Endocrine Abstracts

April 2024 Volume 100
ISSN 1479-6848 (online)

Society for Endocrinology Endocrine Update 2024

Society for Endocrinology

published by bioscientifica

Online version available at
www.endocrine-abstracts.org

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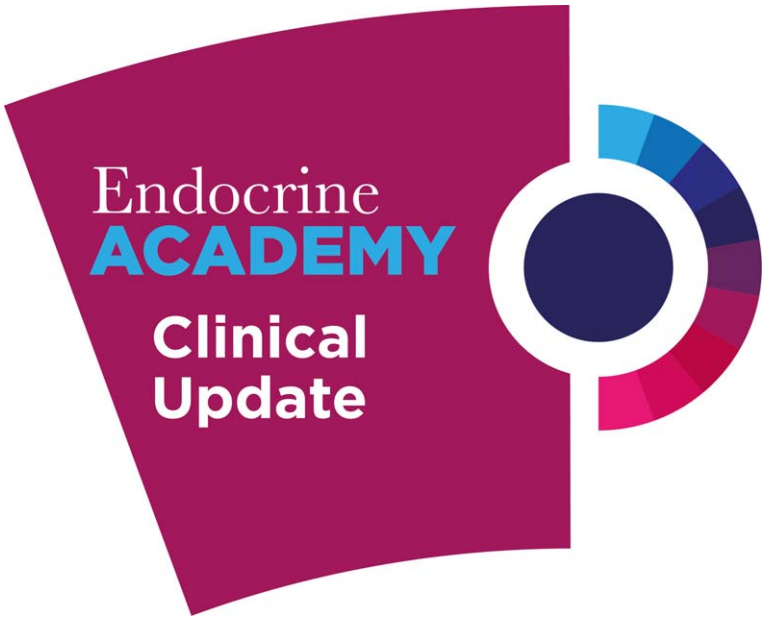

Society for Endocrinology Clinical Update 2024

Endocrine Abstracts

Volume 100
March 2024

Society for Endocrinology Clinical Update 2024

Hilton Birmingham Metropole Hotel, National Exhibition Centre

25–27 March 2024, Birmingham, United Kingdom

Programme Chair
Professor Maralyn Druce (*London*)

Strands, Convenors and Facilitators

Disorders of the hypothalamus and pituitary (I)	Convenor: Professor Niamh Martin (*London*) Facilitator: Professor Niamh Martin (*London*) Facilitator: Dr Marie Freel (*Glasgow*)
Disorders of the hypothalamus and pituitary (II)	Convenor: Professor Niamh Martin (*London*) Facilitator: Dr Rob Murray (*Leeds*) Facilitator: Dr Tisha Seejore (*Leeds*)
Disorders of the thyroid gland	Convenor: Professor Simon Pearce (*Newcastle*) Facilitator: Dr Catherine Napier (*Newcastle*) Facilitator: Kristien Boelaert (*Birmingham*)
Disorders of the adrenal gland	Convenor: Professor Michael O'Reilly (*Dublin*) Facilitator: Professor Michael O'Reilly (*Dublin*) Facilitator: Dr Yasir Elhassan (*Birmingham*)
Disorders of the gonads	Convenor: Dr Richard Quinton (*Newcastle*) Facilitator: Dr Richard Quinton (*Newcastle*) Facilitator: Dr Channa Jayasena (*London*)
Disorders of the parathyroid glands, calcium metabolism and bone	Convenor: Dr Victoria Stokes (*Cambridge*) Facilitator: Dr Victoria Stokes (*Cambridge*) Facilitator: Dr Ruth Casey (*Cambridge*)
Disorders of appetite and weight	Convenor: Dr Saira Hameed (*London*) Facilitator: Dr Saira Hameed (*London*) Facilitator: Dr Chioma Izzi-Engbeaya (*London*)
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Workshop A: Disorders of the hypothalamus and pituitary (I)

WA1.1

Concurrent AVP disorder with acute decompensated HF: any tweak to the management

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The last few decades had seen major breakthroughs in the management of Heart Failure (HF) especially in relation to the modulation of the pathogenetic mechanistic pathway. One of these is the AVP pathway antagonism via the V2R which is promising. However, the influence of the HF complex pathophysiologic pathways in the context of AVP disorder is not well defined. We present an 83-year-old man with long-standing AVP related disorder presenting with acute decompensated HF. He has a background bipolar affective disorder on Lithium treatment for more than 25 years prior to the initial presentation with osmotic symptoms. He also has long standing gynecomastia, loss of libido, and erectile dysfunction. His other past medical history includes AF, T2DM, CKD3, and recently Dementia. Examination showed slightly small testis (15 ml), normal body hair, genitalia, visual field, and bilateral gynecomastia. The initial biochemistry showed sodium of 145, plasma osmolality 304, urine osmolality 303, eGFR of 44, adjusted calcium 2.67, potassium 4.3, 9 am cortisol and testosterone of 327 and 4.6 respectively, FSH 1.9, LH 2.4, IGF-1 31.6, prolactin 214, ferritin 101, Oestradiol 85, FT4 16.9, eGFR of 54. Due to other pituitary hormone deficiency, he had a pituitary MRI which was normal and water deprivation test (WDT) showed baseline plasma osmolality of 317, urine osmolality of 317. Post-DDAVP, the urine osmolality rose to 565 (43% rise) which was interpreted as partial Cranial AVP deficiency. She was therefore started on Desmopressin 100 mg TDS which initially improved his symptoms. However, over a course of 14 years, he developed resistance requiring 600 mg per day of DDAVP to control his osmotic symptoms until his recent presentation with shortness of breath and fluid overload. He was diagnosed with acute decompensated HFpEF, and started on high dose Intravenous Furosemide which was co-administered with the DDAVP leading to difficult fluid mobilization. We weaned vasopressin to 300 mg daily with slightly improved diuresis, however, there was associated troublesome nocturia and this became difficult to manage. This patient had the possibilities of either AVP deficiency (other pituitary hormone deficiency) or AVP resistance (long-term Lithium therapy) and with an inconclusive WDT, he was treated as AVP deficiency. The case illustrates the interaction the two pathologies could have upon each other from the pathophysiologic point of view and if AVP disorder management could be a tweak for the HF treatment in patient with both disorders without use of diuretic.

DOI: 10.1530/endoabs.100.WA1.1

WA1.2

A rare case of AVP deficiency secondary to chloroma

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Case
60yr old male presented to his GP with symptoms of polydipsia, polyuria, reduced appetite and weight loss of about 1 stone over 6-7 weeks. Routine bloods showed abnormal blood film with left shift in neutrophils, moderate thrombocytopenia (61), basophilia and occasional blasts (1%). Morphology was suggestive of Chronic Myeloid Leukaemia (CML) or alternate myeloproliferative disorder (MPD). He was referred to haematology for further management and had specialist bloods and a bone marrow examination. Due to ongoing symptoms of polyuria, polydipsia, repeat bloods showed increasing sodium (153 mmol/l), high serum osmolality (320 mmol/kg) and low urine osmolality (171 mmol/l). Reviewed by Endocrine Consultant, a clinical diagnosis of AVP deficiency was made and he was treated with Desmopressin (DDAVP) 100 mcg PO nocte. On DDAVP, the sodium rapidly normalised. MRI pituitary showed absent posterior pituitary high signal and small lesion at the base of the pituitary stalk, differential diagnosis included a proteinaceous or midline inclusion cyst, hamartoma or possibly low grade glioma. Haematology results showed a Philadelphia chromosome and final diagnosis being chronic phase CML, treated with oral Dasatinib (tyrosine kinase inhibitor) by the haematologists. From a CML point of view he had a normal Full Blood Count within two months and was in a major Molecular Remission four months after starting Dasatinib treatment. MRI at 3 months showed remission of the hypothalamic enhancing lesion and still showed an absent posterior pituitary bright spot. His Haematology Consultant suggested that the lesion could have been a chloroma related to the CML, which responded to the Dasatinib treatment. A repeat MRI at 9 months showed normal appearances of the infundibulum, hypothalamus and posterior pituitary bright spot.

Discussion
Chloroma also known as Myeloid sarcoma (MS) is a rare condition characterized by the presence of solitary or multiple tumours consisting of immature myeloid cells, at an extra medullary site. Most commonly, it occurs concurrently with acute myeloid leukaemia, myeloproliferative disorders or myelodysplastic syndrome. Symptoms usually occur as result of mass effect or organ damage.
Conclusion
AVP deficiency secondary to chloroma is very rare (six case reports in the literature). This case shows an early presentation with AVP deficiency concurrently with the diagnosis of CML, with Dasatinib treatment resulting in resolution of the presumed hypothalamic chloroma and subsequent reappearance of the posterior pituitary bright spot. In this case the principle of 'Occam's razor' resulted in a unifying diagnosis in a patient presenting with two seemingly unrelated rare medical conditions.

DOI: 10.1530/endoabs.100.WA1.2

WA1.3

Diabetes insipidus and compressive thyroid enlargement in adult multi-organ langerhans cell histiocytosis

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Langerhans Cell Histiocytosis (LCH) is a neoplastic histiocytic disorder that is rare in adults. LCH can present as a single or multi-site disease (mostly bone/skin). The most frequent endocrine abnormality associated with LCH is Arginine Vasopressin Deficiency (AVP-D), followed by growth hormone and gonadotropin deficiency. We present the case of a 34-year-old female with complex, sequential multi-system involvement. She had a background history of untreated Graves' disease. She initially presented to the emergency department with a spontaneous pneumothorax, and jaundice due to severe liver dysfunction. The pneumothorax was managed with a chest drain, and later video assisted thoracoscopic surgery (VATS) pleurodesis. Further imaging revealed hepatic cystic lesions, hepatosplenomegaly, severe cystic lung disease and a diffusely enlarged thyroid causing narrowing of the trachea and jugular veins. Following urgent thyroid surgery, histology from the thyroid gland showed infiltrates consistent with LCH. Subsequent to the thyroidectomy, the patient developed hypotonic polyuria, severe polydipsia, and subclinical thyrotoxicosis. Daily fluid intake was up to 6.5L with output reaching 9.5L. Desmopressin was commenced for AVP-D, with good response. MRI pituitary showed thickening and enhancement of infundibulum which although nonspecific, is supportive of LCH. Biochemical pituitary testing showed suppressed gonadotropins, low Insulin-like Growth Factor 1, subclinical hyperthyroidism and normal morning cortisol. Treatment with Cladribine and Prednisolone was initiated. Desmopressin dose and fluid balance required regular adjustment during the chemotherapy treatment. She continued to have significant complications including surgical emphysema, dysphagia, and persistent bilateral pneumothoraces. LCH should be considered in the differential diagnosis of AVP-D associated with pituitary stalk thickness. Multi-disciplinary care involving endocrinology is an essential part of care for LCH patients.

DOI: 10.1530/endoabs.100.WA1.3

WA1.4

Anterior to posterior pituitary dysfunction - crossing the DI-VIde

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De novo vasopressin insufficiency (VI) is extremely rare in patients with pituitary adenoma who have not had biopsy or surgery and raises the question of differential diagnoses including malignancy and infective or inflammatory disease affecting the pituitary. Here we present a case of a patient initially presenting with cystic pituitary adenoma subsequently developing VI. A 24 year old woman presented to her GP with headache and secondary amenorrhoea. MRI brain revealed a cystic pituitary lesion. Pituitary MRI demonstrated a 17 mm, T1 hyper-intense proteinaceous cyst with a suprasellar component and significant displacement of the infundibulum of normal thickness. She was found to have a persistently elevated prolactin in primary care at around 900 mU/l and referred to Endocrinology. Initial early morning basal pituitary function showed persistent monomeric hyperprolactinaemia (prolactin 896 mU/l [100-550 mU/l]) and

borderline secondary hypothyroidism (TSH 1.57 [0.3-4.2 mU/l], free T4 8.0 [9-23 pmol/l], free T3 3.3 [2.4-6 pmol/l]), but otherwise normal pituitary function. Repeat serial pituitary MRIs have shown progressive spontaneous reduction in size of the pituitary lesion from the original scan in December 2021 of 17 mm × 11 mm × 12 mm to 11 mm × 3 mm × 5 mm in January 2023 with resolution of the suprasellar component, resolution of the high signal on T1 imaging and reduction in the infundibular deviation. Images were reviewed in local radiology meeting and felt to represent probable resolution of haemorrhage into a cystic pituitary adenoma. This has been accompanied by spontaneous restoration of regular menses and fully normalisation of anterior pituitary function. She had originally reported excessive thirst with no polyuria on initial assessment in endocrine clinic, on subsequent review she reported marked polydipsia, polyuria and nocturia, passing up to 11L of urine daily. Formal water deprivation test confirmed VI. On review of serial imaging and biochemistry in the regional pituitary MDT, the images were still felt to be most consistent with a cystic adenoma of the pituitary. There was an absence of the posterior pituitary bright spot. There were no imaging features suggestive of inflammation, furthermore the patient had never received steroids which could have treated an undiagnosed inflammatory lesion. In view of the spontaneous reduction in size of the lesion, malignancy was not suspected. She is currently being managed with intranasal desmopressin. We plan to re-image in 6 months and reassess clinically for resolution of VI.Does the panel have any thoughts on further differential diagnosis or management strategy?

DOI: 10.1530/endoabs.100.WA1.4

WA2.1

Lymphocytic hypophysitis, with diabetes insipidus

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Background
Lymphocytic hypophysitis is a rare pathology of the pituitary gland which presents with features of hypopituitarism due to inflammation of the pituitary gland and/or a sellar mass lesion. It is an autoimmune condition and is the most frequent histopathological subtype of primary hypophysitis. Given that it is relatively rare, diagnosis and treatment can be challenging.
Case Description
A 60-years-old female with history of type 2 diabetes referred to endocrinology team with severe fatigue, generalised arthralgia, polyuria (6 l/da), polydipsia(3-6 l/day) and nocturia (4-6 times/day). Initially she was reviewed by ophthalmology team for Right 6th cranial nerve palsy which was initially assumed to microvascular complication related to her diabetes, but in view of her recent headaches since the palsy started, an MRI scan was arranged which showed bulky Pituitary gland. A referral was made to endocrinology team for further review. A dedicated Pituitary MRI scan was advised which showed enlargement of the pituitary mass with extension into the cavernous sinuses and quite a lot of surrounding dural inflammation, with no optic chiasm involvement. Reference laboratory results revealed raised Serum Osmolality (302 mosmol/kg; normal range 275–295 mosmol/kg), Urine Osmolality (280 mosmol/kg) and serum sodium (141 mmol/l; normal range 133–146 mmol/l), other pituitary hormones profile were unrevealing. Her only endocrine deficit is of ADH, resulting in diabetes insipidus. This has responded well to a low dose of desmopressin (DDAVP) of 50 mg TDS at the beginning but later it needed titration up. This has controlled her thirst well and prevented nocturia. She was referred to pituitary MDT for consideration of a pituitary biopsy. Histology was proved to be Lymphocytic hypophysitis with a low mitotic index. High dose of prednisolone 40 mg daily was started to try and supress the inflammation. Later, repeat MRI has shown significant improvement, with normal pituitary appearances now and resolved right 6th cranial nerve palsy.
Conclusion
It is important to have a wide differential diagnosis when managing pituitary masses. Clinical correlation with atypical MRI findings is useful to determine the diagnosis of LH.

DOI: 10.1530/endoabs.100.WA2.1

WA2.2

Partial central AVP deficiency

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A 54 year old male was referred for evaluation of Diabetes Insipidus in 2021 with a 12 month history of polyuria, polydipsia and nocturia 3-4 times per night. He always carried water with him and drank 750 ml overnight. He had a history of Ulcerative Colitis, enteropathic osteoarthritis and asthma. He was on Secukinumab monthly. Partial Central Arginine Vasopressin (AVP) deficiency was confirmed by a water deprivation test (serum osmolality >293 mOsm/kg, urine osmolality 300-750 mOsm/kg and <750 mOsm/kg post DDAVP). MRI Pituitary showed a thickened infundibulum with an absent posterior pituitary bright spot. He was trialled on 0.2 mg desmopressin nocte, titrated up to 0.1 mg BD and 0.2 mg nocte based on symptoms. The following tests were normal – sex steroid axis, morning cortisol, thyroid function, IGF-1, HbA1C, calcium, AFP, hCG and serum sodium. Autoantibody screen was negative. IgG4 was elevated at 5.998 g/l (normal range 0.039–0.864) and Serum ACE 67 U/l (normal 8–65). Following discussion with Rheumatology, a CT TAP in 2022 showed no retroperitoneal fibrosis, bilateral sacroiliitis or mediastinal lymph node enlargement. Bronchoscopy to evaluate for sarcoidosis and/or TB was negative. Repeat MRI pituitary in 2022 showed the pituitary infundibulum remained thickened although slightly improved. But in 2023 increased thickening of the infundibulum was reported consistent with progressive hypophysitis. Central AVP deficiency arises from inadequate production or secretion of arginine vasopressin, usually due to neurohypophyseal damage. The causes include trauma, neoplasm, vascular accident, granulomatous disease including sarcoidosis, infection including TB, inflammatory and autoimmune hypophysitis, drug-induced or idiopathic. The water deprivation test is the gold standard for diagnosis, and partial central AVP deficiency is confirmed if urinary concentration rises to 300-800 mOsm/kg with a greater than 9% rise after administration of DDAVP. Treatment with desmopressin aims for symptom control (Refardt J *et al*. Diabetes Insipidus: An Update. Endocrinol Metab Clin North Am. 2020). Hypophysitis is a rare inflammatory disorder involving the pituitary gland and infundibulum. At least 5 clinicopathologic types have been described: IgG4-related, lymphocytic infundibuloneurohypophysitis, granulomatous, xanthomatous, necrotizing disease or, more common recently, immune checkpoint inhibitor use. Pituitary biopsy is required for definitive diagnosis (Melmed S *et al*. Williams Textbook of Endocrinology 14th Edition). Our patient is currently clinically well and symptom-controlled on desmopressin. The risk of a pituitary biopsy is thought to outweigh the benefits of a clinical diagnosis at present. We are considering treatment with high- dose glucocorticosteroids in light of the recent progressive hypophysitis noted on MRI.

DOI: 10.1530/endoabs.100.WA2.2

WA2.3

Normocytic anaemia: The clue to a brewing diagnosis of craniopharyngioma and the unmasking of AVP deficiency post-steroid replacement

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A 53-year-old Lithuanian man presented with worsening right sided vision (hand movements) and recurrent headaches on a background of previous haemorrhagic strokes. A CT head/angiogram revealed a hyperdense suprasellar mass. His local endocrinology team reviewed and started emergency treatment for presumed pituitary apoplexy (hydrocortisone 50 mg IM/IV 6 hourly) and he was blue-lighted to a tertiary centre for neurosurgical input.
Investigations
Blood tests revealed a hypotonic hyponatraemia (Na 124 mmol/l, Serum Osm 251 mmol/kg, urine Osm 643 mmol/kg, Urine Na 62 mmol/l), normocytic anaemia (Hb 110 g/l Hct 0.3 MCV 84 fL) and an elevated CRP of 21 mg/l. His pituitary profile revealed panhypopituitarism with cortisol 27 nmol/l, ACTH <3 ng/l, Free T4 12.6 pmol/l, TSH 0.08 mU/l, Prolactin 630 mU/l, IGF1 41 mg/l, LH <1 unit/l, FSH <1 unit/l, testosterone <0.5 unit/l. An MRI scan showed a large heterogenous enhancing suprasellar lesion with involvement of the hypothalamus and optic pathways with a wide differential.
Progress and Treatment
Upon transfer, staff noted a polyuria of >450 ml/h with a rise in sodium from to 137 mmol/l. 5% glucose was started intravenously to match urine output. A urine osmolality of 187 mmol/kg revealed a diagnosis of AVP insufficiency which had been unmasked after steroid replacement. 0.5-1 mg s/c DDAVP was started to maintain normonatraemia with repeated dosing once the urine output rose to >200 ml/hr for 2 subsequent hours. A CTCAP, lumbar puncture and ophthalmology review occurred prior to transsphenoidal surgery to relieve pressure on the optic apparatus. A frozen section mid-operation aided diagnostically to facilitate maximal debulking. The histology showed evidence of pus and solid epithelial tumour in keeping with an infected craniopharyngioma.
Conclusions
The patient made a good recovery and was able to read letters with both eyes. Hydrocortisone was weaned to replacement doses (10/5/5 mg), and other hormone replacement initiated (levothyroxine 100 mg OD, 100 mg oral DDAVP at night, testogel 2 pumps daily). Interestingly, blood tests as far back as 2021

show evidence of a normocytic anaemia and low haematocrit, suggesting possible developing hypogonadism even at this stage. It is important to be vigilant for the unmasking of cranial DI post-steroid replacement - the addition of high dose glucocorticoid causes a reduction in CRH mediated AVP production which is usually tonically inhibited by cortisol. Thankfully, this patient's thirst mechanism was intact to facilitate normonatraemia but a subsequent weight gain at follow-up has revealed possible hypothalamic dysregulation of appetite. This will be assessed further with repeat imaging following a course of external beam radiotherapy to treat residual disease.

DOI: 10.1530/endoabs.100.WA2.3

WA2.4

Isolated arginine vasopressin deficiency

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An 84-year-old lady presented with a month's history of polyuria and polydipsia. She reported waking up seven times during the night to pass urine and constantly feeling thirsty. Her measured 24-hour urine output was 4.9 L. She was otherwise doing well with a past medical history of hypertension, hyperlipidaemia, gastro-oesophageal reflux disease and prolonged hospital admission 20 years ago for Guillain Barré syndrome. Her drug history included Lisinopril, Atorvastatin, Amitriptyline and Omeprazole. She did not smoke or drink alcohol. Physical examination was normal, including a neurological assessment. Investigations showed a serum osmolality of 303 mOsm/kg, an inappropriately low urine osmolality of 95 mOsm/kg and a serum sodium of 144 mmol/l within normal range. Her copeptin level was low at 1.7 pmol/l. Her thyroid function tests, cortisol and HbA1c levels were normal. Her eGFR was adequate at 80 mL/min/1.73 m2, with normal potassium and calcium levels. She was diagnosed with arginine vasopressin (AVP) deficiency and started on oral desmopressin. She achieved good symptom control with oral desmopressin 300 mg daily. An MRI pituitary scan showed a normal posterior pituitary bright spot, pituitary stalk and infundibulum. A central, discrete, small hypo-enhancing lesion in the pituitary was detected, with mild deviation of the stalk to the left. The anterior pituitary hormone profile was normal. She then became increasingly unwell and presented to the emergency department 3 weeks later with acute confusion, vomiting and febrile at 38^0C. Her sodium level was within normal range at 144 mmol/l with improved serum and urine osmolality of 300 mOsm/kg and 559 mOsm/kg respectively. She was transferred to the high dependency unit. Desmopressin was converted to subcutaneous administration. The differential diagnoses included infectious encephalitis, metabolic or autoimmune encephalopathy, central venous thrombosis, lymphoma or malignancy. All investigations including CT chest, abdomen and pelvis, autoimmune screen, lactate dehydrogenase (LDH), angiotensin converting enzyme (ACE) and blood film were normal. Clinical improvement was noted with aciclovir and a drop in white cell count was noted on CSF results. She was therefore treated empirically for viral encephalitis for 2 weeks. An MRI head scan showed extensive deep white matter ischaemic changes. This case highlights the workup and management of AVP deficiency, complicated by probable viral encephalitis. The diagnosis is likely idiopathic AVP deficiency but a vascular impairment of the inferior hypophyseal artery system is possible in view of extensive ischaemic changes in the brain. IgG4 related hypophysitis is a rare but remains a possible diagnosis. IgG4 level and pituitary MDT outcome is pending.

DOI: 10.1530/endoabs.100.WA2.4

WA3.1

A case of suprasellar mass with arginine vasopressin deficiency: when necessary acute steroid use serendipitously aids differential diagnoses

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Arginine vasopressin deficiency (AVP-D) is a rare condition that can happen following brain surgery or trauma, as well as conditions affecting the hypothalamus and pituitary gland. Here we describe a case of 76-year old man who had AVP-D secondary to large suprasellar mass of unknown aetiology. He presented with generalised malaise, weight loss, polyuria and polydipsia. Past medical histories include type two diabetes mellitus with Hba1c 52 mmol/mol, Graves' thyrotoxicosis on carbimazole, asthma and hypertension. Random capillary blood glucose monitoring was satisfactory. Blood results showed acute kidney injury with hypernatraemia. The initial fluid balance monitoring, although performed poorly, as well as paired serum and urine investigations on admission did not meet the diagnostic criteria of AVP-D. He was therefore treated for acute kidney injury. Following some improvement in kidney function with intravenous fluids and with malignancy concern, CT head scan was performed which showed suspicious 1.9 cm suprasellar pituitary lesion. CT thorax, abdomen and pelvis did not show any malignancies. Subsequent MRI pituitary showed an enhancing multi-lobulated suprasellar mass lesion, with the main bulk situated in the hypothalamic region and encasing the third ventricle, associated with mass-effect and adjacent vasogenic oedema. He was therefore started on dexamethasone treatment. Subsequent strict documented urine output exceed 5 l/daily with significant nocturia. Repeat paired serum and urine investigations revealed AVP-D and pituitary profile showed panhypopituitarism. ESR was found incidentally raised. Desmopressin therapy was commenced and gradually improved his urine output and electrolytes. He was referred to neurosurgical multi-disciplinary team, with plans to investigate the suprasellar mass, including serum and CSF tumour markers as well as the potential need for biopsy. A repeat MRI Head was done a week apart after and this time it showed significant size reduction of the lesion. This was accompanied by some improvement in the ESR. As there was no evidence of mass effect now, and to avoid 'masking' the diagnosis on subsequent investigations, dexamethasone was changed to hydrocortisone accordingly for hypocortisolism cover. His serum and CSF tumour markers so far have been negative and we are awaiting for decision to proceed for biopsy. The likely cause being inflammatory or lymphoma is high on list in view of the serendipitous improvement in clinical picture following glucocorticoid therapy. In this case, we want to highlight for discussion this rare presentation of AVP-D, potential challenges in managing inpatient fluid balance, and steroid use when clinically indicated but risking interfering with the diagnostic investigations.

DOI: 10.1530/endoabs.100.WA3.1

WA3.2

A case of arginine vasopressin deficiency (AVP-D) due to lymphocytic hypophysitis

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Case history
29-year female presented with sudden onset unquenchable thirst, drinking 7 litres fluids/day, waking 4–5 times at night to drink with polyuria and nocturia. She felt lethargic, nauseated with headaches and weight loss. Past Medical History: Hypertension, following Membranous nephropathy in childhood (previously treated with Tacrolimus and steroids). Examination was unremarkable, with full visual fields.
Biochemical Investigations
Confirmed partial hypopituitarism and suggested AVP deficiency. Serum osmolality 294 mmol/kg, Urine osmolality 77 mmol/kg, Sodium 140 m mmol/l, Cortisol 115 nmol/l, TSH 0.36 mU/l, FT4 9.5 pmol/l, IGF1-15.5 nmol/l, Prolactin 1032 mIU/l, FSH 6.1 IU/l, LH 1.3 IU/l, Oestradiol <92 pmol/l, Water deprivation test: Approximately 200 ml/hour dilute urine (urine osmolality average 75 mmol/kg) passed until 1600 hours when Desmopressin was given. 1 hour post DDAVP 2 mg IM, urine volumes reduced to 100 ml/hr and then to 20 mls/hr at 2 hours. Post DDAVP administration, the urine osmolality rose from 76 to 146 mmol/kg at 1 hour, increased to 411 mmol/kg at 3 hours. Weight reduced from 66.5 Kg to 64.4 kg. Plasma osmolality rose from 281 mmol/kg to 295 mmol/kg. Further Investigations to elicit cause of AVP deficiency: Autoantibody screen, IgG subclass, serum hCG and AFP tumour markers: negative. CSF hCG, AFP and cytology unremarkable, extended TB culture negative. Pituitary MRI: Significantly thickened and avidly enhancing infundibular stalk, deviated to right of midline. NM Whole body PET CT: Symmetrical increased tracer uptake within nasopharynx. Nasoendoscopy unremarkable, nasopharyngeal biopsy: Benign follicular lymphoid hyperplasia. Repeat MRI head and whole spine 3 months later: Marked reduction in degree of pathological enhancement of infundibulum.
Management
Started on replacement Desmopressin and prednisolone, then levothyroxine to excellent effect with resolution of all symptoms. Estrogen to be considered at next clinic appointment.
Conclusions
AVP deficiency is a rare disorder affecting 1 in 25000 people. Differentials include granulomatous, inflammatory, autoimmune, and neoplastic disorders. In this age with abnormal imaging there was particular concern about possible neoplasia. The case was discussed at pituitary MDT with results of PET CT and MRI pituitary. They recommended MRI whole brain and spine followed by CSF examination. Follow up MRI showed dramatic resolution of the stalk findings and CSF were normal. A presumptive diagnosis of lymphocytic hypophysitis was

made. Primary hypophysitis has a prevalence of 0.2–0.88% and annual incidence 1 in 9 million, with lymphocytic hypophysitis being the most common form of primary hypophysitis (71.8%)

DOI: 10.1530/endoabs.100.WA3.2

WA3.3

A case of temporary vasopressin insufficiency following treatment of hyperglycemic emergency

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67 year old lady presented to emergency department with general decline, osmotic symptoms and weight loss of 10 kg in the past 6 weeks, worsening over the past 10 days. She had been reviewed in weight loss clinic 6 months prior, however no aetiology was identified (normal glucose level at the time). No other systemic complaints. Past medical history was unremarkable except for a fracture of right ankle. She was hyperglycaemic with a mixed picture of Diabetic Ketoacidosis and Hyperglycaemic Hyperosmolar state. (pH 7.156, Bicarbonate 11.1, Ketones 6.4 mmol/l, Glucose 43.1 mmol/l, Calculated Serum osmolality-371 mmol/l). Her initial sodium was 155 mmol/l. She was started on fixed rate intravenous insulin and fluids as per DKA/HHS protocols. She was noted to be polyuric (urine output >50 ml/kg /24 hours, with pale urine color) and hypernatremic which was attributed to severe hyperglycemia. DKA resolved by 12 hours of treatment and she was switched to variable rate insulin with fluids. She remained persistently hypernatremic despite normal range glucose levels and aggressive fluid resuscitation (and kept in positive fluid balance) and was managed in ITU. Her sodium rose progressively from 155 on admission to 178 mmol/l over 24 hours. She was reviewed by Endocrinology team at this point. Further investigations requested (paired osmolalities): Serum osmolality 345 mosm/kg, Urine osmolality 370 mosm/kg, Urine sodium 56 mmol/l, Serum sodium 171 mmol/l, Urea 4.1 mmol/l, Creatinine 53 micromol/l). Random cortisol (15:30- 539 nmol/l), TSH 0.86 mIU/l, FT4 15.5 pmol/l, Prolactin 241 mIU/l, Estradiol 92 pmol/l, LH 6.5 IU/l, FSH 7.9 IU/l, C peptide 12 pmol/l (174-960). CT Head reported partial empty sella (MRI pituitary awaited). CT Pancreas ruled out pancreatic malignancy. Endocrinology team diagnosed possible vasopressin insufficiency based on hypernatremia with raised serum osmolality, inappropriate low urine osmolality with ongoing polyuria. A trial dose of Desmopressin 2 mg IV was administered following which the urine output dropped to almost nil, and sodium gradually improved from 155 mmol/l from 171 mmol/l. No further desmopressin doses were administered, polyuria/hypernatremia resolved. She was confirmed to have T1DM (low C-peptide levels, positive GAD and IA-2 Antibody). MRI pituitary showed thickened pituitary stalk and absence of bright spot. Aim of discussion is possible mechanism of this temporary vasopressin insufficiency following diabetic emergency management, as well discussion of MRI findings and persistent secondary hypogonadism.

DOI: 10.1530/endoabs.100.WA3.3

WA4.1

A case of cranial diabetes insipidus- is it idiopathic or something else?

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A 24 year old student was referred from her GP in 2022 with a one month history of polyuria and polydipsia, drinking up to 15 litres of water a day. Renal function, serum glucose and Hba1c were unremarkable but urinalysis showed a specific gravity 1.010. On further questioning her symptoms had progressively worsened over the past 6 months and reported weight gain of 6 kg in 6 months and intermittent headaches but regular menstrual cycles. She had no past medical history of note and was not taking any regular medications nor supplements. Initial biochemistry showed a sodium 147 mmol/l, potassium 4.2 mmol/l, normal renal function with a GFR >90, pituitary profile was within normal limits and serum osmolality was 297 mosmol/kg with a urine osmolality of 75 mosmol/kg. Water deprivation test was consistent with a diagnosis of cranial diabetes insipidus and she was subsequently started on desmopressin with a good clinical response. Pituitary imaging showed a thickened infundibulum contacting the undersurface of the optic chiasm without compression. The pituitary gland was normal in size and shape with no focal lesions. Subsequent interval MRI showed stable appearances and posterior pituitary bright spot demonstrated. Given the unchangeable appearances on pituitary imaging, further investigation into the aetiology of diabetes inspidius is being sought. So far, pelvic imaging has been carried out consistent with polycystic morphology of the right ovary and skeletal survey is unremarkable. She is currently awaiting a PET scan and discussions with the local pituitary MDT are ongoing. Diabetes insipidus or arginine vasopressin deficiency is a rare condition affecting 1 in 25,000 people. It is caused by a reduced production of or failure to respond to anti-diuretic hormone (ADH) resulting in polyuria and polydipsia[1]. Most causes of cranial diabetes insipidus are due to trauma, neurosurgery or pituitary tumours with more rare causes including infiltrative disease, infections, genetic defects or are idiopathic[2,3]. A diagnosis of diabetes insipidus in a young person can be difficult given lifelong medication, potential side effects and regular contact with hospital services. This case demonstrates a clear diagnosis and clinical response to treatment but the cause remains unclear.

DOI: 10.1530/endoabs.100.WA4.1

WA4.2

Acute severe hyponatraemia in arginine vasopressin deficiency

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This case describes a 23-year-old male with known epilepsy, who was admitted to hospital with generalised tonic-clonic (GTC) seizures and acute severe hyponatraemia. He had been feeling generally unwell for two days, but had not doubled his steroids. He has panhypopituitarism due to Langerhans' histiocytosis, including arginine vasopressin deficiency (AVP-D). His medication included antiepileptics, hydrocortisone, (nasal) desmopressin (DDAVP), levothyroxine and topical testosterone. He was intubated and transferred to the intensive care unit (ICU) upon having further GTC seizures and Type 2 Respiratory Failure with consequent acidosis. Serum sodium was 113 mmol/l, urine osmolality 691 mOsm/kg and urinary sodium 70 mmol/l; renal profile and serum glucose were normal. Cerebral oedema was evident on CT. Hypertonic (2.7%) saline, 150 ml, was given as an intravenous bolus, causing a rise of only 3 mmol/l. Therefore, a further 150 ml bolus of hypertonic saline was given. DDAVP was delayed to avoid further reduction in serum sodium, but the urine output rose rapidly (>300 ml/h) and was followed by a rise in serum sodium to 129 mmol/l. The reinstitution of DDAVP 1 mg SC led to a fall in serum sodium to 124; the rise in serum sodium was more than 8 mmol/l in 24 hours, a cause for concern. This complex case illustrates the challenges with managing acute hyponatraemia in AVP-D. The presence of cerebral oedema with seizures may suggest rapid occurrence of hyponatraemia. The major threat to health was worsening of this oedema with risk of coning and therefore the aim of treatment should be about this. Traditional concern about rapid correction leading to osmotic demyelination syndrome (ODS) has been questioned by a recent retrospective study, which showed more rapid correction to be associated with lower mortality compared to slower change and poor correlation with ODS (1). The urine osmolality showed that DDAVP was still therapeutically present, but the urine sodium suggested inadequate amount of steroid for physiological stress; the hyponatraemia was probably due to continued use of DDAVP without appropriate increase in steroid replacement. Nevertheless, restarting DDAVP should not be delayed beyond 24 hours from the last dose and should be restarted as soon as urine out output exceeds 100 ml/h. Close monitoring of urine output as well as other physiological parameters behove management in a critical care setting (2).

DOI: 10.1530/endoabs.100.WA4.2

WA4.3

An interesting case of diabetes insipidus

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I present a case of a 32 year old Vietnamese woman who presented on 3rd September 2023 with abdominal pain and vomiting. Her blood tests showed; Hb 151g/l, WCC 18.3, Na 130 mmol/l, K 1.8 mmol/l, Ur 4.7 mmol/l, Creatinine 91 umol/l, Corrected Calcium 2.93 mmol/l, Phosphate 0.54 mmol/l, Lipase 191 unilts/l. Venous Blood Gases showed pH 7.25, Bicarbonate 15.6, Lactate 1.9, pCO2 4.5, Glucose 7.0 mmol/l. She had a background of treated TB aged 25, recent diagnosis of H. Pylori gastritis, and gave birth in September 2022. Her son was born with congenital complete heart block and she had positive Anti-Ro and Anti-La antibodies. She was managed in the ITU and received concentrated potassium infusions and Hartmann's. Her urine output after admission to ITU was up to 8 L per day with doses of 0.5 -1 mg parenteral DDAVP intermittently. The DDAVP was not effective at reducing her urine output initially. Her Sodium climbed to 161 mmol/l after 48 hours and her calcium and potassium normalised

within 24 hours. They suspected Sheehan's syndrome. She had a Cortisol checked at 0600 on 7th September which was 251 nmol/l and then started Glucocorticoid replacement. She started regular 100 mg twice daily oral DDAVP on 9th September, and she remained on 10/5/5 mg oral hydrocortisone. She was discharged on 12th September on 100 mg DDAVP at night and replacement doses of Hydrocortisone. At this point her Urine Output was about 2 L per day. She had an MRI Pituitary on 8th September which showed a potentially thickened pituitary stalk and a loss of posterior pituitary bright-up. She returned for an Insulin Tolerance Test on 24th October. The Nadir glucose was 1.4 mmol/l. The peak Cortisol was 476 nmol/l, and GH was 4.03 mg/l. Hydrocortisone was stopped. She then had a Water Deprivation Test 5th December. At the start of the test the Serum Osmolality 291 mmol/kg, with a Urine Osmolality of 140 mmol/kg. At 8 hours the Serum Osmolality was 298 mmol/kg with a Urine Osmolality of 228 mmol/kg. Upon clinical review she notices an ongoing good response to low-dose DDAVP and she is being managed as Cranial Diabetes Insipidus secondary to presumed Lymphocytic Hypophysitis. We suspect that her lack of improvement initially, despite Desmopressin, is due to nephrogenic DI secondary to hypokalaemia and gradient washout secondary to a history of polyuria.

DOI: 10.1530/endoabs.100.WA4.3

WA5.1

Acute hyponatraemia and polyuria in an elderly patient - a urinary tract infection or something more?

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An 82 year old lady was admitted under the general medical take with a fall and reduced consciousness. She had a history of two previous trans-sphenoidal surgeries for Cushing's disease 30 years prior, with subsequent cranial diabetes insipidus and panhypopituitarism. Trans-sphenoidal surgery failed to control her cortisol excess, and resulted in a bilateral adrenalectomy. Medication history included full hormone replacement therapy including oral desmopressin 100 mg three times daily. Initial biochemistry revealed significant hyponatraemia with a sodium of 110 mmol/l (reference range 133-146 mmol/l). Plasma osmolality 232 mOsm/kg (275-295 mOsm/kg), with paired urine osmolality of 263 mmol/kg (50-1200 mmol/kg) and urinary sodium 97 mmol/l. Cortisol was low in keeping with known adrenalectomy, and thyroid function tests demonstrated secondary hypothyroidism with a suppressed TSH and normal T4. Clinically, the patient was hypovolaemic, and fluid replacement was initiated with slow IV 0.9% saline, and desmopressin was withheld. Due to low conscious level, a CT head was performed which revealed no acute change. A capillary blood sugar was checked and was found to be low at 2.2 mmol. Prompt treatment to reverse hypoglycaemia was given, as well as IV hydrocortisone given the history of adrenalectomy. Sodium gradually responded to fluid resuscitation and a lower dose of desmopressin was re-introduced due to polyuria, to avoid over-correction of sodium. She was admitted to the medical high dependency unit to monitor her conscious level and facilitate frequent blood sampling. A collateral history was obtained from the patient's next of kin who explained that the patient had been suffering from polyuria, likely secondary to a urinary tract infection given raised inflammatory markers. However, she believed the polyuria to be secondary to her diabetes insipidus, treating with extra doses of desmopressin at home. The profound hyponatraemia was acute, as her biochemistry was within normal range a few months prior to admission. It was felt likely that this was a case of hypovolaemic hyponatraemia secondary to excess desmopressin. This case highlights the importance of patient education when prescribing hormone replacement, ensuring that sick day rules are followed.

DOI: 10.1530/endoabs.100.WA5.1

WA5.2

A curious case of refractory hypernatraemia

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80-year-old female admitted with a fractured neck of femur was found to have hypernatraemia refractory to treatment. On initial assessment, she was polydipsic and hypovolaemic. She had a background of chronic kidney disease. During admission, her serum sodium rose to 167 mmol/l, eGFR was stable at 69 mL/min and her calcium and potassium were within normal limits. Her HbA1c was 40 mmol/mol excluding diabetes mellitus. On further assessment, she reported polyuria (up to 7L/day) in the months preceding her admission. Osmolality testing revealed a raised serum osmolality 317 mmol/kg with a reduced urine osmolality 137 mmol/kg. A water deprivation test was performed with partial response. Her urine osmolality increased from 106 mmol/kg to 372 mmol/kg following the administration of Desmopressin. There was no history of head injury. Her pituitary profile, vasculitis screen and MRI head were normal. She was managed for partial cranial diabetes insipidus and started on Desmopressin 100 mg once daily. This led to a significant decline in her serum sodium over the next few days (159 mmol/l to 136 mmol/l) and Desmopressin was held. Her serum sodium subsequently increased, rising to 160 mmol/l. She was restarted on Desmopressin, and eventually stabilised on a very low dose of 50 mg on alternative days. She remains well at follow up. This case describes an insidious presentation of partial cranial diabetes insipidus of unknown aetiology in a patient presenting with a fall and hypernatraemia. Careful assessment achieved clinical and biochemical improvement with a very low dose of Desmopressin. Hypernatraemia is not an uncommon presentation in the elderly and diabetes insipidus should be considered as a differential diagnosis, particularly in those refractory to conventional treatment.

DOI: 10.1530/endoabs.100.WA5.2

WA5.3

Cranial diabetes insipidus (CDI) secondary to langerhans cell histiocytosis (LCH)

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A 46 years old male with a background history of hypertension and asthma for which he was taking irbesartan and clenil inhaler respectively, was referred to the Endocrine service with a 3 weeks' history of polyuria, polydipsia, nocturia and occasional headaches. On initial screening, diabetes mellitus and hypercalcemia were excluded. Initial biochemistry showed a sodium level was 144 mmol/l (135-144) with a serum osmolality of 300 mOsm/kg (275-295). A diagnosis of Diabetes Insipidus was suspected and a water deprivation test was arranged. At the start of the test, serum osmolality was 313 mOsm/kg with a urine osmolality 172 mOsm/kg (300-900). This was followed by 6 hours of polyuria with a urine output (UOP) in the range of 200-400 ml/hour and recorded weight loss of 3 kg. Following administration of 2 microgram intramuscular desmopressin (DDAVP), the urine osmolality increased to 573 mOsm/kg and the UOP fell below 100 ml/h. The results of this test were discussed at the departmental results meeting and it was unanimously concluded that this is in keeping with partial cranial diabetes insipidus (CDI). The patient was commenced on oral DDAVP 100 micrograms twice daily which resulted in improvement in the urinary frequency and resolution of the nocturia. MRI scan of the pituitary gland showed thickening and enhancement of the entire infundibulum and a primary infundibular lesion was suspected. The anterior pituitary hormone profile showed secondary hypogonadism (Table 1).

Table 1.

Test	Results	Reference range
IGF-1	16.2 nmol/l	7-28
Prolactin	470 mU/l	60-300
LH	2.3 IU/l	1-9
FSH	3.0 IU/l	1-9
Testosterone	3.3 nmol/l	6-27
TSH	1.9 mU/l	0.35-4.7
Free T4	8.7 pmol/l	7-21

During follow-up, the patient mentioned a 2 months history of left arm and hand weakness together with right-sided jaw pain. On clinical examination there was evidence of reduced left upper limb power (3/5) with brisk reflexes and an extensor plantar response bilaterally. XR orthopantomogram showed significant destruction of the right mandible. A PET-CT confirmed a destructive and metabolically active lesions in the mandible and left scapula. At this stage, LCH and Erdheim-Chester disease were considered as differentials and the biopsy of the mandible revealed histology consistent with a diagnosis of LCH. He was referred to the Oncology service for chemotherapy. From an Endocrinological stand point, his symptoms were well controlled on DDAVP 200 mg (0600 hours), 50 mg (1400 hours) and 200 mg (2200 hours).

DOI: 10.1530/endoabs.100.WA5.3

Workshop B: Disorders of the hypothalamus and pituitary (II)

WB1.1

Treatment of Acromegaly

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A 42-year-old man presented to an outside hospital in 2015 with a 5-year history of increasing shoe size, ring size and low mood. During this 5-year period, he was also diagnosed with type 2 diabetes mellitus and obstructive sleep apnoea. On examination, he had signs consistent with acromegaly. This was confirmed on biochemical testing with an IGF-1 > 1200 mg/l, along with partial hypopituitarism and raised prolactin. His formal visual fields testing demonstrated a bilateral upper field defect. His MRI scan showed a large pituitary adenoma with compression of the optic chiasm. He was started on Cabergoline and hormone replacement with testosterone and levothyroxine. He was offered trans-sphenoidal surgery, which was complicated by postoperative CSF leak, meningitis and the development of seizures requiring anti-epileptic medications. Despite surgery, he had on-going symptoms and a persistently raised IGF-1 and he therefore underwent external beam fractionated radiotherapy. He was started on Lanreotide and up-titrated to maximum dose. 6 years after his initial diagnosis, although he had an improvement in his symptoms, he was still reporting symptoms of growth hormone excess and was particularly anxious to have corrective maxillofacial surgery to his jaw. He had a low energy state, stiffness and swelling in both of his hands and underwent bilateral carpal tunnel release surgery. He reported excessive sweating even with minimal exertion and had restless sleep with his sleep apnoea. He was referred to our centre. His IGF-1 remained raised at 272 mg/l (73.9-228.5 mg/l), although his growth hormone was in the safe range. He had a repeat MRI scan which showed a large predominantly residual tumour sitting close to the optic chiasm and stretching the right pre-chiasmatic optic nerve. The anatomy, together with the previous surgical complications, was thought unfavourable for further surgery. The tumour was too close to the optic nerves for stereotactic radiosurgery. The decision was then made to stop the Lanreotide and start on Pegvisomant. 2 years following starting Pegvisomant his latest IGF-1 is 216 mg/l. His symptoms have improved and he is now awaiting OMFS surgery. The primary treatment option for acromegaly is trans-sphenoidal surgery and can lead to complete remission of disease in 50% of patients with macroadenomas. Medical therapy options, in those not cured following surgery or not suitable for surgery, include growth hormone receptor antagonists, somatostatin receptor ligands and dopamine agonists. Radiotherapy can also be used in conjunction with the above to target inaccessible tumour and where medical therapy is not tolerated.

DOI: 10.1530/endoabs.100.WB1.1

WB1.2

Considerations in the young female patient with acromegaly

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A 28-year-old female presented with oligomenorrhoea and bilateral headaches in 2018. Initial blood testing revealed raised prolactin, prompting further assessment of pituitary function. This showed a high IGF-1(132 nmol/l), subsequent oral glucose tolerance test confirmed the diagnosis of acromegaly. It is worth noting that she did not exhibit many of the typical clinical features of acromegaly. MRI demonstrated a left-sided pituitary macroadenoma invading the cavernous sinus. She had normal visual fields. Transsphenoidal surgery was undertaken; histopathology showed a somatotroph adenoma, MIB-1 5% and raised mitotic activity – a higher risk subtype. Post-operative IGF-1 remained elevated (85-95 nmol/l) and the MRI showed residual disease. She was commenced on 4-weekly Lanreotide 120 mg injections, which partially improved headaches. IGF-1 remained elevated despite Lanreotide. Cabergoline 0.25 mg once weekly was added and uptitrated to 1 mg twice weekly. Further treatment at this point was delayed as the patient wished to have a family. Genetic testing undertaken for MEN-1 and AIP were negative. Our patient subsequently became pregnant. Cabergoline was discontinued and Lanreotide was reduced to 4-weekly intervals. She required Metformin in pregnancy for Gestational Diabetes Mellitus (GDM). Lanreotide was discontinued at 24-weeks given patient wanted to breastfeed post-partum. Visual fields were monitored each trimester. Post-partum, elevated IGF-1 levels persisted (61.9 nmol/l), headaches returned, visual fields worsened, prompting recommencement of Lanreotide. Subsequent MRI pituitary showed stable appearances. At 14-months post-partum, our patient became pregnant again. Lanreotide injections were paused at 9-weeks pregnant. She developed GDM (diet-controlled), pregnancy-induced hypertension and obstetric cholestasis. Post-partum IGF-1 levels remained elevated (83.7 nmol/l), prompting recommencement of Lanreotide. Headaches worsened and subsequent MRI showed stable radiological disease. IGF-1 levels fell but remained above range. Despite multiple interventions, the persistence of residual disease and ongoing symptoms led to an MDT recommendation for radiotherapy. The decision was influenced by the ineffectiveness of cure with further surgery and the completion of the patient's family. While awaiting radiotherapy Pegivisomant is being commenced, aiming to better control Growth Hormone levels and alleviate ongoing symptoms. This case demonstrates the importance of keeping an open mind when considering atypical clinical presentations of acromegaly, the escalation of treatment and management plans in acromegaly. We are also reminded of the importance of tailoring surgical management to the young female patient whose priority is fertility preservation and the use of somatostatin analogues in pregnancy. Finally, the case highlights the importance of the endocrinologist's role of remembering to undertake genetic testing in appropriate patients.

DOI: 10.1530/endoabs.100.WB1.2

WB1.3

Management of acromegaly with anxiety

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Summary
Due to the insidious nature of the condition, acromegaly is often diagnosed years after onset of symptoms. By this time, patients will often have developed metabolic and cardiovascular complications. But for this patient, he was most distressed by his changing physical appearance. The delay in diagnosis and subsequent wait for outpatient investigations and management progression caused him severe psychological distress.

Clinical Case
A 39 year old man was referred to an endocrinology outpatient clinic in a district general hospital during August 2022. He presented with an 8-year history of increasing acral overgrowth (shoe size change 6 to 9), prominence of the brow, prognathism, teeth separation, macroglossia with new lisp, enlargement of his nose, hyperhidrosis, severe weight gain, and perceived thorax distortion. His wife described new heavy snoring. Photographs from ten years ago showed a demonstrable difference in his physical appearance. He was otherwise a healthy man with no other PMH. Despite years of symptoms and frequent visits to his GP, he had ultimately diagnosed himself through research on the internet. He was extremely self-conscious and distressed about the physical changes and wanted immediate treatment to prevent them becoming permanent. He was very anxious whilst waiting for his outpatient investigations. He pursued frequent clinical communication requesting confirmation of appointments and immediate results. His baseline IGF-1 level was 1021 mg/l. Acromegaly was confirmed via Oral Glucose Tolerance Test (September 2022) with Growth Hormone level > 100 mg/l at baseline, and 88.3 mg/l at 2 hours. Otherwise normal pituitary hormone profile. Pituitary MRI (November 2022) showed a 23 mm pituitary macroadenoma. He had appropriate visual, cardiac and colonic screening; there was only slight enlargement of the left atrium found. After discussion at the endocrinology pituitary MDT in December 2022, he was referred for surgical resection. In April 2023, after an agonising 8 months since diagnosis, he had a successful endoscopic transsphenoidal resection of the pituitary macroadenoma at a tertiary hospital (the author had coincidentally moved to this hospital's endocrinology department at that time!). He did suffer symptomatic severe hyponatraemia (Na 124 mmol/l) 1 week after surgery requiring re-admission, but this quickly resolved with fluid restriction and slow sodium tablets. At his 6-week post-surgery endocrinology outpatient appointment, he was delighted with his results and reported resolution of his anxiety. He could already see improvements in his acromegalic features – he had lost weight, his shoe size had reduced, and his snoring had stopped (much to his wife's delight!).

DOI: 10.1530/endoabs.100.WB1.3

WB2.1

IGF-1 secreting pituitary macroadenoma: a textbook case of acromegaly

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A 34-year-old obese gentleman was referred in 2017 in view of larger coarsening hands (noted when wearing his wedding ring), bilateral palm paraesthesia, increased sweat production in his palms, and weight-gain despite not having changed his lifestyle. His past medical history included Grave's disease treated

with Carbimazole. On examination, the patient was noted to have a cavernous voice and prominent supraorbital ridges along with generalised facial coarseness. Initial investigations showed an elevated insulin-like growth factor 1 (IGF-1) level of 931 ng/ml and increased fasting Growth Hormone (GH) levels. MR Pituitary reported a 10 mm hypo-enhancing nodule in the right pituitary, bulging the superior margin and resulting in displacement of the pituitary stalk to the left. A prolonged Oral Glucose Tolerance Test (OGTT) in February 2018 resulted in a trough level of GH at 9.96 mg/l; consistent with a diagnosis of acromegaly. A trial of Octreotide LAR 20 mg SC at 4-week intervals was commenced while monitoring IGF-1 levels. The dose of Octreotide was up-titrated according to IGF-1 levels, resulting in dosage increase to 40 mg at 4-week intervals due to insuppressable IGF-1 levels. A Glucagon Stimulation Test in July 2018 revealed an inadequate cortisol response with a baseline cortisol of 81 nmol/l and a peak cortisol of 142 nmol/l. Therefore, Hydrocortisone 10 mg-5 mg-5 mg was started. Repeat MR Pituitary December 2018 reported an increased size of the pituitary macroadenoma (13 × 12 × 10 mm) with no cavernous sinus invasion or optic chiasm compression. Complications pertaining to the underlying condition included hyperplastic polyps noted on colonoscopy. He eventually developed severe obstructive sleep apnoea in 2018 (AHI 52, OHI 47.6, Snore Index 26.6) requiring continuous positive airway pressure at night. Osteopenia was also diagnosed in 2018 via DEXA scanning progressing to osteoporosis in 2020. Hypertension was diagnosed in 2019, treated with perindopril, as well as right-sided carpal tunnel syndrome in 2019. The patient underwent Trans-Sphenoidal Surgery in September 2019 with follow-up MR Pituitary in 2020 reporting no evidence of residual/recurrent adenoma. Repeated post-operative OGTT resulted in suppressible GH levels. Lowest IGF-1 level attained was 274 ng/ml, despite suppressed prolonged OGTT. Nonetheless, IGF-1 levels were noted to keep progressively rising such that a decision was made to recommence the patient on octreotide LAR.

DOI: 10.1530/endoabs.100.WB2.1

WB2.2

Acromegaly: challenges in managing post-treatment elevated growth hormone (GH) /insulin like growth factor-1 (IGF-1) levels and the role of pasireotide"

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Background

The post-treatment follow-up of acromegaly involves assessing treatment efficacy through biochemical evaluation, imaging studies for residual/recurrent disease, and monitoring clinical signs. IGF-1 normalization, typically achieved 12 weeks post-surgery, is considered a success; however, delayed normalization has been observed. Discordant GH/IGF-I results may indicate persistent somatotroph GH secretion and tissue responsiveness. We present a case where maximal medical treatment and two surgeries failed to normalize IGF-1 levels, leading to the utilization of Pasireotide.

Case

A 59-year-old lady attended follow up endocrine clinic in Oct 2023 with elevated IGF-1 levels (>1.3 × ULN (Upper Limit of Normal). She was first diagnosed with acromegaly in 2002. Despite surgical debulking and ongoing medical treatments (Lanreotide and Cabergoline), her IGF-1 remain persistently elevated. A repeat surgical debulking in 2012 achieved partial success, leaving a small residual disease. The patient declined radiotherapy due to concerns about side effects. At that point, Pegvisomant was considered as an option, however, funding was not available for the patient. Given the absence of symptoms, slightly elevated IGF-1 levels (1.2 × ULN) were deemed acceptable, and medical treatment continued. In 2017, Cabergoline was discontinued due to intolerance, and Quinagolide was added to manage persistently elevated IGF-1. Repeat MRI in 2022 showed a reduction in residual disease size. Despite tolerating Quinagolide well, IGF-1 levels rose again in 2023, leading to the initiation of Pasireotide after multidisciplinary team discussion.

Discussion Points

1. Discordant IGF-1 levels post-acromegaly treatment and its impact on long-term management.
2. Challenges and considerations in managing residual acromegaly post-surgery, particularly when surgical and medical interventions show limited success.
3. Effectiveness and considerations for using Pasireotide in cases of persistent acromegaly with elevated IGF-1 levels despite conventional treatments.
4. Discuss the potential benefits and side effects associated with Pasireotide in this context

DOI: 10.1530/endoabs.100.WB2.2

WB2.3

A case report: hair loss associated with lanreotide for the treatment of acromegaly

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A 56 year old female who attends the general endocrine outpatient appointments for acromegaly secondary to pituitary macroadenoma diagnosed in March 2022. She has a history of breast cancer (HER2+), papillary thyroid cancer and is under active treatment for metastatic non-small cell lung cancer (adenocarcinoma) diagnosed in 2019. Her initial MRI pituitary was performed in March 2022 after an interval scan from oncology to assess disease response to treatment identified a pituitary fullness. Her MRI demonstrated a 1.3 × 1.6 × 1.5 cm solid sella mass consistent with a pituitary macroadenoma. Her initial pituitary panel was performed after the MRI, which demonstrated normal thyroid function, gonadotropins consistent with menopause, normal ACTH, prolactin slightly elevated at 1103 mU/l and IGF-1 120 nmol/l with growth hormone 14.30 mg/l (see table 1). She underwent two synacthen tests, which were both normal. In order to complete the work-up, she also had an HbA1 c performed which was 44. Given her complicated history of concurrent metastatic disease, she was deemed not suitable for pituitary resection. She was commenced on Lanreotide to treat her acromegaly. On subsequent visits, her main complaints were hair loss since commencing treatment for acromegaly and she found that more distressing than any other symptoms caused by her comorbidities. The decision was made to switch her from Lanreotide to Pegvisomant given the distress caused by the alopecia, which resulted in marked improvement.

Table 1. Trend of IGF-1 from diagnosis to present

Date	4/4/2022	20/6/2022	12/4/2023	27/6/2023	10/7/2023	16/10/2023
IGF-1 level (range 4-23 nmol/l)	120	134	11	40	38	23

This case highlights alopecia, a documented side effect of lanreotide treatment, which has been reported as a common side effect (>/=1/100 to <1/10) as described in the summary of product characteristics. Although this patient was on concurrent treatment with osimertinib (tyrosine-kinase inhibitor) for her metastatic lung disease, the side effect of alopecia was accounted for by the lanreotide given the temporal relationship of the timing of hair loss and subsequent improvement with pegvisomant. Furthermore, routine screening for known side effects of treatment should always be undertaken on routine endocrine clinic visits for patient wellbeing.

DOI: 10.1530/endoabs.100.WB2.3

WB3.1

A young Acromegalic patient (AIP+) with poor response to SRLs and discordant GH / IGF1

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A 23-year-old Caucasian male was referred to Endocrinology with symptoms spanning over 7 years. He was substantially taller than other members of his family measuring 6'3". He initially presented to Ophthalmology with preseptal cellulitis and noted to have visual field defects with acromegalic features. His pituitary profile showed GH > 100 mu/l, Total T4 104 nmol/l (normal: 60–140 nmol/l), Prolactin 234 mu/l, cortisol 240 nmol/l with flat GST. There was no Diabetes Mellitus and he was normotensive. OGTT showed unsuppressed GH and MRI revealed a pituitary macroadenoma with suprasellar extension. He was diagnosed with Acromegaly secondary to a pituitary GH-secreting adenoma. He underwent TSS and immunostaining showed a pituitary adenoma positive for GH and prolactin, negative for ACTH, FSH, LH and TSH. Post-operatively, his GH and IGF-1 remained elevated. A comparison of GH day curves showed greater response to Bromocriptine than Octreotide. He was discharged on Cabergoline in addition to hydrocortisone. Three months post-operatively, he underwent external beam radiotherapy as his GH and IGF1 remained elevated. MRI showed reduction in size of the pituitary macroadenoma with a small nubbin of suprasellar extension. He underwent re-do TSS 1 year later; histology again confirming pituitary adenoma with similar IHC. Despite this operation, he continued to have elevated GH and IGF1 three months post-operatively. He commenced Octreotide LAR 30 mg IM monthly alongside Cabergoline. He also received Octreotide s/c prn for management of chronic headaches. This eventually normalised his GH, but IGF1 remained elevated resulting in GH/IGF1 discordance. A trial of Pegvisomont was discontinued due to significant side-effects. A year later, MRI pituitary showed empty sella with only a small amount of enhancing pituitary

tissue not suitable for gamma-knife radiosurgery. Genetic testing showed Aryl Hydrocarbon Receptor interacting protein (AIP) mutation. Long term complications: He developed hypertension requiring treatment with three antihypertensive agents, as well as T2DM. An echocardiogram showed ventricular hypertrophy, but no other structural abnormality. He developed significant skeletal complications involving cervical and lumbar spine (requiring decompression and laminectomies at the age of 31) as well as hip and knee arthropathy. Post-operative hypopituitarism was managed with hydrocortisone, L-Thyroxine and IM Testosterone. Conclusively, his IGF1 has not normalised, though GH has suppressed to target <1 mg/l (mean GH 0.3 mg/l). The current focus of management relates to screening of several long-term complications associated with acromegaly in particular requesting colonoscopy, DXA scan and assessment of OSA.

DOI: 10.1530/endoabs.100.WB3.1

WB3.2

Psychological aftermath of acromegaly: a case report

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Acromegaly is associated with osteoarthritis due to soft tissue swelling. Our patient was first diagnosed with acromegaly in 2001 at the age of 51, subsequently undergoing a transsphenoidal pituitary adenoma resection in 2002, followed by postoperative radiotherapy in 2003, with subsequent development of anterior hypopituitarism. He has comorbidities of osteoarthritis, (having previously undergone bilateral total hip replacements and a left total knee replacement), bunionectomy with pinning of the right great toe in 2014, well-controlled T2DM, and a colonic polyp. He currently takes Hydrocortisone/levothyroxine/Tostran gel/Pegvisomant(GH receptor antagonist)/Omeprazole/Tramadol/Calcichew/Rosuvastatin/Metformin/Naproxen, and Lanreotide(somatostatin analogue). Although his acromegaly remains well controlled with a normal IGF-1, he still suffers from significant joint pain and experiences limited mobility as sequelae of his acromegaly. Due to his joint problems as a result of his acromegaly, he unfortunately had to stop working as a warehouse operative in 2011. Since leaving work, he has felt anergia and a lack of motivation. In an attempt to overcome this, between 2011 and 2020, he was volunteering regularly. On days when he was volunteering, he felt engaged and well, but on days when he was not working as a volunteer, he would find himself sleeping excessively with an absence of purpose. All of these activities finished with the Covid-19 pandemic, and since then, he has not been able to perform any voluntary work. His symptoms have since worsened, with a pronounced feeling of 'pointlessness' and continuing weariness. He believes his motivation would return if he regained structure to his life. Frustrations have also arisen due to no longer being able to perform simple 'DIY' household tasks, due to difficulty bending over and balancing on ladders. In January 2024 he was seen by an endocrinologist in a regional chronic fatigue syndrome clinic. It was felt that he did not have chronic fatigue syndrome but rather was experiencing reactive low mood as a result of a major change in his functional level over the last decade or so. On consultation with a clinical psychologist, it was felt that a referral to his local Social Prescribing Team would facilitate some low-intensity cognitive behavioural therapy while also putting him in touch with organisations who could potentially provide him with some structured and meaningful voluntary work. He continues to follow up with his endocrinologist.

DOI: 10.1530/endoabs.100.WB3.2

WB3.3

An unusual presentation of acromegaly (somatotroph adenoma with growth hormone resistance due to anorexia nervosa)

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42 year old female presented to ENT clinic in Nov 2020 with otitis externa and underwent CT mastoid which showed an incidental finding of right sellar / parsellar mass, confirmed later by Pituitary MRI in Nov 2020. Referred with an invasive pituitary parasellar adenoma with a size of 2.4 cm, sellar lesion which extends infrasellarly and into the cavernous sinus. Raised GH level which failed to suppress on OGTT with a low normal IGF-1 level. She had mild symptoms associated with acromegaly (sweating and possible change to show size) with nil significant phenotypic features of acromegaly. She had a raised prolactin and had an episode of galactorrhoea one to two year prior to this which was not persistent and was disregarded in past. Background of severe anorexia under the Psychiatric unit, secondary amenorrhea on oestrogen replacement therapy along with severe Osteoporosis and was on Densoumab injections. Pituitary MDT 16 Feb 2021, diagnosed with Somatotroph Adenoma and growth Hormone resistance due to anorexia nervosa with evidence of disease progression on repeat Pituitary scan. Octreotide test showed good response with raised IGF binding proteins 163 ($10\times$ upper limit). Underwent Trans sphenoidal surgery on 12th July 2021 with a good post operative recovery. Post operative bloods revealed a IGF level: 4.7, GH >200, Prolactin: 1239, octreotide test dose and was discharged on Hydrocortisone. Post operative MDT October 2021: Underwent the ITT test post operative, which achieved minimal cortisol response to hypoglycaemia but adequate baseline cortisol levels. Growth hormone values suggest persistent disease with failure to suppress on OGTT. Comparison of Post operative imaging: showed good decompression but suspicious residual on the right side as well as in the cavernous sinus. Histology: adenoma seen with obvious bone invasion. Decreased immunostaining thought to be related to surgical damage of tissue. Pit1 positivity & GH positivity.. Densely granulated GH producing somatotroph adenoma. Ki67 1% Repeat Pituitary MDT review in Nov 2021: Post operative MRI scan showed residual tissue in the aspect of the right para sellar region with normal IGF levels and persistent raised GH levels with an outcome advised no indication for further surgical intervention and to continue with surveillance programme and continue Hydrocortisone Repeat clinic review in February 2022 showed low IGF-1 at 5.6 nmol/l. Prolactin was mildly elevated at 558 mU/l, Cortisol was reassuring at 461 nmol/l. Marked as treated acromegaly with marked elevation of growth hormone but without an IGF 1 response with continued surveillance.

DOI: 10.1530/endoabs.100.WB3.3

WB4.1

An incidental diagnosis of acromegaly

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The case is presented of a 42 year old female who was admitted to hospital with an acute exacerbation of sarcoidosis. A CT of sinuses was performed which incidentally noted that the pituitary gland appeared enlarged. An MRI of the pituitary confirmed a moderately enhancing $21\times26\times22$ mm pituitary macroadenoma which was displacing the chiasm superiorly. The patient reported that she had to increase the size of her wedding ring three times in the last three years and her shoe size had also increased. She also reported that her facial appearance had changed and gaps were present between her teeth. She had no subjective visual disturbance. Multiple skin tags were noted on examination. There were no overt change in her bowels or weight loss. In addition to sarcoidosis, she had a history of asthma, vitiligo and hypothyroidism. IGF-1 was 736 mg/l. The remainder of her pituitary profile was normal. An oral glucose tolerance test with growth hormone was consistent with a diagnosis of acromegaly. HbA1 c confirmed pre-diabetes and she was commenced on Metformin. Formal visual field testing confirmed bitemporal hemianopia. She was commenced on Sandostatin LAR 10 mg every 28 days and referred for urgent review to a tertiary neurosurgical centre. Due to prolonged courses of steroid therapy for her sarcoidosis, she was commenced on maintenance hydrocortisone while awaiting a short synacthen test. She had a screening colonscopy with two polyps removed. On review in the outpatient clinic one month later, she reported an ongoing and significant headache since commencing Sandostatin LAR. CT brain noted a heterogeneous appearance of the known pituitary adenoma which may indicate some small volume internal haemorrhage. She was transferred to a tertiary neurosurgical centre and underwent an endoscopic transsphenoidal resection. She was well on review post-operatively and passed a short synacthen test. Post-operative IGF-1 was 692 mg/l. The remainder of her pituitary profile was normal. This case highlights the importance of taking a thorough history as this patient had many clinical features suggestive of acromegaly.

DOI: 10.1530/endoabs.100.WB4.1

WB4.2

A challenging case of acromegaly in a young patient desiring fertility

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A 33-year-old patient with background of Bilateral achilles tendonitis, was referred to Endocrinology with raised IGF-1 and concern of acromegaly. Her symptoms included arthralgias and change in hand and feet size. Pituitary profile

confirmed elevated IGF-1 181 nmol/l, otherwise normal pituitary profile. On OGTT, there was failure to suppress Growth hormone. Pituitary MRI revealed large macroadenoma with suprasellar extension, extension into right cavernous sinus with optic chiasm compression and upward displacement. Surgery was advised, with initiation of adjuvant somatostatin analogue (lanreotide)therapy, but this caused gastrointestinal side-effects, needing addition of creon, which allowed her to continue lanreotide. Transsphenoidal surgery allowed significant debulking of disease with small residual left around carotid-artery. Histopathology revealed Somatotroph tumour with MIB1 index 10%. Genetics screen returned negative. Post op investigations unfortunately demonstrated persistent IGF-1 elevation 67 nmol/l and residual intrasellar tissue on MRI. It was advised to manage her medically in view of her wishes to complete her family, therefore lanreotide was restarted. Cabergoline was added at 0.5 mg once weekly but discontinued soon due to gastrointestinal side-effects. Lanreotide frequency was increased to 120 mg every 3 weeks. A year later, IGF-1 was mildly raised:32 nmol/l. She became pregnant leading to cessation of lanreotide but unfortunately had a miscarriage. She stayed off lanreotide and conceived again. She was monitored with visual-field assessment in each trimester. Pregnancy was uneventful apart from development of diet-controlled GDM. Post partum MRI revealed stable radiological disease and IGF-1 was 37 nmol/l. An 8 mm terminal ileum Neuroendocrine Tumour (NET) was identified on her routine colonoscopy. Polypectomy was not possible, so right hemicolectomy was undertaken to remove well-differentiated Grade1 NET Ki67 $<$ 1% pT2pN1(1/16)LV1PN1R0. Lanreotide was reinitiated but optimal control of IGF-1 level wasn't achieved. As her family was completed, she was re-reviewed in our pituitary clinic for definitive management options. Neurosurgeons felt that the small residual couldn't be removed safely, hence she was referred for radiotherapy. Her lanreotide was switched to pegvisomant. She has received 45 Gy fractionated stereotactic radiotherapy and is awaiting a repeat MRI scan 6 months post-radiotherapy. We plan to follow her up in Endocrine clinic with annual pituitary profile and would reassess her pegvisomant dose in 6 months post-radiotherapy on basis of IGF-1 levels. Her last IGF-1 was finally in the normal range at 25.5 nmol/l.

Conclusion

This case elucidates how challenging it can be to manage acromegaly, especially in young patients who desire fertility and illustrates various treatment options available for management in acromegaly.

DOI: 10.1530/endoabs.100.WB4.2

WB4.3

Endocrine metabolic disorders secondary to acromegaly, description of a clinical case in a south american patient

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Introduction

Acromegaly is caused by excessive secretion of growth hormone (GH), usually by a pituitary adenoma, and a concomitant excess of insulin-like growth factor 1 (IGF-1). Excess GH and IGF-1 exert many actions on the cardiovascular (CV) system and especially on cardiovascular disease (CVD) risk factors which are common, especially in active acromegaly, but often persist after adequate treatment in patients with controlled disease.

Clinical case

This is a male patient in the fifth decade of life with a history of acromegaly under pharmacological management as well as heart failure with LVEF of 15%, type 2 diabetes requiring insulin, angioplasty of the anterior descending and circumflex artery at cardiac level and management with angioplasty of the two carotid arteries presented simultaneously at the age of 42 years. She is under management for comorbidities. Currently with a NYHA class III with contraindication for surgical management of pituitary adenoma due to high surgical risk. She is being managed with octreotide and cabergoline by Endocrinology. Continued management by Cardiology and Internal Medicine.

Discussion

In large population cohorts, normal or high IGF-1 levels are associated with lower prevalence of cardiovascular risk factors (CVD) and mortality. IGF-1 administration shows protective effects, but both low and supraphysiological levels are associated with risks. IGF-1 resistance in dysmetabolic states explains contradictory associations between IGF-1 and CVD. In higher risk populations, the relationship between IGF-1 and blood pressure is inverse, changing in cohorts with elevated IGF-1 levels, such as in patients with acromegaly. Although an independent effect of excess HC/IGF-1 on the vasculature has not been demonstrated, controlled and uncontrolled acromegaly is associated with microvascular damage, endothelial dysfunction, and proinflammatory changes. The underlying mechanisms involve metabolic alterations, oxidative stress and inflammation. This case report highlights the importance of analyzing the cardiovascular effects of acromegaly and the need for comprehensive risk factor management.

DOI: 10.1530/endoabs.100.WB4.3

WB5.1

Comprehensive overview of acromegaly management

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A male patient was diagnosed with acromegaly in July 2007 (at the age of 38). His biochemistry showed IGF-1 123 (14.6-39.9) nmol/l; paradoxical rise in GH during OGTT; and evidence of hypopituitarism (Testosterone 5.2 nmol/l, LH 4.0 iu/l FSH 3.7 iu/l, SHBG 8 nmol/l and prolactin 112 mu/l) HBa1c 6.5%. MRI Pituitary revealed a poorly enhancing mass within the right side of the pituitary gland within a slightly expanded pituitary fossa. There was no parasellar extension, no compression of the optic apparatus. He remains normotensive throughout. He underwent two trans-sphenoidal surgeries in 2007; both resulted in significant intra-operative bleeding due to anomalous blood vessels. No pituitary tissue was identified histologically. He went on to receive external beam radiotherapy in 2008. A third trans-sphenoidal surgery was attempted in 2009, but again resulted in profuse venous bleeding. In 2010 he went on to receive stereotactic radiotherapy to accelerate achievement of biochemical control. Over this time medical therapy was introduced to aid biochemical control whilst awaiting the effects of the radiotherapy. Unfortunately, he was intolerant of somatostatin analogues, commencing Pegvisomant after a positive outcome from an IFR submitted to NHS England. The patient discontinued pegvisomant in 2022, as he no longer wished to self-inject. Off of GH lowering medications he now has good biochemical control of his disease (GH $<$ 0.1 mg/l, IGF-3.8 nmol/l, HbA1c 41 mmol/mol). MRI Pituitary in 2023 showed a slight reduction in the overall adenoma size. Unfortunately, his disease was complicated by severe degenerative arthropathy affecting mainly the wrists and knees which has required multiple intraarticular steroid injections and regular analgesics. He remains under regular review with the rheumatology and orthopaedic teams. The severity of the arthropathy has impacted negatively on his mood, quality of life and led to significant functional limitation. Additionally, he suffers from chronic sinus disease with purulent discharge from the nose, under review by the ENT team. Surveillance colonoscopy, Bone Densitometry and echocardiography have shown normal studies.

Learning points

This case demonstrates how Acromegaly frequently require multiple therapeutic modalities introduced both in parallel and concurrently to achieve long-term biochemical control. Additionally, the case demonstrates how associated complications can significantly affect the quality of life and daily functioning. It is therefore important to adopt a holistic approach in managing patients with acromegaly aimed at both biochemical remission and management of comorbidities with timely multidisciplinary team involvement.

DOI: 10.1530/endoabs.100.WB5.1

WB5.2

Acromegaly presenting with plantar fasciitis and headaches

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50 M presented to our hospital with plantar foot pain and clawing of the toes in his right foot for a period of 12 months and a 4 month history of headaches. He was initially managed with physiotherapy and neurology undertook MRI scans. MRI: The pituitary gland is enlarged due to a right-sided hypoenhancing lesion measuring 9.5 $\times$ 9 $\times$ 6.5 mm. No further pituitary lesion is identified. The pituitary infundibulum is at the midline. The optic chiasm is not displaced. On assessment in the endocrine clinic patient reported multiple skin tags and

inability to wear his rings anymore. Patient also reported ongoing Lab work up showed: IGF1 98 nmol/l (8.5-31 nmol/l), OGTT showed inadequate suppression of GH:

22/03/23	10:05	10:25	10:55	11:25	11:55	12:25
Glucose (curve) mmol/l		5.6	7.2	6.4	4.9	6.0
Growth hormone (curve) mg/l	6.9	6.7	5.7	4.6	5.3	6.2

Rest of Pituitary function were within normal limits. Patient was commenced on Lanreotide therapy whilst waiting for definitive management of the adenoma causing GH excess. TSS with good resolution of GH excess. Post op no loss of Pituitary function with post op Cortisol 381 and rest of pituitary function within normal limits. IGF1 in the immediate post Op FU : 37.7 (8.5-31 nmol/l). A further appointment showed a rise in IGF1:

21/09/23 09:06 IGF1: 43.0 (H)
27/11/23 09:30 IGF1: 51.1 (H)

Patient underwent a GH day curve: GH day curve:

Time	GH
9:30 am	1.5
11:30 am	1.7
13:30 pm	1.7
3:30 pm	2.1
5:30 pm	2.6

Further MRI showed: There still remains a 6 mm hypo-enhancing lesion in in the right side of the pituitary fossa. This also returns a similar signal on the T2-weighted sequences to the tumour on the preoperative scan and and may represent a small residuum Postsurgical changes also possible. Patient was referred for pituitary radiotherapy after discussion in the local MDT as there is residual disease. Patient currently awaits radiotherapy.

DOI: 10.1530/endoabs.100.WB5.2

WB5.3

Acromegaly: the diagnosis to management

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42 years old male referred to endocrinology for the symptoms of joint pains, lethargy, sweating and low testosterone levels. Medical history was consistent with obstructive sleep apnea established on CPAP machine. On examination high BMI, prominent lower jaw, and large hands were noted. Investigations confirmed raised IGF-1: 550 ng/ml (normal range 101-267), Low baseline cortisol 126 nmol/l, Low testosterone: 3.1 nmol/l, low LH:2 IU/l/FSH:1IU/l with normal thyroid function test TSH:2.98 mU/l, T4:12.4 pmol/l. GH Day curve suggested mean growth hormone 0.97 mg/l. MRI pituitary suggested Left microadenoma 0.9 mm confined to within the gland. Hormone axis was further assessed with oral glucose tolerance test which indicated nadir Growth hormone 0.9 mg/l. Insulin tolerance test showed peak Cortisol of 555 nmol/l. Testostrone replacement commenced and was referred to surgeons after discussing in Pituitary MDT. In view of low baseline cortisol, he was initiated on hydrocortisone 10 mg/5 mg/5 mg. He underwent Transsphenoidal resection and the histology was consistent with densely granulated somatotroph. Post operatively IGF-1 were noted to be 232 ng/ml (69-208). Cortisol incremented to 529 nmol//l on Insulin tolerance test hence weaned off hydrocortisone. Post-surgery MRI Pituitary was normal. 6 monthly oral glucose tolerance tests were all <0.3 mg/l, indicating a very good result. Insulin tolerance test shows undetectable growth hormone levels with AGHDA score 23/25 Initiated on growth hormone replacement along with testosterone replacement.

DOI: 10.1530/endoabs.100.WB5.3

Workshop C: Disorders of the thyroid gland

WC1.1

Metastatic papillary thyroid cancer

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32 male presented with painless neck swelling for 3 weeks and finding was consistent with MNG. Us neck showed right lobe is enlarged and contains a 11 mm × 12 mm × 15 mm irregular, echo poor nodule with calcification. BTA classification is U5. (Malignant) and followed with Right thyroid nodule FNA was consistent with Oncocytic variant of papillary thyroid carcinoma Thy5. Initially TFTS showed TSh : 1.00 miu/l Free T4 : 17.9 pmol/l. Patient underwent total thyroidectomy with level 6 node dissection and histology was consistent with PT3 bm pN1 a pR1. After surgery his thyroglobulin level keep on rising and peak to 39.89 mg/l. Due to extracapsular and local lymph node invasion TSH recombinant with 5 Gbq radioiodine was given and us thyroid and thyroglobulin was measured after the radioiodine treatment and thyroglobulin drop to <0.9 mg/l. After radiotherapy repeat us neck showed lymph node in level 3/4 and planned for core biopsy which showed Metastatic PTC and planned for right neck dissection. Patient under went right neck dissection and found to have 2/38 lymph node positive for metastatic PTC. Patient having repeated us neck every year over last 5 year to assess for recurrence of disease. We aim to keep TSH <0.1 miu/l and initially started on levothyroxine 150 mg which was escalated to 200 mg and on current dose of levothyroxine his latest TSH: <0.01 miu/l and T4: 24.0 pmol/l, Thyroglobulin level: <0.9 mg/l. After 6 year of follow up us neck showed 2 mm ill-defined hypoechoic region within the right thyroid bed is currently indeterminate which need further us scan in 6 months' time.

DOI: 10.1530/endoabs.100.WC1.1

WC1.2

Primary hodgkin lymphoma of the thyroid: a case report

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Introduction
The thyroid lymphoma (TL) is a rare disease, accounting for less than 2% of thyroid neoplasms. The majority of cases are of the non-Hodgkin (NHL) B-cell lineage and large cell type.
Objective
To present a rare case documented in the literature of Primary Nodular Sclerosis Hodgkin Lymphoma (HL) of the thyroid, in a 20-year-old male patient.
Methods
The clinical history and records of the case, biopsy reports, immunohistochemistry, CT scans, and other extension studies were reviewed for subsequent analysis, summarization, and presentation.
Case Report
A 20-year-old male patient, born and residing in El Vigía/Mérida, presents with a clinical picture evolving over 6 months characterized by a sensation of pain and discomfort in the anterior neck region, profuse nocturnal sweating, and weight loss. Subsequently, there was a sudden increase in volume in the lateral cervical region, mainly on the right side, followed by progressive growth in the anterior neck region, reaching approximately 10 × 10 cm, accompanied by dysphagia. A cytology by fine needle aspiration was performed, yielding a presumptive diagnosis of chronic thyroiditis. Subsequently, a partial right lobectomy was carried out with a biopsy report indicating Hodgkin's lymphoma (HL), nodular sclerosis type (October 2, 2014). Immunohistochemistry reported immunostaining for CD30 and CD15, suggesting primary thyroid HL. The patient underwent four cycles of ABVD protocol without complications. Upon completing the protocol, clinical, laboratory, and imaging reassessment were conducted, all of which were within normal limits. Remission has been maintained up to the present date.
Comment
Primary thyroid lymphoma is defined as a lymphoma that exclusively affects the thyroid gland (stage I) or invades tissues adjacent to the thyroid (stage II) (2). Our patient, as reported in the literature, was diagnosed in the context of a multinodular goiter. However, unlike the literature where the most common cases are Non-Hodgkin Lymphomas (3), this case involves Hodgkin Lymphoma, and it is in a young male patient, with no similar cases reported (4). The proposed treatment followed the standard protocol, intravenous polychemotherapy with doxorubicin, vinblastine, dacarbazine, and bleomycin (ABVD) for four cycles, followed by consolidation with radiotherapy, resulting in a satisfactory response.
Conclusion
We present a case of Primary Thyroid Lymphoma in a 20-year-old male patient, associated with a diagnosis of goiter. This is a rare and uncommon occurrence, both within the lymphoma group and among thyroid tumors.

DOI: 10.1530/endoabs.100.WC1.2

WC1.3

Genetic testing in medullary thyroid cancer - the key to unlocking a diagnosis of MEN2

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Introduction
This case report described a patient who presented with medullary thyroid carcinoma (MTC) requiring a total thyroidectomy and radial neck dissection. Genetic testing performed in the context of MTC revealed RET proto-oncogene mutation. Baseline screening identified bilateral pheochromocytomas requiring treatment with bilateral adrenalectomy.
Case report
60-year-old male patient presented with a neck lump which had been present for few years. Fine needle aspiration was in keeping with MTC, preoperative Calcitonin was 2324 ng/l. He underwent total thyroidectomy and radical neck dissection 2013. He remains under follow up and his Calcitonin fluctuates from 35-135 to date. Genetic testing revealed a heterozygous mutation in RET gene [(Heterozygous for c.1901G>A p.(Cys634Tyr)] confirming a diagnosis of MEN2 in 2019. This is no known family history of MEN related tumours in his family. His serum calcium results were consistently normal. The classical symptoms of pheochromocytoma are absent, although the clinic blood pressure was mildly elevated. Screening for pheochromocytoma with fractionated plasma metanephrines was performed in the context of known RET mutation. The first set of plasma metadrenaline was 5 times and normetadrenaline was 1.6 times the upper limit of normal. This was confirmed on repeat testing. Given the RET gene mutation and significant elevation of metadrenaline, the pre-test probability of a pheochromocytoma was very high. Subsequent MRI adrenals showed multiple nodules within both adrenal glands measuring up to 2.2 cm without any signal dropout on opposed phase imaging. Functional imaging with MIBG scan revealed avidity in bilateral adrenal nodules. Pre-operative preparation with alpha blockade to minimize the operative risks due to a sudden surge of catecholamines was undertaken. He underwent laparoscopic bilateral adrenalectomy without any complications. Histology was consistent with bilateral pheochromocytomas. Plasma metanephrines 6 weeks post-operative were normal. The patient continues surveillance follow up due to the life-long risk of recurrence of pheochromocytoma and monitoring for the MTC.
Learning points
1. All patients with MTC should be offered genetic screening.
2. MEN2 is an autosomal dominant disorder characterized by MTC (100%) with an increased risk of developing pheochromocytoma (50%) and parathyroid hyperplasia (20-30%) due to the mutations in the RET gene.
3. Pheochromocytoma is rarely the initial manifestation and is often identified during screening.
4. Bilateral pheochromocytomas are common in patients with MEN2.
5. Genetic testing should be performed for immediate family members to allow early diagnosis followed by timely intervention to reduce the morbidity and mortality associated with MEN2.

DOI: 10.1530/endoabs.100.WC1.3

WC2.1

Radiofrequency ablation of toxic thyroid nodule

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Background
Radiofrequency ablation (RFA) is an outpatient image-guided thermal ablation procedure that is an alternative to surgery for treating thyroid nodules. It is minimally invasive, cosmetically superior and associated with less risk of hypothyroidism.
Case
We discuss a case of 53 years old female who presented with palpitations, feeling hot, sweating, tremors, weight loss, and pins and needles. On examination, thyroid

was palpable and there were no eye signs. Her investigations showed a low TSH and high FT4 and the rest of investigations, including TPO and TSI, were normal. US/S neck showed a solitary hot nodule measuring 18 mm which was hyperechoic. She was treated with carbimazole 15 mg OD and propanolol 10 mg TDS with limited benefit. She declined surgery and radioactive iodine was not an option because she had a young child. Therefore thyroid nodule RFA was performed in Turkeyafter which she became euthyroid and eventually came off carbimazole. Her post ablation scan showed decrease in size to 12 mm andnodule became isoechoic.
Discussion
The various treatment options available for autonomously functioning thyroid nodule (AFTN) are medical, surgical, radioiodine and RFA. We discuss the emerging literature surrounding the efficacy of RFA treatment, which can lead toTSH normalisation in 71.2% of patients, normalising TFTs in 45-50% of medium sized AFTN and greater than 80% of small AFTN. Whilst thyroid RFA is emerging as a safe and effective treatment for the non-surgical management of thyroid nodules, we will also discuss the recent American Thyroid Association (ATA) consensus in September 2023 that addresses the safe implementation and utilisation of the techniques.

DOI: 10.1530/endoabs.100.WC2.1

WC2.2

Diffuse large B-Cell non-Hodgkin lymphoma masquerading as multi-nodular goitre - a case report

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Thyroid nodules are very common findings in clinical practice. Only a fraction of these thyroid nodules are malignant and reliably differentiating those remains a challenge. We present a case of a man who presented with an enlarging neck mass causing compressive symptoms. This was diagnosed as a multinodular goitre (MNG). However, histopathological analysis revealed it to be diffuse large B-cell non-Hodgkin lymphoma (DLBCL). A 50-year-old male was referred to our endocrinology service by primary care through the 2-week-wait referral system. He had a background of congenital deafness, asthma and retinitis pigmentosa for which he was registered as blind. He had an 8-week history of a neck lump with compressive symptoms including dyspnoea and dysphagia. A collateral history from his mother confirmed the sub-acute onset of the neck lump. He was seen by primary care and an ultrasound (US) scan was done prior to referral to endocrinology. This revealed multiple thyroid nodules, the largest measuring 49 × 37 × 35 mm and graded as U3 indeterminate. He was seen in our service within 2 weeks of the referral. On examination of the neck, there was a large irregular goitre which was rather firm and moved only slightly on swallowing. His thyroid function tests were normal. He had a repeat US neck done that revealed a large hypoechoic mass involving both thyroid lobes measuring 4.7 × 5.5 cm on the left and 2.3 × 3.4 cm on the right side in axial diameter. The mass showed only minor internal vascularity on colour Doppler. There was US evidence of right sided lymphadenopathy measuring at least 1.4 cm in short axis diameter. The mass was extending into the isthmus with tracheal deviation. This was graded as a U5 nodule and hence a fine needle aspiration cytology (FNAC) was performed using an aseptic technique. Given the extent of the mass, a computed tomography (CT) was arranged and revealed a lobulated homogenous cervical mass surrounding the thyroid gland and supraclavicular fossae, extending into the anterior mediastinum. The FNAC was reported as CD-20 positive lymphoid cells, suggesting DLBCL. He was referred to haematology and has since received 6 rounds of chemotherapy and 15 rounds of radiotherapy. Although there have been case reports of non-Hodgkin's lymphoma of the thyroid, we present a unique case where DLBCL presented as MNG which, on further investigation, was found to be a cervical mass encircling the gland and masquerading as MNG.

DOI: 10.1530/endoabs.100.WC2.2

WC3.1

Recurring papillary thyroid carcinoma in a young lady

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A 13-year-old girl was noted to have a right-sided thyroid swelling on being reviewed by her paediatric endocrinologist. Neck examination confirmed a nodular mass in the right thyroid lobe, rubbery in nature, non-tender, mobile on swallowing but not on extrusion of the tongue. There was no thyroid bruit. She was clinically euthyroid with no dysthyroid eye disease or peripheral stigmata of thyroid dysfunction. Thyroid Ultrasound reported a grossly enlarged right thyroid lobe due to an in-homogeneous, solid, ill-defined, multi-loculated nodule approximately 3 × 5 cm. Thyroid Scintigraphy confirmed a large cold nodule in the same location. She underwent Total Thyroidectomy and Radioactive Iodine (I-131) Ablation Therapy (RAIT) 80-mCi in October 2006 with further RAIT 120-mCi in November 2007. Histology reported papillary carcinoma (incompletely excised) in the Right thyroid lobe and Micropapillary carcinoma (completely excised) in the left thyroid lobe on a background of Hashimoto's Thyroiditis. Additionally, parathyroid parenchyma was noted in the periphery of the left lobe and two nodules of thymic tissue were attached to the right lobe. Radioactive iodine uptake (RAIU) scans post-ablation showed no uptake. Treatment with Levothyroxine 100 micrograms daily was commenced post-operatively. Calcium levels remained stable. Thyroglobulin remained suppressed for 14 years post-operatively until a rising level of 1.1 mg/ml was noted in October 2021. Anti-Thyroglobulin antibody levels were persistently negative. Thyroid Ultrasound revealed a few suspicious lymph nodes on the right side of the neck, largest measuring 1.1 cm × 0.8 cm. A similar abnormal node in the midline of the neck above the previous thyroid isthmus measured 0.9 cm × 0.6 cm. Fine needle aspiration (FNA) of this lymph node revealed metastatic papillary thyroid carcinoma. Surgical consultation advised against surgical intervention, and a 3rd dose of RAIT 120-mCi was administered in February 2022. RAIU scan post-ablation showed no uptake. A stimulated serum thyroglobulin level was taken and found to be 38.5 ng/ml indicating the possibility of Iodine refractory disease requiring surgical intervention. Thyroid Ultrasound post-RAIT revealed stable findings. Multi-disciplinary team (MDT) discussion advised surgical intervention via Central neck and Right neck dissection. Right extended selective neck dissection (II-IV, VI, VII) was performed in January 2023. Histology confirmed metastatic papillary thyroid carcinoma was present in 9 lymph nodes (9/20). The largest metastatic tumour deposit was present in one central neck lymph node, measuring 7 mm in diameter and showing extra nodal extension- P1nb. Post-operative follow-up imaging showed no disease recurrence. Intended TSH suppression (below 0.1 micIU/ml) is being achieved.

DOI: 10.1530/endoabs.100.WC3.1

WC3.2

Differentiated thyroid cancer: long-term follow-up and management options for persistent/recurrent disease

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Background
The management of differentiated thyroid cancer involves multiple modalities such as surgery, radioactive iodine ablation therapy (RAIA), external beam radiotherapy (EBRT), thyroid-stimulating hormone (TSH) suppression, and chemotherapy in cases of persistent or recurrent disease. Long-term follow-up incorporates Dynamic Risk Stratification (DRS) using thyroglobulin (Tg) and neck ultrasound. This case focuses on a 65-year-old patient with Follicular Thyroid Carcinoma (FTC) who experienced persistent disease after 10 years of regular follow-up, emphasizing the significance of extended monitoring in thyroid cancer cases.
Case
The patient presented with lower back pain, and an X-ray showed lytic lesion at L1 vertebra. Subsequent MRI indicated possible metastasis. CT thorax, abdomen and pelvis did not reveal any primary cancer. Eventually a biopsy of lesion lead to the discovery of a metastatic deposit from FTC. Following stabilization of spinal metastasis, the patient underwent total thyroidectomy and high-dose RAIA treatment. Despite four RAIA doses, the patient's thyroglobulin levels remained elevated, prompting additional treatments, including External Beam Radiotherapy (EBRT) and TSH suppression therapy. Following these interventions, his thyroglobulin levels remained at around 600-800 mg/l. The patient had a reasonable quality of life and was asymptomatic. Therefore, a decision was made for regular monitoring of thyroglobulin and to continue TSH suppression with levothyroxine. However, after 8 years of stable follow-up, thyroglobulin levels began to rise again. The discussion involves the planning of further RAIA and potential consideration of systemic chemotherapy with Sorafenib if the disease persists.
Discussion Points
- Addressing patient concerns, including the risk of thyroid cancer for family members, side effects of RAIA and EBRT, genetic implications for children, and future cancer risks.
- Emphasizing the significance of long-term follow-up, particularly in distinguishing between low-risk and high-risk cases.
- Exploring various treatment options for persistent or recurrent thyroid cancer, including the potential use of systemic chemotherapy. This case underscores the need for comprehensive and extended follow-up strategies in thyroid cancer

management, considering the specific challenges and potential interventions for cases of persistent or recurrent disease

DOI: 10.1530/endoabs.100.WC3.2

WC4.1

Follicular thyroid cancer

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Introduction
Follicular thyroid cancer (FTC) is a tumour of the thyroid epithelium with follicular differentiation and invasion into capsule or vessels. Constitutes 10% of all thyroid cancers, may be minimally or widely invasive. metastases in 20% of cases by haematogenous spread, rarely to lymph nodes. Twice as common in females as males, mean age 50years. Treated with thyroidectomy, radioactive iodine ablation and TSH suppression with levothyroxine.
Case Description
34 year lady, background Asthma on asthma inhalers, epilepsy-off medications since age 17years, Found to have 5 cm thyroid nodule, U2 in June 2020 and Normal thyroid function during an inpatient stay with appendicitis. She felt nodule was bigger during an asthma attack in December 2022, euthyroid clinically with enlarged right lobe of thyroid. Repeat USS showed 5 cm thyroid nodule in right lobe with U3 features, FNAC Reported Thy 2-normal. Since cytology report and USS features incongruent a repeat FNAC was requested. Unfortunately, 2 nd FNAC reported Thy1-insufficient sample. 3 rd FNAC done reported Thy 3f-indeterminate for follicular cancer. Discussed with patient on need for surgery; all results communicated to patient at each stage. She had right hemithyroidectomy in April 2023. Histology returned Follicular thyroid cancer, PT3a, pNx, pMx, Pv1, pRx. Discussed in the Thyroid cancer MDT and Completion thyroidectomy with Radio-active iodine ablation recommended. She was booked for completion thyroidectomy but incidentally found to be pregnant during anaesthetic assessment. She decided to keep the pregnancy so plans for completion thyroidectomy deferred till after delivery of the baby. Seen at 14 weeks gestation with TSH 2.4 and FT4 10.1 pmol/l. She was started on levothyroxine 50 mg with aim to get TSH under 2 miu/l and for further review by surgical team on delivery. USS Thyroid June 2020 5.1 $\times$ 3.0 $\times$ 2.5 cm isoechoic nodule with a halo and predominantly peripheral vascularity in right lobe of thyroid (U2). No retro-sternal extension. January 2023 5.1 cm $\times$ 2.6 cm $\times$ 2.8 cm right thyroid nodule, no real change since previous scan, slight heterogeneity of the nodule with some internal vascularity; in view of the patients age, the nodule reclassified U3 and FNA performed. No lymphadenopathy. Histology Encapsulated angio-invasive follicular thyroid carcinoma, 50 mm maximum dimension, tumour in the inferior shave margin, incomplete excision. Pathological staging pT3 a pNx pMx pV1 pRx.
Learning points
Important not to overlook patient symptoms even though in this case the size of the nodule was unchanged, features had changed. Repeat investigations essential if results of USS and cytology incongruent

DOI: 10.1530/endoabs.100.WC4.1

WC4.2

Hyperfunctioning thyroid nodule

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We present a case of 40 years old lady who was referred to us with a thyroid nodule in her right lobe. She was well, but on specific questioning reported weight loss of about 3 kgs over the past month and some mild heat intolerance. The nodule was 2 cm in size and the patient was clinically euthyroid. Thyroid function tests demonstrated a suppressed serum TSH with a mildly elevated serum T3. A thyroid ultrasound scan was performed which demonstrated that the palpable nodule was located in the upper pole of the right lobe of thyroid, and this nodule was hyperfunctioning or "hot". There was less than a 1% chance that nodule was malignant and fine needle aspiration biopsy (FNAB) is not indicated. Uptake throughout the remainder of the thyroid was relatively suppressed. The patient had an autonomous functioning thyroid nodule and was referred for radioiodine therapy.
Discussion
Thyroid nodules are very common with 50% of people over fifty years having thyroid nodules on ultrasound. The great majority of these nodules are not malignant. Thyroid nodules under 1 cm in size do not need to be investigated with thyroid scans, ultrasounds, blood tests or FNAB. There is a very low chance that such nodules are malignant and these can be watched clinically to detect if the nodule is growing. Physical exam findings that increase the concern for malignancy include: Nodules larger than 4 cm in size, firmness to palpation, fixation of the nodule to adjacent tissues, cervical lymphadenopathy, and vocal fold immobility. Provided that the patient is not thyrotoxic, the best investigation of a thyroid nodule is a FNAB. In this setting, most thyroid nodules are hypofunctioning or “cold” on thyroid scans and there are no ultrasound findings that can exclude malignancy. Prior to ultrasound guided FNAB, the size of the nodule can be measured accurately which may help in future management of the patient. Despite a sensitivity of 65-98% and a specificity of 72-100% for thyroid cancer, unfortunately, FNAB biopsies are far from perfect with about 20% of FNAB’s being non diagnostic and may miss malignant nodules in up to 5% of patients.
Conclusion
In the euthyroid patient, FNAB is the best investigation for patients with nodules greater that 1 cm in size. Nodules less than this size can be left for surveillance in primary care.

DOI: 10.1530/endoabs.100.WC4.2

WC5.1

A case of metastatic papillary thyroid carcinoma

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45 year old female referred to the endocrine clinic by GP for further management of her ongoing thyroid issue. Patient had recently moved from China. In China during her general health check, doctors over there found that she had 2 small thyroid nodules in her left lobe of thyroid and they recommended hemi-thyroidectomy for that. No significant family history of any thyroid disorders. Post hemi-thyroidectomy she went back for another surgery for lymphatic leakage post hemi-thyroidectomy. Histopathology was sent which showed papillary thyroid carcinoma (classic), Capsular invasive, no clear vascular and nerve tract invasion was observed. Lymph nodes in cervical region were positive for metastasis, but not in tracheal region. She was then started Levothyroxine. She then moved from China to UK. Over here we organised a repeat US scan of her thyroid and CT scan of chest abdomen and pelvis with contrast. US showed unremarkable left thyroid. CT scan showed tiny nodules in right middle lobe, lung otherwise clear. Her TSH was 0.02. Her case was discussed in our thyroid cancer MDT and MDT recommended for completion thyroidectomy and adjuvant radioiodine treatment with repeat CT chest in 3 months time. Patient has been referred for thyroidectomy and radioiodine treatment awaiting outcome from those procedures.
Discussion
It is not common to see distant metastasis from papillary carcinoma, but in this case we see evidence of nodular lesion in right middle lobe of lung. It is difficult to say at this stage whether is it a separate pathology or metastasis from thyroid cancer.

DOI: 10.1530/endoabs.100.WC5.1

WC5.2

High grade follicular thyroid cancer (non-anaplastic)

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70-year-old woman presented with a 2-month history of a left-sided neck lump. Generally well with no swallowing issues, no weight loss, and no systemic upset. Previous history of breast cancer 10 years ago requiring bilateral reduction mammoplasty and radiotherapy. Ex-smoker. There is a strong family history of hypothyroidism. On examination, well and euthyroid. Palpation revealed obvious left-sided anterior neck mass. Nodule was smooth, firm, and minimally tender on palpation. It moved with swallowing. Blood test was unremarkable. Ultrasound scan revealed a 3 $\times$ 3 $\times$ 4 cm mass in the left lobe of the thyroid, with evidence of microcalcification, and classed as U4. No lymphadenopathy. FNA come back as Thy3 F indeterminate. Underwent diagnostic hemithyroidectomy and histology revealed pT3 a high grade follicular neoplasm with some poorly differentiated component and widespread lymphovascular invasion. She had completion thyroidectomy, and awaiting radioiodine ablation.

DOI: 10.1530/endoabs.100.WC5.2

Workshop D: Disorders of the adrenal gland

WD1.1

A case of primary hyperaldosteronism: a timeline

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A 63-year-old gentleman was admitted with right iliac fossa pain, nausea and constipation. Incidentally his potassium was found to be 2.3 mmol/l and he had ureteric stent insertion for right VUJ calculus after the potassium was corrected. Endocrine consultant who reviewed him in the acute medical unit advised an aldosterone to renin ratio (ARR)which was raised with aldosterone 920 and suppressed renin <0.2 but he was still taking Ramipril 5 mg, Amlodipine 10 mg and Doxazosin 4 mg OD despite the correct instructions. A saline suppression test was performed to avoid any further delay in the diagnosis after he came off Amlodipine and Ramipril for 2 weeks. His ARR was raised with Aldosterone level of 730 pmol/l and plasma renin activity of <0.2. Post 2 L of saline infusion, his aldosterone level suppressed to 230 pmol/l with a persistently low PRA <0.2 making the diagnosis of primary hyperaldosteronism unsure (level >240 is highly probable for PA whilst anything <120 is highly unlikely). A dedicated CT adrenal glands showed bilateral adrenal nodularity with a slightly more hyperplastic left gland. He was then referred to Adrenal MDT and AVS results are shown below. He was commenced on Eplerenone 100 mg OD with plan to discontinue the latter 2 weeks prior.

Site	Cortisol (nmol/l)	Aldosterone (pmol/l)	Ratio
Mid IVC	386	2800	7.3
Peripheral	445	2970	6.7
Left adrenal	11859	30200	2.5
Peripheral	404	2830	7
Right adrenal	12191	229000	18.8
Peripheral	597	2640	4.4
High IVC	436	3770	8.6

The above was suggestive of right sided adrenal source of aldosterone excess and thus he had a laparoscopic right adrenalectomy. Post operatively, his BP normalised and he remained normokalemic with a normal ARR and adequate response to synacthen. His adrenal gland histology was reported as nodular and diffuse hyperplasia. During his last endocrine clinic visit, his BP 140/83 whilst on Amlodipine 5 mg OD, Furosemide 20 mg OD, Doxazosin 4 mg OD and he was also commenced on Carbimazole for toxic multinodular goitre picked up on ultrasound when his TFTs showed a primary hyperthyroidism. This case is interesting as the low potassium wasn't picked up for several years until seen by an endocrinologist during the medical take. This case highlights the importance of educating primary care who deal with management of hypertension and other specialists such as urologists who deal with adrenal incidentaloma.

DOI: 10.1530/endoabs.100.WD1.1

WD1.2

Adrenal mass with neurological presentation

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A 70-year old female presented with 2-week-history of lethargy, reduced appetite, altered taste of food, weight loss, night sweats and easy bruising. Her past medical history only included PMR for which she was on low dose of prednisolone. Initial examination was unremarkable. Initial lab results showed unremarkable CRP, thrombocytopenia of 28, deranged LFTs (ALP 754 U/l, ALT 145 U/l, GGT 239 IU/l, Total Bilirubin 30 umol/l) and significantly raised Ferritin of 14837 mg/l. CT CAP showed left adrenal mass measured as 3.7 $\times$ 3 cm. CT adrenals showed indeterminate mass with suspicion of malignancy. Patient steroid dose was doubled and liver biochemistry and thrombocytopenia started to improve. Plasma metanephrines and Aldosterone/renin ratio, sex steroids came back negative. ONDST showed a cortisol of 141 nmol/l. Patient did not feature any signs of Cushing's. A week later, patient developed right 3rd, 6th and V1(ophthalmic) nerve palsies with possible 4th nerve involvement. CT angiography, MRI COW and MRI brain were all normal. LP showed increased protein & lactate with reduced glucose. Microscopy showed some lymphocytes & monocytes but no malignant cells. No evidence of infection. Autoimmune screening including ANCA, ANA, complement levels, liver autoimmune screening, paraneoplastic antibodies and Lyme serology were all negative. Neurology advised to increase steroids and patient was commenced on IV dexamethasone 10 mg OD. Liver biochemistry continued to improve and Ferritin dropped to 1512 mg/l. Myeloma screen came back negative and bone marrow biopsy showed reactive changes. Haematology advised that lymphoma is unlikely. There was no evidence of any lymphadenopathy clinically or through imaging. Adrenal MDT decided to go for adrenal biopsy. Whilst awaiting for the procedure patient developed more severe cranial nerve palsies and repeated MRI showed probable abnormality at both Meckel's caves/medial middle cranial fossae and possible abnormality of CN V and acoustico-facial bundles bilaterally suggesting lymphomatous, malignant or granulomatous infiltration. Adrenal CT guided biopsy showed that the mass had significantly increased in size to about 7 cm within a month since the first presentation. CT CAP was repeated and showed new abdominal lymphadenopathy and new right adrenal mass. Biopsy results came back as diffuse large B-cell lymphoma. Patient was commenced on R-CHOP but unfortunately deteriorated so fast, became aphasic, confused and then developed reduced GCS. End of life care was initiated and the patient died. From day one of presentation till death was around 45 days.

DOI: 10.1530/endoabs.100.WD1.2

WD1.3

A case of ACTH independent Cushing's syndrome with bilateral adrenal nodules

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Case presentation

A 40 year old woman with a history of epilepsy was referred to the endocrine clinic with hypertension and significant weight gain (BMI 42.3 kg/m^2). She had a sleeve gastrectomy performed in Turkey several years previously, resulting in an 18 kg weight loss. However, she regained this weight, most of which occurred in the six months prior to presentation. She had also noted the recent development of striae and was complaining of myopathy, so severe that she struggled to get out of bed each morning. As she clinically appeared Cushingoid and as a result a number of screening tests were carried out, including a low dose dexamethasone suppression test (cortisol was 143 nmol/l) 24 hour urine free cortisol (1406 nmol/24 hours), midnight salivary cortisone (95.8 nmol/l). Given the fact that she failed her screening tests, an ACTH was sent and found to be suppressed (ACTH <3 ng/l), this all supported a diagnosis of ACTH independent Cushing's Syndrome. A CT of her adrenals was carried and discussed at the surgical/endocrine MDT, it was determined that there were bilateral adrenal nodules these measured 2.1 cm on the right and 3 cm on the left. Metyrapone has been added to help with the symptoms of hypercortisolaemia and the MDT are in discussions regarding the best course of treatment for this lady. Currently the plan is to carry out sequential adrenalectomies starting with the larger adenoma (left). Postoperatively her response will be monitored but may possibly require a right sided adrenalectomy.

Time	Cortisol
09:00	717
10:00	684
11:00	656
12:00	673
13:00	749
14:00	681

Fig.1: Cortisol day curve prior to commencement of metyrapone

Discussion

This case has proven challenging as her clinicians are uncertain if one or both of her adrenals are contributing to her Cushing's syndrome, if this could be determined and she is found to have one normal adrenal gland she may avoid lifelong steroid replacement and the morbidity attached to this. On review of the literature there have been cases where adrenal vein sampling (AVS) has been used to localise hypercortisolaemia, however these are primarily case reports[1–4]. Raj *et al* has developed an algorithm to help localise the cortisol-producing adenoma in subclinical Cushing's disease using an adrenal vein to peripheral vein ratio comparing cortisol and metanephrine gradients[4]. Perhaps future research could be carried out investigating the feasibility of AVS in the diagnosis and lateralisation of cortisol-producing adrenal adenomas.

DOI: 10.1530/endoabs.100.WD1.3

WD1.4

Phaeochromocytoma: a case of recurrent disease

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A 56 year old lady underwent laparoscopic adrenalectomy for an incidental right adrenal mass. Plasma metanephrines were elevated pre-op and histology revealed PCC with a PASS score of 0/20 with SDHB immunostaining $+$. She remained asymptomatic until 9 years later when she presented with palpitations and worsening hypertension. Plasma metanephrines were 3-4 times above reference range. She was

also found to have goitre and USG/FNA revealed THY4 lesion for which she underwent total thyroidectomy. Thyroid Ca (pT3 NxMx follicular variant papillary thyroid carcinoma) – Rx with Radio-Iodine. Following diagnosis of bony metastasis from anatomical imaging and no avidity of the metastases with I131, MIBG, Gallium Dotatate and FDG PET were arranged. Out of the three imaging modalities, The FDG-PET showed the most metastatic deposits: nodal, splenic and extensive bone metastases (C2, right humeral head, body of sternum inferiorly, T11-2, L4). However, MIBG and Gallium scan were less sensitive, with the Gallium Dotatate showing the least metastatic deposits. She was commenced on denosumab and also doxazosin for alpha-blockade. She continues to undergo on going surveillance including annual metanephrines. This case highlights the relative inaccuracy of PASS score in predicting malignant behaviour in PCC. This patient presented with metastatic disease 9 years after initial surgery despite an R0 resection and no local recurrence. No pathogenic variant was detected in the usual PCC-PGL genes. It is also interesting to note less sensitive performance of Gallium Dotatate when compared to other functional imaging modalities in identifying metastatic sites which is often the case in Cluster 2 PCC. The current recommendation is for 10-year surveillance in PCC post-resection without a germ line mutation however, rarely, metastatic disease can occur after this period. This calls for more accurate scoring systems and possibly other sensitive tumour markers for surveillance. Analysis of the tumour for any possible somatic mutations may become a necessity in the future.

DOI: 10.1530/endoabs.100.WD1.4

WD2.1

Reninoma: a rare cause of hypertension in pregnancy

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A reninoma is a tumour of the afferent arteriolar juxtaglomerular cells that secretes the enzyme renin, leading to hyperactivation of the renin-angiotensin-aldosterone system. It is a cause of pathological secondary hyperaldosteronism that results in severe hypertension and hypokalaemia. Fewer than 200 cases have been described, seven of which were associated with pregnancy. We present the case of a 29-year-old woman referred with hypertension and hypokalaemia at 10 weeks' gestation of a dichorionic twin pregnancy. She was treated with Labetolol 600 mg four times daily, Methyldopa 1 g three times daily and Nifedipine LA 60 mg twice daily to maintain a blood pressure of approximately 130/90 mmHg. Her medical history included hypertension, diagnosed aged 19. She had one previous uncomplicated singleton pregnancy. There was no family history of hypertension or endocrinopathy. Recumbent plasma renin concentration was elevated at 67.7 ng/l (3-6 ng/l), and plasma aldosterone was elevated at 1425 pmol/l (<440 pmol/l). Tests for hypercortisolism and catecholamine excess were negative. Echocardiography revealed borderline concentric left ventricular hypertrophy and no coarctation of the aorta. Urine protein:creatinine ratio was elevated at 53.4 mg/mmol (<45 mg/mmol). A 2.4 cm solid, right renal lesion was identified on ultrasound. Further characterisation with magnetic resonance imaging demonstrated a heterogenous high signal area that indented the renal sinus fat and extended into the medullary area of the kidney. A biopsy of the lesion was arranged, and histopathology confirmed a juxtaglomerular cell tumour. No evidence of pre-eclampsia was seen. The patient proceeded for a right total nephrectomy at 16 weeks' gestation. Macroscopically the lesion was a well circumscribed, haemorrhagic, tan-coloured mass lesion measuring 3.2 × 2.5 × 2.6 cm. The tumour was microscopically characterised by diffuse proliferation of tumour cells with moderate amounts of eosinophilic cytoplasm and vesicular nuclei. The tumour cells were positive for CD34, SMA, and vimentin and negative for CD117. Electron microscopy of the tumour showed rhomboid shaped granules characteristic of renin in tumour cells. The remainder of the kidney was unremarkable. The postoperative course was complicated by hypotension, and anti-hypertensive medications were discontinued. Supine plasma renin level measurement 7 weeks postoperatively was normal at 10.3 ng/l (<16 ng/l), 15% of the original value. Two infants were born via elective Caesarean section at 33+4 weeks gestation. Reninoma is a very rare and potentially curable form of hypertension, particularly in women of childbearing age. Plasma renin concentration was three times greater than the expected value for this stage of pregnancy. Management in pregnancy is challenging and involvement of the multi-disciplinary team is vital.

DOI: 10.1530/endoabs.100.WD2.1

WD2.2

A patient with two forms of PA - pituitary adenoma and primary aldosteronism

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Background
Clinically relevant pituitary adenomas (Pit PA) affect approximately 1:1200 of the general population, and may manifest with hormone hypersecretion, hypopituitarism and compression of the visual pathways. Primary aldosteronism (Adr PA) is now recognised to account for 5–14% of all cases of hypertension and is associated with excess morbidity when compared with primary hypertension. Here, we report a patient who was noted to have a history suggestive of Adr PA whilst being investigated for Pit PA.
Case
A 45-year-old man attended his primary care physician with a 6-month history of reduced sexual function. Laboratory investigation demonstrated partial hypogonadotrophic hypogonadism [LH 2.6 U/l (RR 1.5-9.3); FSH 8.8 U/l (RR 1.4-18.1); total testosterone 6.7 nmol/l (RR 7.2-31.3)], with associated mild hyperprolactinaemia [prolactin 719 mU/l (RR 45-375)] and possible partial central hypothyroidism [Free T4 10.3 pmol/l (RR 10.5-21.0); TSH 0.7 mU/l (RR 0.35-5.5)]. Serum cortisol was normal with no evidence of Cushing's syndrome clinically or biochemically (UFC 42 nmol/24h; LNSC 0.5 and 0.9 nmol/l) Serum calcium was normal. Formal visual field testing showed a left temporal defect, and subsequent pituitary MRI revealed a 34 × 26 × 19 mm macroadenoma with suprasellar extension. Whilst being investigated for Pit PA, parallel investigations were initiated for suspected Adr PA based on the patient's history of hypertension (treated with amlodipine) and unprovoked hypokalaemia. Plasma renin concentration (PRC) was low (3 mU/l), which coupled with a plasma aldosterone concentration (PAC) of 790 pmol/l, yielded a markedly raised aldosterone:renin ratio (263.3). Adrenal MRI demonstrated a possible nodule in the body of the left adrenal gland, with thickening of the medial limb; the right adrenal appearances were unremarkable. Subsequent ACTH-stimulated adrenal vein sampling (AVS) indicated a bilateral origin of PA:

	IVC	Left adrenal vein	Right adrenal vein
Aldosterone	1,160	44,200	32,500
Cortisol	1,037	17,585	14,114
A:C ratio	1.12	2.51	2.30

The patient was changed to mineralocorticoid receptor antagonist (MRA) therapy with good control of blood pressure and correction of hypokalaemia. At trans-sphenoidal surgery, a macroadenoma was resected, with immunohistochemistry showing positivity for FSH. Transcription factor expression is negative.
Conclusions
Although, the co-occurrence of Pit PA and Adr PA in our patient may represent a simple coincidence, the possibility that they are linked [either through an underlying genetic predisposition (e.g. MEN1) or a novel pathophysiological pathway (as previously proposed for macroprolactinomas and Adr PA – Williams *et al*, JCEM, 2015)] remains.

DOI: 10.1530/endoabs.100.WD2.2

WD2.3

A case of synchronous phaeochromocytoma and renal cell carcinoma

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A 57 year old man with a history of hypertension and type 2 diabetes mellitus (HbA1c 80 mmol/mol) presented with right sided flank pain and weight loss. He reported a history of intermittent palpitations and headaches. CT with contrast demonstrated a right renal mass and right adrenal mass. MRI adrenal showed a 2.4 cm T2 hyperintense right adrenal lesion that demonstrated a stricture diffusion with no signal dropout on out of phase imaging and a 2 cm mass in the upper pole of the right kidney. He was referred to the endocrine clinic for review of the adrenal mass and diabetes management pre-operatively. Biochemical evaluation of the adrenal mass revealed elevated plasma metanephrines, normetanephrine 2640 pmol/l(0-1180), metanephrine 2190 pmol/l(0-510) and 3-metoxytyramine <100 pmol/l(0-180). He was commenced on doxazosin for blood pressure management and diabetes care was optimised in the peri-operative setting. He underwent a robotic right radical nephrectomy and adrenalectomy. Histology confirmed a clear cell renal cell carcinoma (RCC) limited to the kidney and an encapsulated tumour (30 mm) in the adrenal gland (PASS score 2). Post-operatively, his plasma metanephrine has normalised. His blood glucose levels have improved (HbA1 c 53 mmol/mol). There was no family history of RCC, phaeochromocytoma or paraganglioma. He subsequently underwent genetic testing which did not identify any genetic mutation. Our patient may yet have a genetic mutation that has yet to be found and further screening could be considered in the future.

DOI: 10.1530/endoabs.100.WD2.3

WD2.4

Advanced and aggressive metastatic adrenocortical carinoma in a 30-year old gentleman

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30 M referred to the Surgical Same Day Emergency Care (SDEC) clinic with 2-month history of abdominal pain to left loin and RUQ and worsening back pain for 1-week. Abdomen was soft with tenderness to the RIF, LIF and bilateral loin area. Bloods demonstrated a CRP of 210, sodium 145, potassium 3.2, creatinine 63, ALP 572, ALT 73, bilirubin 12 with normal WCC and neutrophils. A CT abdomen pelvis demonstrated a large left adrenal 10 cm × 11 cm × 13 cm solid mass with some central necrosis, which extended to the left renal vein, infrahepatic IVC and L2 lumbar vein, and metastases to the liver, spine, pelvis and sternum. A history of weight gain and perceived facial puffiness was elicited. Further examination demonstrated Cushingoid facies, purple abdominal striae and elevated blood pressure of around 180/100 mmHg. Initial biochemistry demonstrated a random cortisol of 1300 and low potassium. During work up including biochemistry, liver biopsy and MDT, pain was the primary issue for our patient. The palliative care team were involved for analgesia and lead up-titration of opioid, amitriptyline and radiotherapy for bony lesions. CT chest demonstrated a likely metastatic right lung nodule and thoracic spinal metastases. Biochemistry revealed: LH <0.3, FSH 0.5, Testosterone 5.8, TSH 0.69, Free T4 5.8, Cortisol 1388, LDH 968, ACTH <3.8. Plasma testing ruled out a phaeochromocytoma. Urine steroid profile showed increase in metabolites of 11-deoxycortisol, DHEA, cortisol, progesterone, 17-hydroxyprogesterone alongside pregnenetriol and tetrahydro-11-deoxycortisol. Metyrapone 250 mg TDS was commenced and subsequent testing demonstrated a drop in cortisol to 550 (1388) after three days. During admission, this patient became intermittently pyrexic, tachycardic and developed a new oxygen requirement and was diagnosed with a Klebsiella bacteraemia of unclear source. Liver biopsy demonstrated findings consistent with adrenocortical carcinoma, however it was noted that GATA3 was unusually positive and synaptophysin was very weak. Sadly, this died unexpectedly overnight with a cause of death attributed to 1a) Klebsiella Bacteraemia 1b) Metastatic Adrenocortical Carcinoma (ACC). Full work up was not possible (e.g. 24 hour urine free cortisol, dexamethasone suppression test or salivary cortisol), however results including urine steroid profile, supressed ACTH and response to Metyrapone established good proof of cortisol excess and evidence towards a diagnosis of ACC. This case illustrates highly aggressive ACC and highlights a presentation that includes florid Cushing's and non-specific symptoms secondary to direct organ invasion by tumour growth as well as more distant metastases.

DOI: 10.1530/endoabs.100.WD2.4

WD3.1

Primary aldosteronism in a young man with a family history of hypertension and stroke

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A 25 year old Afro-Caribbean man was referred for adrenal vein sampling for suspected Conn's syndrome and the finding of a right adrenal nodule. He initially presented to his local hospital with vomiting. He had hypokalaemia, which persisted even after the vomiting had resolved. He required oral potassium supplementation to maintain a normal serum potassium level. He gave a history of fatigue and occasional muscle cramps during the last 3 years. Intermittent spontaneous hypokalaemia was apparent on checking his historical blood tests during the same time. His GP had started him on amlodipine 10 mg once daily about 6 weeks earlier but his BP was above the recommended target of 140/90, despite compliance with the medication. He was otherwise fit and well. He is a non-smoker, rarely drinks alcohol, and does not use illicit drugs. His father died of a stroke and uncontrolled hypertension at the age of 45. His paternal grandfather also died of a stroke. His younger brother aged 18, was healthy with no known hypertension. On examination, he was normotensive on eplerenone 50 mg twice daily and amlodipine 10 mg once daily. His BMI was normal. He did not have any Cushingoid features. Biochemical testing, when he was potassium replete and not on eplerenone, showed a suppressed renin (2.0 mU/l), high aldosterone (827 pmol/l), ARR 413.9 (<91) and failure of aldosterone to suppress on saline infusion (819 from 1320 pmol/l). A biochemical diagnosis of primary hyperaldosteronism was therefore confirmed. The 1 mg overnight dexamethasone suppression test showed an appropriately suppressed cortisol of 33 nmol/l, thereby excluding Connshing syndrome. Cross-sectional imaging confirmed a right adrenal adenoma (a 15 mm nodule with unenhanced attenuation of 0 HU on CT and a homogeneous lipid-rich nodule on MRI) Metanephrines were not required since the unenhanced attenuation of the adrenal nodule was less than 10 HU. Adrenal vein sampling was not deemed necessary since he was younger than 35, had marked hyperaldosteronism, spontaneous hypokalaemia and a solitary adrenal adenoma. Genetic testing for CYP11B1/CYP11B2 chimeric gene and germline KCNJ5 mutations were negative. Following the reassuring genetic test results, he was referred directly for laparoscopic right adrenalectomy for the 15 mm aldosterone-producing right adrenal adenoma.

DOI: 10.1530/endoabs.100.WD3.1

WD3.2

Primary hyperaldosteronism in a patient with cushing's disease in remission

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A 47-year-old man attending Endocrine services for the management of Cushing's disease in remission, presented with resistant hypertension which warranted further investigation. He initially presented in 2013 with Cushing's disease and underwent successful transsphenoidal surgery. Postoperatively he was diagnosed with ACTH deficiency, partial growth hormone deficiency, and diabetes insipidus for which he was prescribed hydrocortisone 10 mg daily and desmotab 0.2 mg nocte. During his outpatient follow-up, he continued to be hypertensive despite remission of disease, and treatment was escalated over the subsequent six years until he eventually required five agents – ramipril 10 mg, amlodipine 10 mg, bisoprolol 10 mg, spironolactone 100 mg, doxazosin 8 mg. At this point, an ambulatory blood pressure monitor recorded daytime average blood pressure of 142/85 mmHg and nighttime average blood pressure of 150/88 mmHg. He had episodes of spontaneous hypokalaemia and symptoms suggestive of obstructive sleep apnoea. Initial investigations ruled out Cushing's disease recurrence, with cortisol 11 nmol/l post-1 mg overnight dexamethasone suppression test. Additional biochemical work-up revealed elevated aldosterone 877 pmol/l, and a fully suppressed renin <5 mIU/l, with normal potassium 3.9 mmol/l and normal plasma metanephrines, taken whilst off beta-blockers. Aldosterone-renin ratio was 175.4 suggestive of primary hyperaldosteronism. Difficult to control hypertension significantly compromised the interpretability of biochemical workup. Equally, a saline suppression test was not suitable. Cross-sectional imaging revealed a 1.2 cm left adrenal nodule with attenuation of 35 Hounsfield units and a general decrease in volume of the adrenal glands in keeping with his status of ACTH deficiency. Confirmatory testing was required and following multidisciplinary team discussion, he proceeded to adrenal vein sampling. On the first attempt at adrenal vein sampling, there was a failure to cannulate the right adrenal vein. Repeat testing was successful and lateralized to the left adrenal gland, with a lateralization index of 39.5 and a contralateral suppression index of 0.71. The patient is listed for robotic left adrenalectomy in early 2024. The key learning points from this case centre around the diagnostic workup of primary hyperaldosteronism including the interpretability of renin and aldosterone concentrations in antihypertensive agent use, and the interpretation of adrenal vein sampling results. It also highlights the importance of considering alternative endocrine diagnoses in patients attending the outpatient clinic.

DOI: 10.1530/endoabs.100.WD3.2

WD3.3

Bilateral phaeochromocytoma heralding a diagnosis of MEN 2A

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Pheochromocytoma is a rare catecholamine producing neuroendocrine tumor arising from the adrenal medulla. Approximately 40% of cases are hereditary and the remaining are sporadic. There are several familial syndromic disorders associated with phaeochromocytoma including: von Hippel-Lindau (VHL) syndrome, multiple endocrine neoplasia type 2 (MEN2) and, neurofibromatosis type 1 (NF1). Bilateral phaeochromocytoma should prompt suspicion of a hereditary familial syndrome such as MEN2 or VHL or SDHx or less commonly associated with inherited pathogenic variants in genes including; TMEM127, NF1, or MAX. We hereby present a case of bilateral phaeochromocytoma

heralding a new diagnosis of MEN2 A in a kindred. A 32-year female, who had a past medical history of goitre, Grave's thyrotoxicosis, supra ventricular tachycardia/atrial flutter, diabetes mellitus and hypertension was investigated for secondary causes of hypertension. She had a history of hypertension, palpitations, on and off headaches and anxiety. Her mother was also diagnosed with hypertension at the age of 29 years. Other than hypertension and a palpable goitre, there were no other remarkable clinical findings. Biochemical testing revealed elevated plasma metanephrines, normetanephrines and 3 methoxytyramine levels at 2039, 148087 and 1703 pmol/l respectively. Subsequent MRI imaging identified large bilateral indeterminate adrenal masses without evidence of signal drop out. A diagnosis of bilateral phaeochromocytoma was confirmed and the patient was planned for laparoscopic bilateral adrenalectomy. After adequate alpha blockade with doxazocin, carvedilol was added for blood pressure control. Tumor multi-focality prompted testing for suspected familial syndromes. The calcium levels were mildly raised (2.63 mmol/l) with unsuppressed PTH (4.13 pmol/l) and a fasting calcitonin level was 157.90 ng/l. The patient underwent an uncomplicated bilateral laparoscopic adrenalectomy. The histopathology samples showed bilateral phaeochromocytoma and an extra adrenal sympathetic para-ganglioma in infra renal aortic nodal area. Post operatively, due to elevated fasting calcitonin, she underwent a total thyroidectomy which confirmed bilateral, nodal metastatic medullary carcinoma of thyroid, c-cell hyperplasia, and diffuse parathyroid hyperplasia in a single gland. The genetic analysis was positive for a pathogenic RETc.1900T > G p.(Cys634Gly) variant. Her three children (13, 9 and 7 years) were also found to have inherited the RET variant and are awaiting prophylactic thyroidectomy and her father has also been diagnosed with the same variant and medullary thyroid carcinoma and is awaiting surgery. This case highlights the association of bilateral phaeochromocytoma with familial syndromes and importance of genetic analysis as phaeochromocytomas may be the presenting tumor phenotype in endocrine neoplasia syndromes such as MEN2A.

DOI: 10.1530/endoabs.100.WD3.3

WD3.4

Unravelling silent phaeochromocytoma in MEN-2A

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A 75-year-old patient was referred to the endocrinology department following the incidental discovery of a right adrenal mass during a CT scan of abdomen and pelvis conducted due to Doppler negative unilateral leg swelling which was present for 1 month. On clinical examination, the heart rate was 82 bpm, weight 78 kg, height 155 cm, BMI 32, blood pressure 185/90 mmHg, no organomegaly or lymphadenopathy and no clinical features of hormonal excess including catecholamine or corticosteroids were detected. The initial investigations including hormone assays were unremarkable ; K+ 4.9 mmol/l, adjusted Calcium 2.47 mmol/l, Plasma metanephrine 23 ng/l (<100), Plasma normetanephrine 84 ng/l (<170), 24 hour Urine metadrenaline 0.99 umol/d (0-1.2), Urine Normetadrenaline 2.67 umol/d (0-3.3), Urine methyoxytyramine 0.79 umol/d (0-2.5), Aldosterone Renin Ratio 25.3 (<80), Overnight dexamethasone suppression test- Cortisol 69 nmol/l (0-50), Androstenedione 0.5 nmol/l (2-5.4), DHEA 0.5 umol/l (0.9-2.1), 17-hydroxyprogesterone <1.0 nmol/l, Plasma chromogranin-A 32 pmol/l (0-60) and Chromogranin-B 78 pmol/l (0-150), CA 19-9 <2 ku/l (0-27), CA 125- 29 ku/l (0-35), CA 15-3 17.7 ku/l (0-26.2), CEA 2.7 mg/l (0-3.8) and Urine steroid profile normal. The CT abdomen and pelvis revealed a 6.6 × 6.4 cm heterogeneous right adrenal mass with a central cystic stellate component and abutting the IVC prompting concerns for adrenocortical carcinoma or metastasis. Completion CT chest showed no extra-adrenal malignancy. The case was discussed in the Adrenal MDT meeting, leading to a laparoscopic right adrenalectomy. Histologic examination of the right adrenal gland revealed a mass arising from adrenal medulla with central cystic degeneration. Cells were strongly positive for synaptophysin and chromogranin on immunohistochemistry. The overall features were consistent with Phaeochromocytoma with PASS score of 7. Due to the rarity of **Silent Phaeochromocytoma** and the substantial size of the mass at diagnosis, additional investigations including an MIBG scan and genetic testing were undertaken. The MIBG scan was unremarkable, however, next-generation sequencing (NGS) identified a pathogenic RET missense variant {2410G > A p.(Val804Met)}, confirming a genetic diagnosis of Multiple Endocrine neoplasia type-2 A (MEN-2A). Patient is now under routine endocrinology follow-ups and awaiting a DOTATATE PET-CT. In summary, silent phaeochromocytomas characterized by minimal or absent symptoms and subtle hormone elevation below traditional diagnostic thresholds, present a formidable diagnostic challenge. Individuals with familial phaeochromocytoma typically exhibit few clinical symptoms and seldom manifest the traditional triad of headache, palpitations, and sweating. This case emphasizes the importance of a nuanced diagnostic approach as undetected cases may lead to hypertensive crises and potentially fatal complications.

DOI: 10.1530/endoabs.100.WD3.4

WD4.1

Follow up for primary hyperaldosteronism – how long is long enough?

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Introduction
Primary hyperaldosteronism classically presents with hypertension and hypokalaemia, though many may be normokalaemic. It is most commonly caused by bilateral adrenal hyperplasia, while 30-40% have a unilateral adenoma or nodule. Aldosterone renin ratio (ARR) is performed, with confirmatory testing if required plus adrenal CT to identify an adrenal lesion. Adrenal venous sampling (AVS) distinguishes between unilateral and bilateral disease. Unilateral adrenalectomy is the preferred treatment, or alternatively medical management with mineralocorticoid receptor antagonists for bilateral disease or where surgery is not suitable, with the aim of preventing adverse cardiovascular outcomes of excess aldosterone. Hyperaldosteronism can rarely be seen in adrenocortical carcinoma (ACC).
Clinical case
A 37 year old gentleman was referred to cardiology in 2004 with hypertension and hypokalaemia (K 2.60 mmol/l). Investigations included ARR (aldosterone 331 ng/l, renin 3.2 mu/l, ratio 103.4 (<25)). CT abdomen was reported as showing normal adrenals. He was managed medically for primary hyperaldosteronism with spironolactone. Over the next 15 years he remained hypertensive, requiring Eplerenone 200 mg and five concurrent antihypertensives, with periodic advice sought from cardiology by primary care. During this time he suffered a stroke and developed chronic kidney disease. He presented to dermatology in 2022 with melanoma. Staging CT revealed a 45 mm indeterminate left adrenal lesion. He was referred to endocrinology and underwent functional testing plus PET scanning. Differentials included primary adrenal disease – functioning or non-functioning, low grade ACC or metastatic melanoma. Repeat ARR was markedly elevated (aldosterone 5500 pmol/l, renin 3.6 mu/l, ratio 1537.8), with mild hypercortisolaemia (144 nmol/l) after overnight dexamethasone suppression. Plasma metanephrines were normal. He underwent laparoscopic adrenalectomy in March 2023 with hydrocortisone cover and post-operative antihypertensive reduction. Despite this, renal function declined post-operatively. Histology revealed a 58 mm adrenal lesion with Modified Weiss score of 2 (>25% clear cells, low mitotic rate, high grade focal nuclear change) and favoured carcinoma over adenoma. Adjuvant mitotane was not indicated. Post-operative ARR normalised to 38.5.
Conclusions
This case demonstrates the classic presentation and biochemical diagnosis of primary hyperaldosteronism, but without obvious adrenal adenoma on imaging. This gentleman was lost to follow up and suffered adverse cardiovascular mortality with persistent hypertension despite multi-agent treatment. At the time of presentation to endocrinology there were several differentials, and while histology report favours ACC over adenoma, the low Weiss score could suggest an adenoma in keeping with primary hyperaldosteronism. AVS at the time of first diagnosis may have offered earlier detection of a unilateral aldosterone-producing adenoma with surgical treatment options.

DOI: 10.1530/endoabs.100.WD4.1

WD4.2

Hirsutism and incidental pheochromocytoma

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A 67-year-old lady was referred to Haematology for evaluation of Polycythemia (Haemoglobin 162 – 172 g/l, PCV 50 – 53%) A simultaneous referral was sent to Endocrinology for hirsutism, noting that her Testosterone level was 24 nmol/l, SHBG 33 nmol/l. Her past medical history was significant for hypothyroidism, hypertension and migraines for which she was on Levothyroxine, amlodipine and candesartan. She was a non-smoker and teetotaller. Her haematology workup was negative including a JAK2 mutation. It was thus understood that her polycythemia was secondary to hyperandrogenism. Hirsutism: Over the past 2 years, she noted

increased facial hair, and increased hair on her shoulders, breasts, and abdomen (Ferriman-Gallwey score 9). Her BMI was 36 with central obesity but no features of Cushing's syndrome; there was no cliteromegaly and she did not report any voice change. She had been menopausal since 20 years. Her hormonal profile showed LH 9.5 miu/l, FSH 31.6 miu/l, oestradiol 166 pmol/l. Prolactin, IGF1 and cortisol level were normal. US pelvis was unable to identify either ovary. A preliminary diagnosis of ovarian hyperthecosis was entertained, though given the high level of testosterone further imaging was requested to exclude ovarian or adrenal tumour. CT abdomen identified 1.6 cm right adrenal nodule (washout curves - indeterminate results) No nodule was seen in left adrenal gland. Both ovaries were visualised and were bulky for a post-menopausal woman, measuring 21 mm (right) and 26 mm (left). She was trialled on prostap 3.75 mg IM monthly. This decreased her Testosterone to 3.2 nmol/l, eventually leading to normal testosterone of 1.2 nmol/l. Alongside, a workup for adrenal incidentaloma showed suppressed cortisol on ONDST, normal aldosterone-renin ratio but marginally elevated plasma normetadrenaline 1357 pmol/l (normal 120 – 1180) confirmed on 2 samples. MIBG showed increased uptake in right adrenal gland in keeping with Pheochromocytoma. She underwent right adrenalectomy and the histology showed pheochromocytoma with low mitotic activity. Post-op, her plasma metadrenaline normalised completely and she only required amlodipine to manage her BP. Genetic testing for pheochromocytoma was negative. She stopped taking prostap after a couple of years as she felt it was related to weight gain. Though her Testosterone started to rise again, it was not to the same extent as before (Testosterone 5.2 – 8 nmol/l) with no recurrence of hirsutism. She was offered Prostap once polycythemia recurred. Long term management for ovarian hyperthecosis would be oophorectomy which she may consider.

DOI: 10.1530/endoabs.100.WD4.2

WD4.3

A case of phaeochromocytoma- optimisation of alpha and beta blockage

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A 42-year-old man from Colchester was referred to our endocrinology service in January 2023. He was having abdominal pain for a year, unresponsive to a trial of PPI. He was also found to have hypertension for one year which was controlled by Amlodipine. An ultrasound organised by his GP revealed gallstones and a substantial right supra-adrenal mass, leading to a referral to the local urology team. Subsequently, CT scan was performed which characterised as a likely phaeochromocytoma, measuring 9 × 8 cm. He has a history of well-controlled asthma and idiopathic Bell's palsy. He has a family history of hypertension. He does not smoke but drinks occasionally. He experienced sporadic episodes of elevated blood pressure, palpitations, tremors, and anxiety. He was seen by local endocrinologist and checked urine normetadrenaline which was >49500 pmol/l, consistent with phaeochromocytoma. He was started on Doxazosin. Clinical examination was unremarkable and no evidence of other endocrine dysfunction. His plasma metanephrine results revealed metanephrine 490 pmol/l(0-510 pmol/l), normetanephrine 21220 pmol/l(0-1180 pmol/l), and 3-Methoxytyramine less than 75 pmol/l(0-180 pmol/l). He was initiated on phenoxybenzamine at St Bartholomew's Hospital and the dose was titrated as an outpatient. He underwent a preoperative NM DMSA scan revealing normal divided renal function. While awaiting elective surgery, he faced recurrent episodes of high blood pressure, palpitations, and anxiety, necessitating local A&E visits. Phenoxybenzamine dose was up titrated gradually, along with cautious low-dose beta-blockade to control symptoms and blood pressure. He underwent an uneventful open right adrenalectomy in April 2023. Plasma metanephrines was normalised postoperatively and follow up MRI showed no residual or recurrent disease. Histological examination revealed a favourable tumour profile with Ki-67 less than 1%, and germ line testing for 13 key predisposition genes indicated no mutations.

Discussion

We present this case to highlight a careful titration of alpha and beta blockade in managing phaeochromocytoma and the significance of preoperative assessments in optimising surgical outcomes.

DOI: 10.1530/endoabs.100.WD4.3

WD4.4

Pheochromocytoma presenting as acute coronary syndrome

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A 63 year old male presented with sudden onset severe chest pain which clinically seemed cardiac in nature. A diagnosis of Non-ST Elevation MI was made and was managed conservatively. Later, after 6 months he again presented with chest pain. On this occasion, CT aorta and CT Thorax, Abdomen and Pelvis was done to rule out aortic aneurysmal rupture, and to look for post-infarct changes in the myocardium, cardiac MRI was done. Cardiac MRI and CTTAP both showed an incidental finding of left adrenal lesion measuring 4.8 cm highly suspicious of adrenal pheochromocytoma. On further exploration, he expressed having headache, sweating, palpitations and persistently raised blood pressure along with chest pain for past 6 months. Radiologists' opinion was sought for further characterization of the mass. The lesion was suggested to have high vascularity due to rich capillary network, arterial phase enhancement and significant washout on PV phase. Investigations showed high levels of urinary and plasma metanephrines. Low-dose dexamethasone suppression test and overnight dexamethasone suppression test showed unsuppressed cortisol levels supporting possibility of co-secreting cortisol. Renin activity and aldosterone levels were normal. He was given adequate alpha blockade with increasing dose of doxazosin and was planned to have elective laparoscopic adrenalectomy. As an intraoperative complication, he developed grade 2 splenic rupture followed by a litre of blood loss due to which spleen was removed. Having sensitivity of 97% and specificity of 93%, the compelling evidence suggests using plasma free metanephrines as primary test of excessive catecholamines for diagnosis of Pheochromocytoma and Paragangliomas (PPGL). Computed Tomography is the first line investigation to confirm the location. PPGL should be ruled out in patients presenting with chest pain and persistently high blood pressure. Our patient did not have a family history of PPGL and the syndromes associated with it. However, one third of patients with PPGL have germline mutations and PPGL may often be a part of hereditary syndromes, so genetic testing is advisable for all the patients diagnosed with PPGL. The incidence of persistently low blood pressure after PPGL removal varies between 20-77% which is attributed to downregulation of alpha and beta receptors. Our patient developed persistent hypotension after the tumor removal which was managed with vasopressors in Intensive care.

DOI: 10.1530/endoabs.100.WD4.4

WD5.1

Delayed presentation of adrenal insufficiency during covid pandemic

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29 year old female presented being generally° unwell with vomiting and black outs in Feb 2021. She was 3 weeks postpartum. It was normal vaginal delivery but the baby was small for date but otherwise healthy. She had past medical history of hypothyroidism on levothyroxine. On examination, she looked pale, unwell and tanned. Observations showed BP80/60 PR88/min, RR18/min temp 36.6° c. ABG showed PH 7.34, HCO3 22.3, Na126, k 5.6 cl 93 urea22.9 creat122 glu4.5 lac0.6. other investigations were •Hb 99, WBC 8.2, Neutrophils 5, Platelets 109, Na 132, K 6.1, Urea18.7, Creat 90, GFR74,•Alb 34, Bili 6, ALP 89, ALT 26, Calcium 2.62•CRP 4•Trop: 231 (0-46) •D-dimer: 715 (0-500), Repeat trop: 329, Cortisol: <30 (09:00 am), BNP: 11486 (0 – 299)ECHO - LV upper limit of normal size with reduced systolic function 38%, Basal LV walls contract well, Dyskinetic septum towards apex. Hypokinetic all other LV walls. Normal right heart size and function, no valvular pathology. ECG showed wide spread Twave inversion. Pituitary profile showed prolactin 1194, IGF1 17.5, Oestradiol<70 FSH 8.5 LH 2 TSH0.17 T4 23.8, Synacthen test showed basal cortisol <30, which did not rise in spite of stimulation. Later on adrenal antibodies were positive and ACTH levels were >2000. When did she became adrenal insufficient? Retrospectively she felt well in December 2019 when she had holiday in Turkey. She consulted GP for lethargy, weight loss and head ache a month later and found to have hypothyroidism with raised TPO antibodies. In May 2020, she had hospital admission for head ache, vomiting, dizziness, abdominal pain with recent increase in levothyroxine to 75 mg. The blood tests done during this admission showed sodium 132, potassium 4.5 and the cortisol level was requested. she felt better after iv rehydration and the low sodium was assumed to be due to dehydration due to vomiting. The cortisol level was <30 but was overlooked. In June 2020, she became pregnant and her symptoms were assumed to be due to pregnancy. it was her 2 nd pregnancy and recalled the pregnancy symptoms were much worse than her first pregnancy. She felt much better when she had steroids during pregnancy. She deteriorated further after pregnancy and presented 3 weeks after delivery.

DOI: 10.1530/endoabs.100.WD5.1

WD5.2

A case of primary aldosteronism with hypertrophic cardiomyopathy and a horseshoe kidney

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A 56-year-old man of Ghanian descent was referred to the endocrine clinic with a 16-year history of drug resistant hypertension. His past medical history was of hypertrophic cardiomyopathy, chronic kidney disease, and horseshoe kidney. He is one of seven hypertensive siblings, two of whom died of complications of hypertension. An incidental finding of bilateral adrenal nodules was noted on abdominal computed tomography. Plasma aldosterone concentration (PAC) was 1020 pmol/l, plasma renin activity (PRA) 1.3 nmol/l/hr, and aldosterone/renin ratio was 785, with creatinine 143 μmol/l and normokalaemia. At his first endocrine clinic appointment, blood pressure (BP) was 170/90 mmHg on spironolactone 100 mg, lisinopril 20 mg, indapamide 1.5 mg, moxonidine 200 mg, doxazosin 16 mg twice daily, and verapamil 240 mg twice daily. A diagnosis of primary aldosteronism (PA) was confirmed by the captopril challenge test. At baseline, PRA was 1.0 nmol/l/hr, PAC 544 pmol/l, and creatinine 186 μmol/l. At 120 minutes from captopril administration, PRA was 0.5 nmol/l/hr and PAC was 528 pmol/l. He was considered for inclusion in PA research studies. Adrenal vein sampling (AVS) was then performed with cosyntropin stimulation.

AVS results

Sample site	Aldosterone (pmol/l)	Cortisol (nmol/l)
Right adrenal vein (RA)	44500	31877
Left adrenal vein (LA)	23100	20486
Low internal vena cava (IVC)	2440	1887
Iliac vein	974	916

Selectivity index (ratio of cortisol in the adrenal vein to low IVC) was 16.9 on the right and 10.9 on the left, confirming successful cannulation of both adrenal veins. Aldosterone to cortisol ratio was 1.39 on the right and 1.13 on the left, with a lateralization index (LI) of 1.23. This demonstrated bilateral aldosterone secretion, precluding surgical intervention or enrolment onto the MATCH (Wu *et al*., 2023) or FABULAS (Argentesi *et al*., 2023) studies. He was managed medically with spironolactone 25 mg, amlodipine 10 mg, doxazosin 8 mg twice daily, and sotalol 160 mg twice daily, achieving a BP control of 132/84 mmHg without postural hypotension. He remains on review in the endocrine clinic. This case of a 16-year-long delay in diagnosis and, consequently, appropriate medical management, illustrates the need for improved awareness of PA amongst clinicians, simplification of the diagnostic pathway, and effective medical strategies for managing PA.

DOI: 10.1530/endoabs.100.WD5.2

WD5.3

A case of pheochromocytoma crisis presented as acute multi-organ failure and cardiac arrest

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Background
Most phaeochromocytomas are unilateral and are not associated with a neuroendocrine syndrome. Although these tumours are often histologically benign, they tend to have potentially lethal presentations.
Case
A 51-year-old female presented in 2016 with headache, vomiting, palpitations, and a cardiac-sounding chest pain for 16 hours. Her ECG showed a junctional rhythm with generalised ST-segment depression. Acute coronary syndrome treatment was commenced. Her symptoms had been intermittent and progressive over 14 months prior to this presentation. On arrival, her blood pressure (BP) was 137/70 mmhg and her heart rate (HR) was 92/min. Whilst in ED; she suddenly deteriorated with worsening breathlessness and escalating chest pain which radiated to her back with a sudden rise of her BP to 250/140 mmhg and HR to 160/min. O2 Saturations were 78% on 15 L oxygen via facemask. She developed ventricular fibrillation and required immediate cardiopulmonary resuscitation. The patient was intubated and transferred to intensive care unit. Glyceryl trinitrate infusion was administered to control her BP. A CT Aortogram showed a 7 cm right adrenal mass, compressing the inferior vena cava. A bedside echocardiogram showed poor contractibility of the left ventricle. The patient developed acute kidney injury and her liver functions were deranged. N-Acetyl Cysteine infusion was commenced. Plasma normetanephrines were 10672 pmol/l and metanephrines were 6885 pmol/l. MIBG scan confirmed right pheochromocytoma diagnosis. She was on intravenous anti-hypertensive treatment (Phentolamine and esmolol) which were later switched to Doxazosin and Bisoprolol. Once stable, the patient underwent laparoscopic resection of her right adrenal pheochromocytoma with uneventful recovery. Genetic testing for pheochromocytomas/paragangliomas (PPGL) was negative. Histopathology confirmed a pheochromocytoma diagnosis with no vascular or capsular invasion or extension into the adjacent fat. The PASS score was 7. And the Ki67 index was approximately 1%. Since the curative surgery, the patient's kidney, liver and heart failures were reversed back to normal. She remains under regular follow up and all of her subsequent post-operative metanephrines and nor-metanephrines are undetectable and is not requiring any anti-hypertensive treatment now.
Discussion
Phaeochromocytoma is classically associated with periodic hypertension and intermittent and variable symptoms like headache, sweating, and palpitations which are difficult to diagnose particularly in females at this age group. These symptoms are attributed to the excessive release of catecholamines from the tumour's chromaffin tissue. Management should focus on initial stabilisation of the disturbed haemodynamic status, followed by adequate pre-surgical α-blockade and β-blockade, if indicated and deemed necessary. Urgent surgical intervention tends to be associated with high surgical morbidity and mortality.
Conclusion
Despite most phaeochromocytoma tumours tend to be histologically benign, they may lead to serious life-threatening complications. However, the disease is curable if detected early and the tumour is resected with appropriate presurgical medical therapy. Finally, pheochromocytoma confirmation warrants further investigations to exclude a multiple endocrine disorder (e.g. MEN-2a)

DOI: 10.1530/endoabs.100.WD5.3

WD5.4

A case of VHL presenting with phaeochromocytoma

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Introduction
Von Hippel-Lindau syndrome is an autosomal dominant condition due to the germline mutation of the VHL gene. Approximately 80% of VHL cases are inherited and 20% occurred because of de novo event. Phaeochromocytomas occur in 10 – 20% of VHL families. Bilateral phaeochromocytomas are more common than extra-adrenal paraganglioma and the majority secrete normetanephrine.
Case
A 25-year-old lady of Asian origin was admitted to the hospital due to the evidence of hypertensive retinopathy and systolic blood pressure of more than 200 mmHg following attendance to the eye clinic with floaters and headache. She had five months history of headache, fatigue and palpitations prior to admission. She has medical history of iron deficiency anaemia due to menorrhagia and family history of hypertension in mother, who is in her 40s. She was screened for endocrine causes of hypertension. Her plasma normetanephrine level was elevated at >25000 pmol/l (reference range 0-730). CT (adrenals) demonstrated left adrenal lesion of 2 cm with indeterminate features and 5.5 cm right adrenal solid and cystic lesion. She was referred to the Adrenal MDT. MIBG scan showed bilateral phaeochromocytomas and an indeterminate tracer-avid retroperitoneal nodule inferior to the right adrenal mass. Her fasting gut hormone profile and bone profile were normal. Further enquiry revealed that her paternal grandmother had VHL mutation, but her father does not carry the gene. Her maternal uncle and maternal grandfather passed away from kidney failure. Her parents are second cousins. Genetic profile for familial phaeochromocytoma and paraganglioma panel R223 was carried out. Her genetic test revealed that she has VHL gene (c.250G>A heterozygote). Her mother was later tested and found to carry the same gene. She was managed pre-operatively with doxazocin and bisoprolol. She had MRI head and spine, which did not identify any paraganglioma. Ophthalmology assessment did not report any retinal angiomas. She had bilateral open adrenalectomy. Histopathology demonstrated left sided phaeochromocytoma of 2 cm (PASS score 1/20), and right sided phaeochromocytoma of 6 cm (PASS score 6/20), ectopic adrenal tissue identified to the right of inferior vena cava with Ki67 of 3.5%. Post operatively, she was managed with hydrocortisone and fludrocortisone replacement. Her plasma normetanephrine levels have normalised.
Conclusion
Genetic screening and counselling is important in VHL syndrome. The management of phaeochromocytoma requires a multidisciplinary approach. Patients should remain on close surveillance for recurrence of phaeochromocytoma and other complications of VHL.

DOI: 10.1530/endoabs.100.WD5.4

Workshop E: Disorders of the gonads

WE1.1

The investigation and management of post-pubertal gynaecomastia

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Background
Gynaecomastia results from the raised oestrogen-to-testosterone ratio caused by relative oestrogen excess or testosterone deficiency. Alterations to androgen sensitivity causes a relative testosterone deficiency that can present in a spectrum, from significant, to subtle alterations of secondary sexual characteristics. Mild androgen insensitivity syndrome (MAIS) should be considered in the differential for those presenting with gynaecomastia with elevated gonadotrophins and testosterone.
Clinical case
A 23-year-old PE teacher was referred for further assessment of right-sided gynaecomastia. Breast ultrasound via two-week wait was non-concerning. Initial biochemistry detected elevated gonadotrophins, testosterone, prolactin and SHBG. The patient reported six months of an enlarging retroareolar lump with no associated galactorrhoea or sexual dysfunction. A scrotal lump was also noticed, with no concerning features on ultrasound. HCG and AFP normal. He attended the gym up to five times weekly and denied the use of anabolic steroids or sports supplements. He used cannabis recreationally and drunk alcohol socially. There was no personal or family history of note. Clinical examination demonstrated normal BMI, musculature, and secondary sexual characteristics. Right sided 2 × 3 cm retroareolar gynaecomastia, with no cervical or supraclavicular lymphadenopathy was detected. Visual fields were intact. Biochemical investigations following six weeks abstinence from cannabis revealed an elevated 9 am testosterone 41.5 (0–29 nmol/l), LH 9.5 (1.7–8.6 u/l) , FSH 3.6 (1.5–12.4 u/l) and rested prolactin 777(0–323 mU/l). Normal SHBG, oestradiol. He was euthyroid, eucortisolaemic, normal IGF-1. MRI pituitary was normal. DXA scan reported normal bone mineral density, and semen analysis, normo-ozospermia. His Karyotype was 46 XY. He awaits the results of genetic screening to confirm a diagnosis of MAIS. Given only mild gynaecomastia, he remains on a watchful wait pathway.
Discussion
The assessment of gynaecomastia is aimed at the detection and management of underlying causes. Elevated gonadotrophins and testosterone in our patient prompted ruling out a functioning gonadotroph adenoma. With no features of hypogonadism other than mild gynaecomastia, Klinefelter's and chromosomal disorders were excluded with karyotype analyses. Clinical suspicion then pointed toward a syndrome associated with resistance to testosterone signalling. Androgen insensitivity syndrome is a rare x-linked recessive condition secondary to over 1000 described mutations in the androgen receptor gene. A range of phenotypes result, and MAIS, due to subtle clinical features may go undetected; reinforcing the importance of defined pathways for investigating gynaecomastia. Management of gynaecomastia for most, including in those with MAIS follows watchful waiting; testosterone replacement recommended only in those with testosterone deficiency, and the use of aromatase inhibitors not routinely advised.

DOI: 10.1530/endoabs.100.WE1.1

WE1.2

Hypogonadotropic hypogonadism in young obese male

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This is a case of 23 year-old male who presented with 2 months history of significant lethargy, erectile dysfunction and lack of libido. He has obesity with BMI of 43, and fatty liver disease. His sense of smell is intact. His random testosterone level was low at 5.8 nmol/l, and repeat 9 am fasting testosterone was 8.4 nmol/l (8.3–13.2), with normal gonadotrophins. SHBG was 15.2 nmol/l (14-71), which is at the lower end of normal. The rest of pituitary profile were unremarkable. Low testosterone was likely secondary to obesity, however in view of patient's age and significant symptoms, how would we approach this case?
Points for discussion:
1. Is pituitary imaging required? 2. Should testosterone therapy be considered for his symptoms? 3. Fertility considerations with testosterone therapy 4. Weight loss approach, should we consider bariatric surgery?

DOI: 10.1530/endoabs.100.WE1.2

WE1.3

A case of CHD7 mutations associated kallman's syndrome

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Kallman's syndrome is a abroad term which refers to association of olfactory alterations and idiopathic hypogonadotropic hypogonadism and it is responsible for approximately 50% of all cases of idiopathic hypogonadotropic hypogonadism. It is classically associated with KAL1 gene mutation. However, it is not caused by this single gene alone, but multiple genes have been found associated. We present a 31-year-old male Nurse with CHD7 associated Kallman's syndrome. He was diagnosed with Kallman's syndrome since age 14 when he presented with delayed puberty and anosmia and has been on hormone replacement therapy. No associated visual or hearing abnormalities and no learning disability. Apart from pituitary incidentaloma about 10 years before his recent relocation to the UK, he has no other past medical history. He went through puberty as expected with Testosterone and the dose was increased slowly until the adult dose was maintained on Testosterone undecanoate 1 g every ten weeks. He was not in a relationship but plan fertility in the future. He is a current smoker, and drinks moderate alcoholic beverages. Examination showed height of 160 cm (similar to parental height), weight 85.5 kg, non-eunuchoidal, BP 130/86 mmHg, small male external genitalia, VF normal to confrontation, right testes was absent with small left testicle. Biochemistry included undetectable LH and FSH with Testosterone 9.6 (few weeks prior next dose of Nebido), haematocrit of 50.4, PSA of 0.35. Other pituitary hormone results are normal. Normal Pituitary MRI with no obvious pituitary adenoma, pelvic MRI showed short right inguinal canal containing small volume soft tissues inferiorly and atrophied left testis in the left hemi-scrotum which necessitated urologist referral. Genetic result positive for CHD-7 with normal Echocardiography. The presence of anosmia in patient presenting with idiopathic hypogonadotropic hypogonadism often gives a way the diagnosis of Kallmann syndrome. However, this is not a single genetic entity but associated with more than 20 genetic mutations, one of which is the CHD7 as our patient presented. It is commonly known to be associated with CHARGE syndrome and accounts for 5-10% of all Kallman's syndrome. It could be associated with or without other phenotypical features of CHARGE syndrome but with milder severity due to missense variants rather than nonsense variants with less severe effect on protein function than those that cause CHARGE syndrome. Although, the phenotype cannot be predicted from genotype, but in our patients, the genotyping allowed comprehensive care and adequate planning on future expectations.

DOI: 10.1530/endoabs.100.WE1.3

WE2.1

Clinical dilemmas: residual high hCG and rising LH & FSH on testosterone therapy post bilateral orchidectomy for testicular tumor

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A 33 year old male is being follow-up for testosterone replacement (rx) after undergoing bilateral orchidectomy. He was diagnosed with a left testicular germ cell tumor at 20-years of age needing left orchidectomy, followed by a right testicular orchidectomy 2 years later in view of a lump in his right testicle. He did not receive any chemo/radiotherapy. Pre-operative LH, FSH and testosterone levels were normal; 2.4 U/l (0.8–7.6), 3.2 U/l (0.7–11.1) and 16 nmol/l (10.5–32) respectively. HCG at diagnosis was 2.9 mIU/ml (0-2.7). He underwent normal puberty. Post bilateral orchidectomy, testosterone undecanoate 1 g IM every 12 weeks was started. Pre-treatment LH was 42.7 U/l, FSH 81.4 U/l, testosterone 2.17 nmol/l and normal hCG(1.2 mIU/ml). Serial hormone levels are shown in **Table 1**. The main challenging dilemmas were a detectable hCG levels, 4 years after surgery and failure of suppression of LH and FSH despite normal/high levels of testosterone (**table 1**). A CT-Trunk excluded the possibility of any possible residual metastatic testicular tumor, or other possible hCG-producing tumor. MRI of the pituitary was normal. This case highlights two important aspects: (i) In men with bilateral orchidectomy, the LH/FSH levels may not be suppressed when exogenous testosterone is administered after bilateral orchidectomy, despite normal/high levels of testosterone. This perhaps may be explained by the absence of the negative feedback of inhibin on LH/FSH, since both testes are removed. Similarly this is seen in post-menopausal women failing to suppress LH/FSH despite HRT, however this can be explained by the low doses of sex hormone requirements needed, which are not enough to suppress LH/FSH. (ii) the pituitary produces a sufficient amount of hCG which can be detected in serum, especially when gonadotrophins levels are high - as seen in our case where hCG was detectable when LH was at its highest (**table 1**). However it is important to

exclude other possible sources of hCG production, especially in patients with past history of malignancy to exclude recurrency or residual tumor.

	Pre-op	Pre-Rx	6 months on Rx	1 year on Rx	4 years on Rx	4.5 years on Rx	7 years on Rx
LH	2.4	42.7	31.0	47.7	48.7	53.6	36.4
FSH	3.2	81.7	65.7	104.4	126.0	102.0	54.7
Testos-terone	16	2.17	7.00	36.5	46.8	38	17.40
hCG	2.9	1.2	<1.0	1	2.8	2.9	1
Estradiol	187			80.4			

DOI: 10.1530/endoabs.100.WE2.1

WE2.2

A case of non-classical congenital adrenal hyperplasia as a rare cause of male subfertility

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48-year-old taxi driver presented with a 2-year history of subfertility and confirmed azoospermia. He had normal libido and normal sexual function. His height was 156 cm and he had a normal blood pressure. His medical history included pre-diabetes. He took no regular medications. He had never smoked and he did not drink alcohol. He denied use of exogenous anabolic steroids. His blood tests showed a normal testosterone level of 17.6 nmol/l (RR10.0-3.0 nmol/l) with low gonadatrophins, LH <0.1 (RRL2.0-12.0 u/l) and FSH 0.2 u/l (RR 1.7-8.0 u/l). There was also polycythaemia with a haemoglobin level of 171g/l(RR130-168 g/l) and haematocrit of 0.52l/l (0.39-0.50l/l). An extended androgen profile showed a raised androstenedione level of 73.6 nmol/l(RR < 9.0 nmol/l), raised dehydroepiandrosterone 22.3 umol/l (RR0.8-6.9 umol/l) and significantly elevated 17-hydroxyprogesterone level of 886.6 nmol/l (RR < 9.6 nmol/l) raising the suspicion of congenital adrenal hyperplasia (CAH). Genetic testing confirmed a diagnosis of CYP21A2-related CAH (non-classical CAH). An ultrasound scan of the testes was carried out to investigate for testicular adrenal rest tumours, which were not seen but the scan did confirm small atrophied testes (testicular volume 2cc). The patient expressed that achieving fertility was his main priority. His partner, aged 41 years, underwent fertility investigations and no cause of subfertility was identified. As such, the patient was commenced on human chorionic gonadatrophin injections with the aim of sperm induction as well as prednisolone 3 mg once daily for CAH. Unfortunately, the patient reported feeling unwell with the prednisolone and attributed it to this medication so the dose was reduced to 1 mg. He also developed type 2 diabetes and commenced metformin. This case highlights CAH as rare cause of subfertility and individualised treatment according to the patient's fertility aims. In this case, the serum testosterone levels were within normal range, but reflected androgen production rather than testicular production. Gonadotrophic injections aimed to stimulate testicular androgen production and subsequent spermatogenesis, while exogenous corticosteroids aim to suppress the adrenal production of androgens. The case also highlights the therapeutic challenges of using corticosteroids given potential adverse effects, such as the development of Type 2 diabetes.

DOI: 10.1530/endoabs.100.WE2.2

WE2.3

Follicular harmony: triumph over hirsutism with the symphonic intervention of gnrh antagonists

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Gonadotropin-releasing hormone (GnRH) antagonists, primarily used in prostate cancer treatment, have found application in androgen-secreting ovarian tumors. Among these, degarelix, a pure GnRH antagonist was found to rapidly suppress testosterone levels within 24 h. Testosterone fell from 14 nM to 1.5 nM within 24 h and to less than 1 nM within 48 h. A 77-year-old woman presented with hirsutism and voice deepening over the past few months. Elevated serum testosterone levels with non suppressed LH and FSH along with polycythaemia suggested either an ovarian tumour or ovarian hyperthecosis. Pelvic MRI showed a solid enhancing lesion arises from the left adnexa. The gynecology-oncology (MDT) recommendation was laparoscopic bilateral salpingo-oophorectomy (BSO) along with omental and peritoneal biopsies. The patient, expressed reluctance to proceed with surgery. A repeat scan indicated stability in the lesion size with no suspicious features. We therefore initiated a trial of a GNRH antagonist, degarelix 80 mg to determine whether the testosterone was suppressible. The table shows a rapid fall in gonadotropins as well as substantial reduction in testosterone levels.

Time (hours)	LH	FSH	Testosterone Extracted	Testo: SHBG ratio	SHBG
Baseline	24.0	45.6	14	43	33
2	15.7	41.1*	-	-	-
4	10.2	34.8*	7.5	27.8	27
6	8.7	36.3*	4.5	16.1	28
8	5.6	31.1*	3.2	13.9	23
24	5.4 to 2.8	23.5* to 29.4	1.5	0.8	-
48 (bd)	1.8 to 1.2	15.3* to 21.5	0.8	0.8 and 1.0	-
72 (bd)	1.0 to 1.0	*15.0 14.4	-	-	40

The patient reported significant improvement in hirsutism, noting thicker hair and decreased frequency of headaches. Fatigue has reduced, and overall well-being has improved. The patient tolerated injections well and expressed eagerness to continue. Testosterone levels have consistently remained below 1 nM since initiating the injections. She has been on this treatment for 4 months, with no adverse features, and further scans have shown no growth. The risk of malignancy is not known in these patients, but the response to a fall in gonadotrophins suggests that the production of testosterone is not autonomous. We recommend that patients in this situation have a "degarelix test" and if the testosterone falls within 24 hours, that the patient can continue the drug. Longer term studies of such patients are needed to confirm whether there is a risk of malignancy in these patients, or whether the fact that the lesion is not autonomous excludes malignancy.

DOI: 10.1530/endoabs.100.WE2.3

WE3.1

Concealed diagnosis behind a young patient with gynaecomastia

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Introduction

Gynecomastia is a condition characterised by the benign proliferation of breast tissue growth in males. Among variety of causes, 3% of cases are due to testicular tumours. [1]. We present a 35-year-old male, who had elevated estradiol levels and gynecomastia, who was found to have a Leydig cell tumour.

Case Presentation

A 35-year-old male was referred to our clinic with 3 month history of bilateral breast growth. He had no significant medical history, non-smoker, and consumed 4 to 5 cans of beer per week. He did not take any regular medications. He reported that he had been going to the gym and taking protein supplements for muscle building about 6 to 8 weeks before the onset of symptoms. He denied using testosterone, androgens, or anabolic steroids. On examination, he had a BMI of 22.5 kg/m^2 and a masculine build with normal secondary sex characteristics. He had symmetrical bilateral gynecomastia, characterized by enlarged and tender glandular tissue. On two occasions, 4 months apart, he had elevated estradiol levels. The testicular examination was normal, with no palpable nodularity or inguinal lymphadenopathy.

Blood Test Results

Test	Result	Normal Range
Oestradiol	433 pmol/l	40-160 pmol/l
Testosterone	24 nmol/l	8.3-30.2 nmol/l
Free Androgen Index	28.7%	20.4-81.2%
SHBG	83.7 nmol/l	13.5 – 71.4 nmol/l
FSH	1.3 iu/l	1-12 iu/l
LH	3.0 iu/l	0.6-12 iu/l
Prolactin	241 miu/l	73-407 miu/l
TSH	Normal	N/A
AFP, hCG, LDH	Negative	N/A

Testicular ultrasound was requested, demonstrating a 14 mm upper pole mass of the right testis with heightened vascularity on colour Doppler. The patient subsequently underwent a right orchidectomy, and the histopathology report confirmed a Leydig Cell Tumor. CT TAP showed no evidence of metastatic disease.

Discussion and Conclusion

Leydig Cell Tumors are usually unilateral neoplasm that arise from the gonadal stroma. The majority of Leydig Cell Tumours secrete the hormones testosterone and estrogen. [2] They are rare tumours which mainly affect men in the age range of 20-60 years old and normally present with negative tumour markers. [3]. Orchiectomy is curative in approximately 90% of cases. [4] In conclusion, it is critical for endocrinologists to consider the possibility of Leydig Cell tumors,

especially in young men who present with unexplained raised estradiol levels and gynecomastia. The key to management is to maintain a low threshold for performing testicular ultrasound, even in cases with normal physical examination findings and negative tumor markers. Early diagnosis and prompt treatment are essential for favorable outcomes.

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DOI: 10.1530/endoabs.100.WE3.1

WE3.2

Unexpected gonadal failure in a well male patient: case report

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Diagnoses
Primary hypogonadism, Gynaecomastia
Case
A 36 year old male presented with bilateral gynaecomastia via his GP. He otherwise felt well in himself and was not significantly affected by this condition. He had initial workup investigations then was lost to follow up and results until 2 years later in my clinic. On review he reported a normal for him libido, normal erections, normal ejaculation. He reported no issues with energy levels, he works in hospitality which involves some long hours but he is generally able to function as usual. He has not had any fractures or features of osteoporosis. He has not noticed any hair pattern changes unusual for him. He was noted to have minimal body hair but felt his hair followed a similar pattern to the rest of the males in his family. His ethnicity is mixed black and Asian. He has no significant medical history and no previous testicular issues that he was aware of. On examination he continues to have bilateral gynaecomastia grade 2-3. He appears overweight with a BMI calculated at 33. His blood pressure was 138/91. Testes as reported on ultrasound, no change as per patient. Socially he vapes, consumes 8units/week alcohol, does not take any recreational drugs or other non-prescribed supplements.
Presenting Investigations
Testosterone 1.9, FSH 32, LH 18, prolactin 133. Repeat showed stable results. Karyotype 46 XY, Semen analysis- Azoospermia. Ultrasound Breasts - both U2. Ultrasound Testes- Both testes appear small without lesions. The right measures 2.5 × 1.1 × 1.6 cm and left measures 2.5 × 0.8 × 1.3 cm. Both epididymis appear normal. The left scrotal sac space has several varices.
Management and Discussion
He hopes to have fertility to father a child. He is in a relationship but they were not currently trying to have a baby. We discussed that if he was to have any success with fertility, whilst unlikely, this should be addressed sooner rather than later. He accepted an offer for specialist referral to consider sperm retrieval and any other options available for his fertility. Apart from gynaecomastia he is currently subjectively asymptomatic and testosterone replacement therapy is unlikely to make a major change to his expected fertility, therefore it may not be indicated at this stage. Thus far he has not been well engaged with his workup and management for this condition so it may not be acceptable to him. In his next appointment we will discuss the options for testosterone.

DOI: 10.1530/endoabs.100.WE3.2

WE3.3

Menopause related libido loss: is testosterone replacement always needed?

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Menopause may cause a constellation of symptoms associated with reduced quality of life. Loss of libido is a common one, although there still is uncertainty about its management in clinical practice. This 50-year-old lady was seen in the endocrine clinic complaining about fatigue and loss of libido. The patient's journey started 3 years earlier when she was commenced on hormone replacement therapy (HRT) in the community. After a short treatment with Evorel Sequi, as libido was not improving, the patient was referred to the endocrine clinic. HRT was stopped to perform a full hormonal screening that came back unremarkable. The patient was started on a new HRT regimen, according to her preferences, with Oestrogel 3 pumps/day and Utrogestan 200 mg/12 days. Additionally, the patient was also advised to start Testogel 2%, half squirt a day for 2 weeks, with an indication to increase the dose to one squirt a day if needed. A few months after starting this regimen, the patient's libido significantly improved, however, she started experiencing some hair growth. On a routine blood test, oestradiol and testosterone levels were significantly elevated (>x3ULN). The patient was reviewed by her GP who stopped Testogel and reduced Oestrgoel to 1 pump/day. When the patient was seen at our clinic, she was complaining about significant fatigue and loss of libido since changing the HRT. Moreover, since starting oral Utrogestan, experienced some headaches and nausea, although preferring to continue oestrogel rather than restarting the patches. She was reluctant to change the HRT again and resigned to her new quality of life. During the consultation the patient reported to have been taking Fluoxetine 20 mg/day for a long time, to help her depression/anxiety secondary to family issues. After a long consultation, the patient accepted the advice to increase Oestrogel to 2 pump/day, try to switch Utrogestan to Norethisterone Acetate 5 mg/12 days, switch Fluoxetine 20 mg to Mirtazapine 15 mg/day, and speak with GP if feeling in need of mental health support. Six months later, the patient reported a significant improvement in her fatigue and libido, not requiring to restart testosterone anymore. Libido management might be difficult during menopause, however selecting the right HRT as well as treating the interfering causes, can lead to improvement of symptoms without testosterone treatment.

DOI: 10.1530/endoabs.100.WE3.3

WE4.1

Hypogonadotrophic hypogonadism and gynaecomastia in a male patient

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A 33-year-old rehabilitated intravenous drug abuser was referred in view of bilateral gynaecomastia. The gynaecomastia developed gradually over a year with the left breast greater than right, and associated with intermittent tenderness but no galactorrhoea. He was found to have a low total testosterone and elevated oestradiol level. The patient claimed to have had undergone normal puberty with normal secondary sexual characteristics. He was able to maintain a beard, and had normal muscle strength. He admits to snoring at night, however denied excessive lethargy. He also lost his morning erections and complained of decreased libido. At presentation, his Methadone dose was being down-titrated. He denied use of over-the-counter medication and denied use of testosterone or anabolic steroids. On examination, the patient was normotensive with an obese body habitus. He was at Tanner Stage V but had evident gynaecomastia. Visual fields were normal to confrontation.
Investigations:

Test	Result	Range
FSH	2.1	U/l
LH	1.6	U/l
Total Testosterone	4.54	10.5-32 nmol/l
Oestradiol	151	0-146 pmol/l
SHBG	25.3	10-57 nmol/l
Albumin	46	32-52 g/l
Calculated Free Testosterone	0.0945	>0.225 nmol/l
Synacthen Test	0 min 195 30 min 548 60 min 689	nmol/l
TSH	1.2	0.3-3 micIU/ml
Free T4	18.46	11.9-20.3 pmol/l
Prolactin	76	45-375 mIU/l
GH	0.06	0-8 mg/l
IGF-1	168	76-265 ng/ml
Serum Osmolality	306	282-300 mOsm/kg
Urine Osmolality	846	500-1200 mOsm/kg
Haemoglobin	14.5	14.1-17.2 g/dL
Haematocrit	42.5	40.4-50.4%

Breast Ultrasound showed bilateral gynaecomastia and MR Pituitary showed a normal pituitary gland. Bone Density showed a Hip T score -1.1 and Spine T score -2.3 in-keeping with osteopenia. Sleep study showed mild OSA for which he was being followed-up by Sleep Clinic. The diagnosis of hypogonadotrophic hypogonadism, possibly secondary to obesity and long-standing opiate abuse as well as methadone treatment, was explained to the patient. He was offered testosterone replacement in an attempt to improve his sexual symptoms, prevent progression to osteoporosis, and possibly reduce gynaecomastia. However, plastic surgery may be required in the future to correct the latter. It was explained that testosterone replacement does not induce fertility, and if family planning is being considered in the future, the treatment

regime would need to be modified to human choriogonadotropin (hCG). To this end, he was started on testosterone undecanoate 1000 mg IM every 12 weeks with a plan to sample trough testosterone levels prior to the third dose.

DOI: 10.1530/endoabs.100.WE4.1

WE4.2

Long-term management of macroprolactinoma on high dose cabergoline with a partial response. two case reports

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Case 1: A 33-year-old male patient with seven years of erectile dysfunction and aspermia presented for a fertility opinion. He had a diagnostic of macroprolactinoma a year ago when Cabergoline was started with a gradual increase of the dose. Upon his initial evaluation in our clinic, on 2 mg Cabergoline weekly, his serum PRL level was × 10 UNL, decreased 70% from the diagnostic, and the tumour shrinkage was 60% from the diagnostic. A gradual increase of the Cabergoline up to 4.5 mg weekly and hypogonadism treatment with recombinant LH was planned. After the couple succeeded in conceiving, the patient was converted to testosterone substitution therapy. A year after increasing the dose to 4 mg Cabergoline weekly, the adenoma shrunk by 30% in volume, and the prolactin level maintained fivefold UNL. Case 2: A 44-year-old female patient with a diagnostic of macroprolactinoma abutting the optic chiasm – with constant treatment on Cabergoline 2 mg weekly in the last 18 months was referred to evaluation for a 2 mm progression of the adenoma. She had normalisation of the prolactin and regular menstrual cycles. The visual field examination reveals a slight abnormality in the temporo-superior quadrant. A gradual increase to 4 mg of Cabergoline weekly was planned with good tolerance. The six-month follow-up in the visual field examination showed a slight improvement. In case adverse effects do not develop, a high dose of Cabergoline remains a therapeutic option. Patients must be informed of the potential long-term side effects of high doses of Cabergoline, mainly the risk of cardiac valvular or pleural fibrosis. Some studies have shown little benefit to further increasing the cabergoline dose beyond 4 mg per week, considered the maximally effective dose while waiting for time effects, leading to hormonal control after several months in a substantial proportion of initially resistant patients. The use of Anastrozole, an aromatase inhibitor, to counter the further increase in drug resistance induced by testosterone supplementation, noted in a few cases, allowing a significant reduction of prolactin concentrations with lower doses of Cabergoline.

DOI: 10.1530/endoabs.100.WE4.2

WE4.3

Irradiation induced primary ovarian insufficiency

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30 year female diagnosed with AML at the age of 3. On diagnosis in 1996 had recurrence of AML 1998 had Bone marrow transplant with Total body irradiation and cyclophosphamide preconditioning 1998. She had suffered with post transplant cardiomyopathy (1999) Primary ovarian insufficiency and Childhood growth hormone replacement therapy (discontinued 2010) and recently found to have possible post irradiation induced Hypercalcaemia. She weighs 40 kg, height 4 ft 11 inches and BMI 17.8. Her dexa scan showed (Osteopenia)- spine T-score -1.1, hip T-score - 1, Bone mineral density 0.881 g/cm^2. She has not sustained any fracture. She was initially started on oral contraceptive pill for many years and but has been changed to Fomestin 2/10 mg 5 years ago and she continue to have withdrawal bleed and with no h/o mood swings and sided effects. She switched her to Evoral sequi patch for a year but sustained rash with patches and stopped using it 1 year ago now has moved to Oestrogel Pump750 micrograms/actuation two pumps every day for two weeks followed by Oestrogel two pumps and Utrogestan capsule 200 mg for next two weeks and continue to have withdrawal bleed. she is not keen for pregnancy and never been pregnant.

	Fsh	Lh	Oestradiol
2008	88.6	26.4	98
May 2015	39.6	19.9	343
Oct 2019	42.6	29.4	441

DOI: 10.1530/endoabs.100.WE4.3

WE5.1

What is optimal sex steroid replacement and treatment of osteoporosis in turner syndrome?

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Background
Turner syndrome (TS) affects around 1:2000 women and is the most common genetic cause of primary ovarian failure (POF). These patients require timely sex steroid replacement and are at increased risk of osteoporosis.
Clinical case
A 34-year-old female diagnosed with TS aged 10 years, attended the endocrine clinic after her care was transferred from Ukraine. She received growth hormone treatment for 4 years from the age of 12 and was commenced on hormone replacement therapy (HRT) aged 16 years. She is currently on Femoston 2/10 mg (estradiol/dydrogesterone), colecalciferol 400 IU BD and calcium carbonate 1.5 g BD. She has regular withdrawal bleeding and a history of wrist fracture. This patient was 158 cm tall, weighed 72 kg (BMI of 28.8 kg/m^2) with normal secondary sexual characteristics. Blood pressure was normal, chest X-ray showed no cardiomegaly and transthoracic echocardiogram was normal. She is awaiting a cardiac MRI. Ultrasound scan of urinary tract and pelvis showed no significant structural abnormalities. There was dyslipidaemia with raised cholesterol (7.6 mmol/l; nr 0.0–5.0) triglycerides (4.9 mmol/l; nr 0.80–1.8), and cholesterol/HDL ratio = 4.3. Given the increased cardiovascular disease risk in TS, atorvastatin 20 mg/day was initiated. Thyroid function tests and adjusted calcium levels were normal. IgA tissue transglutaminase antibodies were within normal range. Vitamin D levels were 40 nmol/l (nr 50–125). A DEXA scan revealed osteoporosis.

Location	T score
Lumbar Spine	-0.3
Hip	-1.3
Neck of femur	-2.5

Advice on weight bearing exercises was given. Given the diagnosis of osteoporosis despite HRT, rheumatology advice is being sought regarding bisphosphate versus the use of agents such as Denosumab.
Clinical dilemmas
1) What is the optimal dose and timing of HRT in patients with TS? 2) Could osteoporosis have been prevented and how is osteoporosis best managed now?

DOI: 10.1530/endoabs.100.WE5.1

WE5.2

Deep voice - when hormone effect is not expected

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A 66-year-old female patient presented post-menopausal with vaginal bleeding. She was on Oestrogen cream. The US showed a right ovarian cyst. The C125 was normal, and the uterine biopsy showed no malignancy. The bleeding continued and she was reviewed 4 months later. The MRI shows evidence of uterine adenomyosis. The right ovarian cyst is likely to represent a right ovarian endometrioma (32 × 28 × 30 mm). She was referred to the endocrine clinic for as increased hair growth and deepening of the voice. She noticed voice changes approximately four to six weeks ago with increased hair growth in her face, on the front and back of her body and her legs. She needed to shave every day. She later stopped shaving on the body hair because it grows very rapidly, however shaving the facial hair daily. she noticed that her sex drive had increased significantly. The Examination showed mild clitoromegaly with hirsutism. The hormonal profile showed a high testosterone of - 25.2 nmol/l, FAI - 86.9, SHBG 29, LH 12.1 U/l, FSH 21.6 U/l, and Estradiol 157. Her case was discussed in the Gynaecology MDT and she underwent laparoscopic bilateral salpingo-oophorectomy. The pathology report showed a Steroid cell tumour of the ovary - Stage1A. Following the surgery, the Testosterone was normal, and hyperandrogenism symptoms gradually resolved. Sex cord-stromal tumours (SCST) are a group of benign and malignant neoplasms. The pure sex cord tumours represent approximately 7-8% of all primary ovarian tumours. They secrete androgens, estrogens, or other steroid hormones that can cause clinical manifestations related to the hormonal profile. Ovarian SCSTs diagnosis is a histologic one. It is suspected preoperatively based on the presence of an adnexal mass combined with signs of estrogen or androgen excess or elevated levels of serum tumour markers. However, the diagnosis is confirmed by a histological specimen. Granulosa Cell tumours are the most common type of potentially malignant ovarian SCST; they comprise 2-5% of all ovarian malignant neoplasms and 90% of malignant SCSTs.

Sertroli cell tumours and sex cord tumours with annular tubules are rare. Sertroli cell tumours are typically benign, but malignant behaviour is more likely in higher-grade diseases. Androgenic effects are common; estrogenic effects are less common. Surgery is the main therapeutic modality for the management of these tumours, while chemotherapy and hormonal therapy may be used in some patients with progressive and recurrent tumours

DOI: 10.1530/endoabs.100.WE5.2

Workshop F: Disorders of the parathyroid glands, calcium metabolism and bone

WF1.1

A case of severe hypocalcaemia

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A 52 year old Syrian gentleman with a background history of hyperlipidaemia and psoriasis presented to the emergency department following a referral from his GP who identified severe hypocalcaemia on bloods in the community. The gentleman had been complaining of symptoms of weakness and lethargy, alongside tingling in his hands and feet for the preceding 4 years. He spoke very limited English, which may have been one of the reasons behind his non engagement with healthcare services. On presentation to the emergency department, he appeared to be comfortable and well. He was haemodynamically stable, with normal cardiorespiratory and neurological examinations. He was noted to have some muscular fasciculations in his extremities, however with no prolonged tetany. His ECG showed a borderline prolonged QTc. Bloods on admission revealed a normal FBC and renal profile, however his serum adjusted calcium was 1.35 mmol/l (2.15 – 2.5). Further biochemical evaluation revealed a corresponding parathyroid hormone level of 0.55 pmol/l (1.6 – 6.9) and a 25-OH Vitamin D level of 37 nmol/l (50 – 125). He had normal magnesium and phosphate levels. He was treated initially with repeated doses of 10% calcium gluconate, followed by a maintenance infusion. Following treatment, his serum adjusted calcium level had improved to 2.3 mmol/l and the patient symptomatically felt much better. Prior to his discharge, a genetic panel had been sent in order to look for an underlying cause of his hypoparathyroidism. He was subsequently discharged on Adcal D3, and carcitriol 1microgram/day. On his follow up in clinic, he was seen with an Arabic interpreter, and reported that his medication had run out 10 days prior, and for that matter had started experiencing symptoms of numbness and weakness once again. Repeat bloods prior to his clinic attendance revealed a serum adjusted Ca of 1.63, PTH of 0.63, and 25-OH vitamin D of 62. His genetic panel had returned negative for a genetic/familial cause of hypoparathyroidism, raising the suspicion that the hypoparathyroidism is autoimmune in nature. The patient did not display any features of other autoimmune conditions. He was issued a repeat script of medication and lifelong compliance was re-iterated. On further follow up, the patient demonstrated excellent compliance with his medication, with significant improvements both clinically and biochemically.

DOI: 10.1530/endoabs.100.WF1.1

WF1.2

Challenges in the management of chronic hypoparathyroidism

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Case
We report a 63-year-old woman who was referred to our Endocrine Bone Unit with difficult to control hypoparathyroidism. Sixteen-years previously, she underwent a total thyroidectomy with radioiodine ablation for multifocal papillary thyroid carcinoma with lymph node involvement. However, surgery was complicated by permanent postsurgical hypoparathyroidism, requiring regular calcium supplementation and active vitamin D (Alfacalcidol 1.25 mg). Over the 10-years prior to referral, corrected calcium values were frequently <2 mmol/l (despite treatment compliance), necessitating up-titration of the Alfacalcidol dose (averaging 1.75 mg daily). However, maintaining a target corrected calcium of 2.1 to 2.2 mmol/l, resulted in hypercalciuria with 24-hour urinary calcium measurements frequently >10 mmol/l (even following introduction of Indapamide and low salt/protein diet), due to the increasing circulating calcium and the permanent loss of PTH-induced active calcium transport in the distal tubule. This was associated with radiological evidence of nephrolithiasis/renal calculi and recurrent episodes of renal colic. Additionally, she had worsening bone mineral density without a history of fragility fractures, secondary to postmenopausal status, previous TSH suppression after thyroid cancer (now in remission), hypercalciuria and maternal osteoporosis history. Bone turnover was not reduced (which can occur where hypoparathyroidism causes adynamic bone) and so based on her fracture risk she was prescribed an oral bisphosphonate. Despite this, bone mineral density fell at both the lumbar spine (T-scores -1.3 to -1.7) and hip (T-scores -2.0 to -2.6).
Outcome
The principal management issues for this patient are: (1) difficult to control hypoparathyroidism, (2) hypercalciuria with nephrolithiasis/renal calculi due to necessary use of calcium/active vitamin D to maintain circulating calcium, (3) worsening bone mineral density. Therefore, given that potent antiresorptive therapies for osteoporosis risk causing hypocalcaemia and adynamic bone in a high-risk patient, a multidisciplinary decision was made to start PTH-analogues (Teriparatide), providing PTH replacement therapy for hypoparathyroidism, anabolic therapy for osteoporosis, and allow a reduction in the Calcium/Alfacalcidol doses.
Discussion
Most cases of secondary hypoparathyroidism are postsurgical with bilateral thyroid surgery the cause in $>80\%$ of patients. Conventional therapy involves the titration of calcium/active vitamin D, with the aim of preventing signs and symptoms of hypocalcaemia, maintaining serum calcium levels slightly below normal/low normal range, avoiding hypercalciuria/hypercalcaemia, and avoiding renal calcifications. PTH-analogues as a replacement therapy for hypoparathyroidism provides an additional therapeutic option, particularly for those who remain uncontrolled or those with side-effects of standard treatment (including calcifications).

DOI: 10.1530/endoabs.100.WF1.2

WF1.3

A case of Looser zones of osteomalacia is confused with fracture

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Background
Hypophosphatemic osteomalacia (HPO)is an uncommon metabolic disease. We describe a case of HPO, where radiological findings of the looser zone (pseudo fractures) were confused with an actual fracture and were scheduled for orthopaedic intervention. Extensive biochemical and radiological investigations followed by an endocrinology review enabled the diagnosis of HPO and prevented surgical intervention.
Case history
A 60-year-old gentleman presented to primary care with extensive bony pains and resultant poor mobility. Endocrine, rheumatology, and orthopaedics teams extensively investigated him. He was found to have multiple fractures in various, and a DEXA scan reported osteoporosis of the hips. An initial pelvis X-ray was reported as bilateral neck of femur fractures (NOF), although clinically, he did not have NOF. Therefore, the Orthopaedic team requested a CT scan of the hip for further clarity before surgery. The CT was reported as Subacute left femoral neck and right femoral shaft. Fracture appearances are in keeping with atypical femoral fractures, and metabolic/pathological causes should be explored, particularly bisphosphonate-related femoral fractures. The patient was re-admitted for elective surgery, for which he drove to the ED and mobilised to the ward. Further endocrine input and biochemical evaluations were requested to review the metabolic aspect, as his calcium and phosphate levels were low. Reviewing all previous investigations, an endocrine team concluded that this is a case of hypophosphatemia osteomalacia (HPO) and resultant pseudo fracture (Loosers zones). Investigations Ad. Calcium 2.11, PTH 13, Vitamin D 108 Renal and Thyroid function Normal ALP 440, Phosphate (0.35- 0.7), Bone turnover markers- P1 NP 88 and CTX (raised), 24 Hour Urine Calcium – Normal Magnesium 0.91, Albumin 42 Protein electrophoresis, PSA and CK normal. Coeliac screen negative MRI left lower leg- Linear non-continuous fracture of the Tibia. MRI spine -Disc bulge CT-TAP- Healing Rib fracture Bone scan- extensive and symmetrical uptake (Not typical of Paget's disease) Treatment Treated with sando Phosphate, active Vitamin D3(calcitriol), and oral calcium. Conclusions Treatment with phosphate and calcium supplements improved his bony pain and mobility. Further radiological evidence of bone healing was noted. Diagnosing HPO remains challenging to Endocrinologists and physicians due to its low prevalence and nonspecific manifestations. Blood tests for electrolytes, particularly serum phosphate and bone mineral density (BMD), are a primary clue for diagnosis. Fracture lines in osteomalacia are very common and can be confused with actual fractures. They may consist of pseudo fractures (Characteristic of HO), actual fractures, or insufficiency fractures.

DOI: 10.1530/endoabs.100.WF1.3

WF2.1

Five pints of milk a day keeps the hypocalcaemia at bay: autosomal dominant hypocalcaemia

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An 18-year-old male, presenting with unexplained weight loss, was found to have asymptomatic hypocalcaemia (adjusted 1.72 mmol/l, range 2.2-2.6 mmol/l) and hyperphosphataemia (2.05 mmol/l, range 0.8-1.5 mmol/l). He had a background of repaired perimembranous VSD, mild learning difficulties and developmental delay. Parathyroid hormone (PTH) was found to be undetectable and 25-OH Vitamin D insufficient (43 nmol/l). Urine calcium/creatinine ratio was elevated (0.81 mmol/mmol). There was no evidence of autoimmune endocrinopathy: no mucocutaneous candidiasis and both thyroid function and 9 am cortisol were normal. Parathyroid autoantibodies were negative. There was no family history, although the patient and his mother were both noted to have short stature and possible facial anomalies. Genetic testing established a heterozygous c.2488G > A activating variant of the calcium sensing receptor gene (CaSR) resulting in amino acid substitution p.(Gly830Ser), which has previously been described in the literature. This confirmed the diagnosis of autosomal dominant hypocalcaemia. It was challenging to achieve normocalcaemia at presentation, requiring multiple intravenous calcium infusions and uptitration to 2 mg alfacidol and 10 Calcichew tablets daily. Calcium then fell to 1.88 mmol/l at clinic follow-up and alfacalcidol was switched to calcitriol 500 ng twice daily. The patient became intolerant of multiple calcium formulations and resulted to consuming up to five pints of milk a day to maintain normocalcaemia. Calcitriol was increased further to 1500 ng daily, but calcium rose to 2.46 mmol/l and so was reduced to 1250 ng and the patient advised to lower dairy intake. The patient has subsequently presented with chronic daily headache and CT imaging demonstrated ectopic intracerebral calcifications. Ultrasound to assess for nephrocalcinosis is awaited. Renal function is maintained with eGFR > 60 and calcium/creatinine ratio is in the normal range (0.43 mmol/mmol). CaSR expression is highest in parathyroid and kidney. Gain-of-function leads to reduced PTH secretion, and consequently reduced calcium release from bone, Vitamin D activation and renal calcium reabsorption. As CaSR is also expressed in the kidney this compounds the effect on calcium reabsorption. Treatment with activated Vitamin D and calcium supplementation increases filtered calcium load, worsening hypercalciuria and leading to nephrocalcinosis and intracerebral calcifications. Paradoxically in this patient calciuria improved with treatment. It is recommended calcium is maintained in the bottom or just below the normal range and thiazide diuretics can be used to reduce calciuria. Future treatment avenues in research trials include calcilytics and long-acting PTH analogues.

DOI: 10.1530/endoabs.100.WF2.1

WF2.2

Strategies to limit renal stone formation in patients with hypoparathyroidism

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A 60 year old female developed iatrogenic hypoparathyroidism and hypothyroidism following a total thyroidectomy, performed for a multinodular goitre, in 1981. Post-operatively, this was treated with levothyroxine 100 mg daily, alfacalcidol 2 mg daily and Adcal-D3 four tablets daily. Other past medical history included hypertension, bilateral cataract extraction and recurrent hypokalaemia with high urinary potassium losses. Hypertension was treated with candesartan 8 mg and amiloride 5 mg once daily. 35 years after first developing hypoparathyroidism, a routine surveillance CT of the renal tract identified asymptomatic 4 mm and 6 mm non-obstructing renal calculi. Following this, 2 × 24 hr urine collections demonstrated high total urine output, and urinary calcium excretion of > 10 mmol/day with normal urinary citrate excretion. Urinary Calcium/Creatinine Excretion ratio was 0.039. Recurrent hypokalaemia prevented the use of indapamide or other thiazide-like diuretics to reduce urinary calcium losses.

Table 1: 24hr urine collection results, concurrent blood results and medication

Urine Collection 1: 24hrs		
Total Volume: 3666 mls [<3l]		
Na^+	47 mmol/l	172 mmol/day
K^+	13.1 mmol/l	48 mmol/day

Concurrent Blood Tests	
Na^+	139 mmol/l (133-146)
K^+	4.2 mmol/l (3.5-5.3)
Cr	72 mmol/l (55-110)
cCa^{2+}	2.28 mmol/l (2.2-2.6)
Phosphate	1.16 mmol/l (0.8-1.5)
Urinary Ca/Cr excretion ratio: 0.039	

Urine Collection 2: 24hrs		
Total Volume: 4056mls		
Creatinine	2.0 mmol/l	8.1 mmol/day (7-13)
Ca^{2+}	2.47 mmol/l	10.01 mmol/day (2.5-7.5)
Phosphate	3.82 mmol/l	15.62 mmol/day (13-42)
Mg^{2+}	1.05 mmol/l	4.3 mmol/day (2.4-6.5)
Citrate		1.64 mmol/day (>1)

Medication
Candesartan 8 mg OD
Amiloride 5 mg OD
Alfacacidol 2 mg OD
Adcal D3 400 u/750 mg 4 daily

She presented for routine clinical review and reported polydipsia, consuming 3-4 l/day. She denied urinary frequency, polyuria, or nocturia. There was no evidence of hypokaleamia, hypercalcaemia or diabetes. On alfacalcidol 2 mg/day, and Adcal D3 400 IU/750 mg 4 tabs/day, blood tests showed: cCa 2.48 mmol/l, Phos 1.62 mmol/l, eGFR 84 ml/min/1.73 m2, Na 139 mmol/l, K 4.5 mmol/l, PTH < 0.3 pg/ml, TSH 0.02 IU/l, fT3 4.7 pmol/l, fT4 18.8 pmol/l. This precipitated a discussion regarding target serum calcium levels when treating hypoparathyroidism, especially in a patient with a history of renal calculi. Strategies for reducing the renal fractional excretion of calcium include both reducing calcium delivery to the glomerulus (by limiting serum calcium concentration) and promoting tubular calcium reabsorption using thiazide-diuretics. Furthermore, these patients are at high risk of nephrogenic diabetes insipidus (vasopressin resistance) due to nephrocalcinosis and the reporting of polyuria necessitates careful assessment.

DOI: 10.1530/endoabs.100.WF2.2

WF2.3

Hungry bone syndrome- how common is it and have you seen it?

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Background
Hungry bone syndrome (HBS) is a prolonged and profound post-operative hypocalcaemic state following parathyroidectomy or thyroidectomy. The incidence is uncommon, cited between 4-13% with surgically treated primary hyperparathyroidism, and can last up to a year post-operatvely. Hypocalcaemia in HBS (usually <2.1 mmol/l) is rapid, and is attributed to the sudden decline in parathyroid hormone (PTH) levels which alters the milieu of PTH-mediated osteoclastic bone resorption in patients with uncontrolled primary hyperparathyroidism, towards osteoblast-mediated bone resorption. The subsequent influx of minerals into the skeleton leads to hypocalcaemia, hypomagnesaemia and hypophosphataemia. This is further accentuated by the failure of the remaining suppressed parathyroid glands to regain activity for a period of time. The spectrum of HBS symptoms includeparaesthesia, tetany, arrhythmias, cardiomyopathy, and seizures.
Clinical case
A 32-year-old fit-and-well man presents to his GP with chronic, non-specific back and knee pain. He was found to have incidental severe hypercalcaemia (3.75 mmol/l (NR 2.20-2.60 mmol/l), leading to hospital admission. Further stratitificaiton showed severe primary hyperparathyroidism (PTH:227 pmol/l; N = 1.6-6.1 pmol/l)ALP of 1578 u/l, and 25-OH vitamin D insufficient 26 nmol/l. NM parathyroid SPECT CT showed a left intrathyroid parathyroid adenoma measuring 3.1 × 2.5 × 4.6 cm. CT-NCAP was also consistent with this, alongside evidence of erosive bone disease at the sacroiliac joints, iliac wings and left humeral head. After immediate management with IV hydration, he underwent left thyroidectomy with parathyroidectomy, with marked intra-operative PTH reduction to 9.9 pmol/l. recalcitrant hypocalcaemia over 3 weeks as inpatient (corrected calcium 1.70-1.95 mmol/l) with associated symptoms of hypocalcaemia which was refractory to treatment. Subsequent histology showed parathyroid carcinoma currently awaits head and neck MDT outcomes.
Specific management
Management of HBS constitutes careful monitoring and replacement of depleted electrolytes. Severe hypocalcaemia <1.9 mmol/l, symptomatic hypocalcaemia, or ECG changes such as QTc prolongation indicate the need for IV calcium replacement. Activate 1,25(OH)2 cholecalferol (Calcitriol) is the treatment of choice since it does not need any PTH activity for hydroxylation. Subsequently IV calcium can be replaced with high dose oral elemental calcium. Careful monitoring at 2-weekly intervals is required to prevent rebound hypercalcaemia when the remaining parathyroid glands start responding.
Learning points
• HBS is a serious complication of parathyroidectomy following severe untreated primary hyperparathyroidism (PHPT) and is characterised by a profound and prolonged period of hypocalcaemia.

• Adequate history regarding duration and severity of PHPT is necessary to guide post-operative management.
• Management of post-operative hypocalcaemia requires IV replacement if: severe <1.9 mmol/l, symptomatic, or associated with ECG changes alongwith Calcitriol
• Careful monitoring of bloods and dose titration of calcium replacement is indicated both in the peri-operative and post-operative periods

DOI: 10.1530/endoabs.100.WF2.3

WF3.1

A case of hypocalcaemic hypoparathyroidism complicated by malabsorption, leading to refractory hypocalcaemia and repeated hospital admissions

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Case Presentation
A 27-year-old female who recently moved to the UK, was referred to Endocrinology with suspected thyrotoxicosis. She was diagnosed with thyrotoxicosis 11 years prior, and was temporarily treated with a 'block and replace' regimen. She had history of traumatic brain injury with no long-term sequelae, and cholecystectomy leading to chronic diarrhoea. She reported swallowing difficulty and a choking sensation. Investigations identified hyperthyroidism due to multi-nodular goitre. Thyroid receptor antibodies were initially negative, but weakly positive on follow up (0.9I U/l), indicating Graves' disease. A thyroid ultrasound revealed three U3 thyroid nodules with maximal diameter of 32 mm. These were benign (THY2) on fine needle aspiration. She remained thyrotoxic despite titration of carbimazole to 20 mg daily, over 3 years. A follow-up ultrasound showed interval increase in nodule size, with maximal diameter of 36 mm and U3 classification. The patient's TSH remained suppressed (<0.01 mU/l) and she remained symptomatic. The decision was made to proceed to thyroidectomy. Simultaneously, she was noted to have asymptomatic severe hypocalcaemia (adjusted calcium 1.46 mmol/l, vitamin D 54.6 nmol/l, PTH 1.4 pmol/l, magnesium 0.63 mmol/l, phosphate 2.50 mmol/l). She reported repeated childhood hospital admissions requiring intravenous calcium infusions, but was unsure of the cause. Parathyroid antibodies were negative. She was diagnosed with hypocalcaemic hypoparathyroidism and was commenced on Adcal-D3, Alfacalcidol and Magnesium supplementation. She suffered repeated hospital admissions, despite titration of Alfacalcidol to 2.5 mg daily, Adcal D3 to 4 tablets daily and Magnesium 10 mmol sachets twice daily. She was initially asymptomatic, however more recent hospital admissions were complicated by seizures alongside hypocalcaemia. She was commenced on levetiracetam and referred for neurological assessment. As her calcium failed to normalise, underlying bile acid malabsorption was suspected, due to ongoing diarrhoea. She was commenced on Colesevelam 1250 mg daily after gastroenterology input. On latest follow-up, her adjusted calcium is stable at 2.12 mmol/l, with magnesium of 0.64 mmol/l. She still awaits thyroidectomy.
Discussion
This is a complex case of refractory hypocalcaemia in a patient with significant co-morbidities. Her previous traumatic brain injury has likely lowered the seizure threshold, with hypocalcaemia possibly exacerbating seizure episodes. Exploring and treating other reasons for persistent hypocalcaemia, including malabsorption, was paramount in this case. Careful consideration and planning will be required prior to thyroidectomy, to avoid post-operative hypocalcaemia. The risk is significant due to her concurrent Graves' disease and hypoparathyroidism. A pre-load regime of higher dose Alfacalcidol has been planned prior to her thyroidectomy.

DOI: 10.1530/endoabs.100.WF3.1

WF3.2

A challenging case of post-operative hypoparathyroidism in the context of metastatic breast carcinoma; a physician's nightmare

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Although not used as first-line, recombinant human parathyroid hormone (rhPTH) has a role in the treatment of chronic hypoparathyroidism especially when the conventional treatment is deemed unsatisfactory. A 48-yr-old female with a history of total thyroidectomy for a benign multinodular goiter and post-operative permanent hypoparathyroidism was referred to us in 2011 due to treatment resistant hypocalcemia requiring intravenous calcium infusions. Her calcium remained mostly in the range of 1.4-2.0 mmol/l. Other than the history of Raynaud's Syndrome and lactose intolerance, her past medical history was unremarkable. She was on Thyroxine 100 micg daily, alfa-calcidiol 1 micg twice-daily and Calcium Carbonate 1 g four-times-daily. Upon evaluation she was found to have ongoing abdominal symptoms for an extended period due to Celiac disease and gluten removal improved her symptoms and calcium level for a brief period. She was also on long-term antacids which could have contributed to the malabsorption of calcium salts. Her calcium control remained challenging, hence various options were tried including supplementation with vitamin-D3, changing to calcium citrate, a trial of liquid form of alfacalcidol, and switching to calcitriol. Regretfully, over the next few years (2015-2020), she went on to develop bilateral recurrent breast cancer requiring surgery, chemotherapy, radiotherapy, and adjuvant endocrine therapy. Her calcium level varied markedly during this period with recurrent admissions requiring calcium infusions. As the initial whole-body scan was negative, and she was stable without any local recurrence or distant metastasis from the oncological perspective, in 2021 she was started on rhPTH(1-84) with a good response and stability over calcium level at 100 mg daily. Unfortunately, it had to be stopped after 2-years due occurrence of bony-metastasis from progressive breast cancer. Immediately after stopping the rhPTH, she went down on a spiral of multiple hospital admissions with symptomatic hypocalcemia. Currently, she is on alfa-calcidiol 14 micg daily, Vitamin-D3 1000 IU daily, Calcium Carbonate 4 g daily along with Thyroxine 125 micg daily and her calcium remains in the range of 1.75-2.2 mmol/l. Most recently, she was given IM ergocalciferol 300,000 iu injection which seemed to have kept her calcium at 2.23 mmol/l. Due to the concerns over the evidence from pre-clinical studies for the risk of osteosarcoma, safe use of rhPTH is still not established in the presence of bony metastasis. Physicians are reluctant to use PTH therapy although the benefits outweigh the perceived minute risks; hence further research is needed to establish the safety.

DOI: 10.1530/endoabs.100.WF3.2

WF3.3

Challenges in management of hypoparathyroidism and severe hypocalcaemia in autoimmune polyendocrine syndrome -Is recombinant human parathyroid hormone or PTH pump an option?

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We present a case of 18 Year male with autoimmune polyendocrine syndrome who presented with seizures to A and E presumed secondary to his profound severe hypocalcemia. Adjusted calcium levels of 1.80 mmol/l.
Background
Primary adrenal insufficiency, Hypoparathyroidism, Pancreatic insufficiency and malabsorption, Pernicious anaemia, Aspergers syndrome and Stem cell deficiency in the eye. On admission he received calcium gluconate stat doses which was followed by calcium carbonate infusion. Following that he stayed in hospital for a few weeks and his calcium was monitored regularly and on several occasions the calcium was critically low requiring infusions. Of note is that his calcium supplements (calcichew were increased to two tablets TDS) and alfacalcidol dose was increased to 2.5 micrograms. Despite increase in the dose his calcium levels were erratic. Due to his pancreatic insufficiency his Creon dose was increased as well. He denied any loose or clay coloured stools, increased stool frequency. Compliance was explored and directly observed treatment was practiced but calcium levels stayed erratic. His calcichew was changed to calcichew forte and dose was increased to 2 tablets QDS and his alfacalcidol dose was increased to 2.75 micrograms and he was discharged when calcium was low normal consistently for a few days off infusion and calcium gluconate. He remained seizure free despite very low calcium levels and had no ECG changes He was discharged from hospital but his follow up blood tests at MSDEC showed very low calcium levels, warranting infusions. (1.84 mmol/l, 1.79, 1.92) and on one occasion he had adjusted calcium of 1.64 mmol/l requiring hospital admission.
Other tests
fecal calprotectin negative
Celiac antibodies negative
Magnesium normal on all occasions (>0.7 mmol/l)
PTH in october 0.8 pmol/L, Vitamin B12 and Folate in range
Vitamin D 16.5
An OGD is requested to look for oesophageal candidiasis his calcichew is switched to calvive tablets. Timing of his Creon tablets is also changed to ensure there was an hour gap between Creon and his calcium supplements.

Discussion
1. Is there a role of Recombinant parathyroid hormone in these patients?
2. Family queried regarding PTH pumps, can this be a potential option in the future?
3. If hypocalcemia persists, is there a scope of increasing alfacalcidol further or calvive should be increased?
4. How frequently should his calcium levels be monitored

DOI: 10.1530/endoabs.100.WF3.3

WF4.1

First presentation of severe hypocalcaemia

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Introduction
Hypoparathyroidism is a rare endocrine disease with a prevalence of less than 40/100,000 people worldwide[1]. It has a variable presentation but can present with life-threatening arrhythmias or seizures.
Case Presentation
A 31-year-old male presented to our Emergency Department following a witnessed tonic-clonic seizure with no previous history of epilepsy. He was not on any regular medications and denied recreational drug use. Examination was largely unremarkable with a normal neurological examination. However, there was evidence of significant tooth hypoplasia and poor dentition. Admission blood tests showed profound hypocalcaemia (adjusted calcium level of 1.47 mmol/l) with an inappropriately low parathyroid hormone (PTH) level (1.6 pmol/l). Vitamin D was low (22 nmol/l). Full blood count, renal function, liver function and magnesium levels were normal. A CT head was unremarkable though subsequent MRI showed Chiari I malformation for which neurosurgical referral has been made. There was no history of neck surgery. He reported longstanding mild paraesthesia in his fingers but was otherwise well in himself with no evidence of tetany or spasms. He denied any previous seizures or fractures but may have had rare nocturnal cramps in his calves. He reported recurrent childhood infections, with resultant hospital admissions in his home country of Lithuania. It was suspected he may have undiagnosed learning difficulties. He had no notable family history. Given findings of severe, symptomatic hypocalcaemia secondary to hypoparathyroidism and Vitamin D deficiency, he was admitted and treated with intravenous calcium gluconate acutely. He was also commenced on Alfacalcidol and Adcal D3 which were titrated to achieve normocalcaemia. A Vitamin D loading regimen was initiated (50,000 units once a week for 6 weeks). He was discharged from hospital once his calcium stabilised >2 mmol/l. Adjusted calcium levels remain at the target lower end of the normal range on oral calcium and Alfacalcidol, with no further seizures. Genetic tests were sent for chromosomal analysis and gene panel tests.
Conclusion
It is essential to rule out calcium and other electrolyte derangements as a contributory factor for new onset seizures. Once hypocalcaemia is identified, a systematic approach is key to determine the cause of hypocalcaemia, which then allows timely treatment.
Reference
1. Bilezikia, J. P. (2020) 'Hypoparathyroidism', Journal of Clinical Endocrinology and Metabolism, 105(6), pp. 1722–1736. doi: 10.1210/clinem/dgaa113.

DOI: 10.1530/endoabs.100.WF4.1

WF4.2

Treatment refractory post-surgical hypoparathyroidism requiring recombinant PTH (teriparatide) administration

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We present a case of a 43 year-old male with permanent post-operative hypoparathyroidism following total thyroidectomy for toxic nodular goitre. His medical history includes Mccune-Albright syndrome and mild right optic atrophy. He had prolonged hospital stay post-surgery due to persistent severe hypocalcaemia with mild hypomagnesemia. Post-surgery, hypocalcaemia was treated with intermittent calcium infusion, oral calcium and D3 supplements and vitamin D analogues of alfacalcidol 4 microgram daily which was switched to calcitriol 2 mg daily due to lack in calcium improvement. He was also commenced on regular oral magnesium replacements. Despite maximal oral and intravenous treatment, normocalcaemia was not achieved hence recombinant PTH of Teriparatide was commenced at 40 mg daily subcutaneously. He was discharged following normocalcaemia and was regularly followed up for calcium monitoring. Hypoparathyroidism and hypocalcaemia is a common postoperative complication after total thyroidectomy. Standard treatment with supplementation of calcium and vitamin D analogues, usually treat this condition. Uncommonly, in some cases including our patient, hypoparathyroidism is refractory to standard treatment and recombinant PTH is required to achieve normocalcaemia.

DOI: 10.1530/endoabs.100.WF4.2

WF4.3

How is the calcium normal?

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A 25-year-old lady with a background of Multiple Endocrine Neoplasia (MEN) type 2 a was referred to the endocrine team during her first pregnancy. She was initially diagnosed with bilateral phaeochromocytomas in Romania in 2018 after presenting with paroxysmal headaches and hypertension, and underwent laparoscopic bilateral adrenalectomies. Subsequently, she was diagnosed with MEN2 a when found to have a RET gene mutation: RET exon 11 C1901 G2a, p.CYs634Tyr. She was the index case in her family. Three months later, she underwent prophylactic total thyroidectomy and total parathyroidectomy. Three other family members have since been confirmed as MEN2a. On referral to the endocrine team, she was 21 weeks pregnant and taking hormone replacement in the form of Hydrocortisone (10, 5, and 5 mg), Fludrocortisone 100 mg od, Levothyroxine 150 mg od, Adcal 1000 mg od, and Calcitriol 0.25 mg od. Our patient became hypercalcaemic in the second trimester. She was advised to stop Calcitriol and adcal. After cessation, she remarkably had normal levels of adjusted calcium for the remainder of her pregnancy, despite low/undetectable levels of both PTH and PTHrP. Literature review states that there is an increase in serum calcitriol levels in the latter half of the pregnancy. The increase in calcitriol can be regulated by other pregnancy hormones, which are normal in hypoparathyroidism, such as prolactin, oestrogen, and placental growth hormone. In case calcitriol dose is not reduced or stopped then in combination with elevated serum levels, there will be an increase in calcium absorption and bone resorption, which result in hypercalcaemia. Calcitriol levels drop during breastfeeding. Her calcium level dropped post-delivery and she was restarted on supplementation. During the last trimester, our patient was diagnosed with pre-eclampsia (PET). Interestingly calcium supplementation in pregnancy may help prevent hypertension; therefore, reducing the chances of PET. Six months post-partum her calcium levels remain in optimal range (low-normal) on calcitriol 0.5 mg od and calcium 1000 mg od. This case teaches us the importance of closely monitoring calcium levels in pregnancy and post partum in patients with hypoparathyroidism.

DOI: 10.1530/endoabs.100.WF4.3

WF5.1

An unusual life threatening presentation of hypocalcemia

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A 40 y /M with no previous CVS/family history, presented with fall. On history, he was feeling unwell, had Appetite loss $\times$ 3 months, progressive SOB, Orthopnoea, PND and palpitations. No chest pain/fever. On Examination, he had tachycardia (160) and irregular rhythm, raised JVP, SpO2 92%, B/l ankle edema, bibasal fine inspiratory crackles in chest, Hepatomegaly(3 cm) CVS :S3 gallop, mild TR, MR. ECG : sinus rhythm with freq ectopics, long QT, paroxysms of tachycardia, T wave inversion V4-V6. CXR revealed cardiomegaly and pulmonary oedema. His Troponin was <0.02 mg/l. Echo showed dilated LV with globally impaired systolic function with LVEF15% due to diffuse hypokinesia, moderate MR, TR. Coronary angiogram was normal, no vessel disease. Clinical Diagnosis of heart failure was made and pt started iv furosemide, digoxin, B blockers. But he started deteriorating and had irregular rhythm on cardiac monitor(ectopics/AF/Atachy). He also started c/o nocturnal muscular cramps and paraesthesia. Was shifted to ITU immediately. Further investigations revealed Calcium:1.03 mmol/l, Phosphate:2.77 mmol/l. Mg 0.63 mmol/l. PTH <0.5 pmol/l. Vitamin D 88 nmol/l, TSH 1.96 CRP $<$ 3. Ultrasound neck: No parathyroid glands identified. So he was started on iv calcium gluconate, iv magnesium and 2 mg Alfacalcidolvit D3) and Adcal. Blood investigations over next few days showed improving ca, po4 and mg levels. ECG: HR improved (70), sinus rhythm, QT normal, Digoxin stopped, Patient's sats improved with no O2 reqt. His overall Condition improved in 2 weeks and was discharged. -3 months

later Patient was completely asymptomatic and Repeat Echo showed EF improved to 59% with improved global LV contractility, No MR. ECG HR 70/mt, normal QT, sinus. -Final Diagnosis was Hypocalcaemic cardiomyopathy secondary to primary hypoparathyroidism (Idiopathic/low Mg) Etiology of heart failure: cardiac myocytes contraction is directly dependent on Ca concentration in the ECF. Low ca leads to lowered cell membrane potential → increased membrane permeability → escape of cytoplasmic proteins from renal tubules. Also decreased natriuresis → result in fluid retention → heart failure. Correction of hypocalcemia promotes natriuresis. HYPOCALCEMIC CARDIOMYOPATHY is reversible Systolic/Dilated cardiomyopathy due to deterioration of the heart muscle's contractility. Often a late manifestation of long standing hypocalcemia. May manifest with arrhythmias(AF, prolonged QT, VT) which is completely reversible on treating hypocalcaemia. Traditional therapy for heart failure, i.e. diuretics/digitalis alone not effective in resolving symptoms. Furosemide could decrease serum calcium level by increasing calcium excretion in urine leading to worsening symptoms. Alfacalcidol is MUST for treatment along with calcium supplementation in primary hypoparathyroidism.

DOI: 10.1530/endoabs.100.WF5.1

WF5.2

Chronic hypoparathyroidism requiring treatment with Natpar (Parathyroid Hormone rDNA)

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A 62-year-old lady was being followed up by endocrine surgeons for multinodular goitre. She underwent an elective total thyroidectomy in April 2017 and histology confirmed a multinodular goitre with no evidence of malignancy. The patient first developed hypocalcaemia immediately post-operatively and was started on Alfacalcidol 0.25 micrograms daily in addition to Levothyroxine replacement. Unfortunately, the patient was lost to follow-up and re-presented at our endocrine clinic in July 2020 with symptoms and signs indicative of hypocalcaemia i.e. peri-oral paraesthesia, tingling in the hands and positive Chvostek's and Trousseau's sign. On taking urgent blood tests, the corrected calcium was 1.77 mmol/l and ECG showed normal sinus rhythm with a prolonged QTC of 488 ms. The patient was then admitted for an intravenous infusion of calcium gluconate while on cardiac monitoring. She received 20 ml 10% calcium gluconate in 50 ml of 5% Dextrose over 10 minutes, after which her symptoms had resolved, then 100 ml of 10% calcium gluconate in 1 Litre 0.9% saline infused at 50 mls/hour. She was concurrently started on Alfacalcidol 0.25 micrograms 8-hourly and Calcium Carbonate 1 g 8-hourly. Unfortunately, despite regular blood tests and up-titration of Alfacalcidol on an out-patient basis, the patient required multiple hospital admissions with symptomatic hypocalcaemia over the span of 2 years. The patient had reached a maximum dose of Calcium Carbonate 1 g 8-hourly and Alfacalcidol 8.5 micrograms daily in October 2022. The decision was taken to start the patient on Natpar (Parathyroid Hormone rDNA) to attempt to prevent the latter. The patient underwent the necessary education on how to administer Natpar subcutaneously and became familiar with the device. She was started on 50 micrograms daily and the Alfacalcidol dose was reduced by 50% as instructed by the drug summary of product characteristics (SmPC). The patient reached a stable level of corrected calcium (ranging between 2.05 and 2.2 mmol/l) on Calcium Carbonate 500 mg 12-hourly, Alfacalcidol 0.5 micrograms daily and Natpar 100 micrograms daily in July 2023 and has since not required further hospital admissions for symptomatic hypocalcaemia or dose adjustments.

DOI: 10.1530/endoabs.100.WF5.2

WF5.3

Genetic disorders and hypoparathyroidism: unravelling complexity through case studies

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Hypocalcaemia, characterized by abnormally low calcium levels, can stem from various aetiologies, broadly classified as parathyroid hormone (PTH) dependent or PTH independent. PTH-dependent causes encompass deficiencies in circulating PTH, either in isolation or as part of complex syndromes or genetic disorders, further categorized into disorders of parathyroid formation, PTH synthesis or secretion disorders, and parathyroid gland destruction disorders. The patient, presenting in his early 30 s with mild symptomatic hypocalcaemia, displayed spectrum of manifestations associated with hypocalcaemia, including weakness, muscle cramps, nervousness, headaches, and hyperexcitability of nerves. Notably, his mother and sister had hypoparathyroidism. Biochemical analysis revealed persistently undetectable PTH levels, corrected calcium of 1.88 mmol/l, vitamin D of 101 nmol/l, GFR of 80 ml/min, HbA1 C of 41, and 24-hour urine calcium of 10.4 mmol/day (normal range: 2.5-8). Despite management strategies involving Vitamin D analogues and calcium supplements to maintain optimal serum calcium levels between 2 to 2.2 mmol/l, patient continued to experience hypercalciuria, leading to recurrent kidney stones. Introducing Bendroflumethiazide to counter tubular excretion of calcium proved unsuccessful, prompting need for ongoing endocrinology follow-up to monitor hypocalcaemia and adjust medications. Genetic testing eventually revealed a heterozygous AIRE mutation, unveiling a compelling case of hypoparathyroidism attributed to autoimmune destruction of the parathyroid gland, specifically associated with autoimmune poly endocrinopathy candidiasis ectodermal dystrophy (APECED) or Autoimmune Polyglandular Syndrome type 1 (APS1). APS1, an autosomal recessive disorder linked to mutations in the AIRE gene on Chromosome 21q22.3, Intriguingly, genetic testing revealed a heterozygous AIRE mutation, presenting an autosomal dominant pattern that suggests the potential existence of an unidentified AIRE variant or more probable that symptoms are unrelated to AIRE variant. Classic triad characterizing APS1—mucocutaneous candidiasis, hypoparathyroidism, and adrenal insufficiency— often accompanied by enamel hypoplasia, alopecia, vitiligo, pneumonitis, hepatitis, autoimmune gastritis, and enteropathy. However, in this instance, patient solely presented with hypoparathyroidism, emphasizing importance of considering APS1 in individuals under 30 with hypoparathyroidism, even if a singular component of the triad is evident. This illustrative case underscores intricate landscape of familial hypoparathyroidism, encompassing genetic complexities and formidable challenge of managing associated complications. It accentuates the imperative of a holistic and individualized approach, integrating genetic analysis, symptom surveillance, and tailored therapeutic interventions. The persistence of hypercalciuria and kidney stones underscores the need for continued vigilance and adaptation of management strategies for optimal patient care.

DOI: 10.1530/endoabs.100.WF5.3

Workshop G: Disorders of appetite and weight

WG1.1

Efficacious use of GLP-1 receptor analogue in type 1 diabetes complicated by class 3 obesity

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Introduction
Prader-Willi syndrome is a multi-system disorder that commonly leads to severe obesity. Hyperphagia plays a key role in the development of obesity and without restriction of calorie intake patients will often develop severe obesity related complications including an increased risk of type 2 diabetes (T2DM). GLP-1 receptor agonists (GLP1-RA) have been developed for use in obesity and T2 DM for weight loss and glycaemic control as well as cardiometabolic positive outcomes. They have been shown to decrease appetite through increased satiety and have been demonstrated as being effective in cases of hypothalamic obesity.
Case history
A 25 year old male with a background of Prader-Willi like syndrome (history of obesity, hyperphagia and developmental delay) was diagnosed with type 1 diabetes (T1DM) aged 18 (Glutamic Acid Decarboxylase and Zinc transporter 8 antibody positive). He was treated with a basal bolus regime, however, due to evidence of insulin resistance (with acanthosis nigricans, hypertriglyceridemia and low HDL) he was started on metformin. Despite this he had continuous excessive weight gain, exacerbated by persistent hyperphagia. At 23 years old he had a BMI 44.95 kg/m^2, HbA1 c 70 mmol/mol, total daily insulin dose 149 units (1.4 units/kg). He also had evidence of mild sleep apnoea on sleep studies. Despite lifestyle changes with diet and exercise, he had limited weight loss. Consequently, he was commenced on a trial of a GLP1-RA both for glycaemic control, weight loss and appetite suppression. Due to intolerance with Dulaglutide, he was trialled on Liraglutide with the dose up titrated to 1.8 mg daily.
Results and management
Treatment with a GLP1-RA resulted in reported appetite suppression. Additionally, there was a 14% reduction in weight with BMI improving to 37.7 kg/m^2 following 14 months of treatment. Glycaemic control also improved (HbA1 c 46 mmol/mol), with a reduction in insulin requirement independent of weight loss (total daily insulin dose 92 units (1.0 unit/kg))
Conclusion
This case demonstrates the efficacious use of a GLP1-RA in a patient with T1 DM and Prader-Willi like syndrome with evidence of insulin resistance and morbid obesity. Use of Liraglutide led to significant weight loss and improvement in insulin sensitivity with a self-reported improvement in hyperphagia. The use of GLP1-RA agonists should be considered in patients in syndromic obesity and diabetes, where weight reduction is an important factor in reducing long term metabolic complications.

DOI: 10.1530/endoabs.100.WG1.1

WG2.1

Continuous glucose monitoring in the management of post-bariatric hypoglycaemia – does it have a place in treatment algorithms utilised by the NHS?

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Post-bariatric-surgery hypoglycaemia (PBH) typically presents at least six months post-operatively, particularly in those who have undergone Roux-en-Y gastric bypass (RYGB), with the literature suggesting that this condition develops in up to 30% of people post-bypass surgery. PBH is characterised by high postprandial insulin and glucagon-like peptide-1 secretion leading to hypoglycaemia 1-3 hours after consumption of meals that are high in carbohydrate content. We present the case of a 48-year-old female, who underwent RYGB in 2009, without prior history of diabetes (all previous HbA1 c results available since 2015 have been in the range of 33-41 mmol/mol). Seven years after RYGB, she first noticed hypoglycaemic events while monitoring during pregnancy, which were mostly asymptomatic. Over the last few years, she has increasingly been experiencing autonomic symptoms 1-2 hours after high-carbohydrate meals, with capillary glucose levels dropping as low as 2.5 mmol/l and symptoms improving after carbohydrate intake (Whipple's triad). She does not report episodes of fasting hypoglycaemia, no other significant medical history other than vitiligo, sigmoid diverticulosis and previous cholecystectomy with subsequent bile acid malabsorption causing intermittent diarrhoea, and with alternative causes of hypoglycaemia excluded biochemically (normal cortisol and fasting glucose), a clinical diagnosis of PBH was made. She had a Freestyle Libre trial; during the fortnight, her time-below-range (<3.9 mmol/l) was 19%, but with a strict low-carbohydrate diet her glycaemic variability was reduced and her symptoms and frequency of hypoglycaemia improved. She was not keen to take acarbose and has tried to manage PBH with dietary modification as per dietitian advice. She follows a low glycaemic-index carbohydrate diet (30 grams for meals, 15 grams for snacks) paired with vegetables, protein and healthy fats, taken every 3-4 hours, but she still experiences autonomic symptoms in daily life, affecting her quality of life. She reports that during the period she used continuous-glucose-monitoring (CGM), she was more confident to modify her dietary choices to prevent postprandial hypoglycaemia, and would be keen to continue using CGM, but the challenge remains that its use in PBH has not been approved by regulatory authorities in the UK. The literature demonstrates that CGM can help patients with PBH detect impending hypoglycaemia, allowing them to adopt dietary modification and early treatment to prevent and reduce post-prandial hypoglycaemia. Although currently not NHS-funded for PBH, CGM could be considered as a treatment tool for PBH in clinical practice alongside dietetic intervention, and it may be particularly important for people experiencing disabling episodes of hypoglycaemia.

DOI: 10.1530/endoabs.100.WG2.1

WG3.1

Nutritional induced polyneuropathy post bariatric surgery

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Neurological complications are frequently recognised with bariatric surgery. We present a case of a young 24 year old female, who had sleeve gastrectomy performed privately in Turkey. She received nutritional supplements following surgery but compliance is uncertain. 3 months post gastrectomy, she was admitted with 2-week history of progressive ascending bilateral lower limb weakness and paraesthesia. She had lost by then 10% of her excess weight. Preceding this episode, she had admission with vomiting and abdominal pain and was found to have gallstones, which is also a known risk with rapid weight loss. Initial differentials were Guillain-Barre-syndrome or transverse myelitis. She was found to be deficient in vitamin B1, vitamin A, vitamin D and folic acid. Lumbar puncture and spinal imaging were unremarkable. Nerve conduction study and EMG revealed significant patchy sensorimotor neuropathy which consistent with nutritional deficiencies following gastrectomy. She made a good recovery with her symptoms following nutritional replacements and long period of rehabilitation. This is a case of nutritional induced polyneuropathy post bariatric surgery. This case elicits the importance of thoroughly examining and observing bariatric patients after surgery, informing of potential risks of neurological complications to individual undergoing the surgery, and the importance of nutritional supplements and its compliance post-surgery.

DOI: 10.1530/endoabs.100.WG3.1

WG4.1

The slimfast plan to surgical success

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We report a case of a 45-year-old gentleman who was seen in the Endocrine Clinic with confirmed phaeochromocytoma. He had a background of obesity; he weighed 123 kg and at a height of 169 cm, his BMI was 43 kg/m^2. This presented a significant risk for laparoscopic abdominal surgery, general anaesthesia and post operative recovery. He was therefore urgently referred to a Tier 3 Bariatric Service and commenced on subcutaneous injections of Semaglutide, initially 0.25 mg weekly for 4 weeks, followed by 0.5 mg weekly for 4 weeks, which was then increased to 1 mg weekly. He was also referred to the specialist bariatric dietitian for a Very Low Calorie Diet (VLCD) in the form of total meal replacement. His diet consisted of increasing his daily water intake to 3 litres and eating three meal replacement bars (232 kcal each) a day in addition to a portion of vegetables. With this he took a multivitamin and Omega 3 supplements. Of note, the increased water intake helped mitigate any postural hypotension symptoms that are commonly associated with uptitration of phenoxybenzamine. After 4 weeks, he had lost 11 kg and by 12 weeks he had lost 15 kg (12% weight reduction from baseline). However, blood tests showed a microcytic anaemia (haemoglobin 128 g/l) with deficiencies of iron (3 umol/l) and vitamin B12 (149 ng/l). He was subsequently commenced on

ferrous fumarate 210 mg twice daily and vitamin B12 intramuscular injections. In view of his micronutrient status, he was advised to increase his daily calorific intake to a total of 1200 kcal with the addition of small meals. After 16 weeks, he underwent a successful left laparoscopic adrenalectomy for definitive treatment of his phaeochromocytoma. The operation was a success with no immediate complications and he was discharged home a couple of days later. He was followed up in clinic after a fortnight, at which point his weight was 105 kg (15% weight reduction from baseline). This case illustrates the results that can be attained through strict adherence to a VLCD in combination with GLP-1 agonist therapy, at the same time as the need to closely monitor for nutritional deficiencies.

DOI: 10.1530/endoabs.100.WG4.1

WG5.1

Orlistat – the forgotten drug

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Introduction
Obesity is a chronic disease which becoming a worldwide pandemic. In the UK it's estimated that around one in every four adults living with obesity. The mainstay of intervention to manage weight is lifestyle modification includes eating a healthy, reduced-calorie diet and regular exercise. There are different pharmacological therapy agents for medical management of obesity, However, currently NICE recommended weight-loss agents are limited to Orlistat and GLP-1 RAs includes liraglutide and semaglutide. Mechanism of action of orlistat is inhibiting the absorption of dietary fats via the inhibition of lipase enzymes.

Case history
A 60-year-old female has been referred by the Surgical Tier 4 Services for consideration of medical management while she awaits a laparoscopic sleeve gastrectomy. As far as her weight is concerned, she describes herself been overweight since she was a child and she reported to gain more weight gradually with a period over the last six decades. She has tried multiple diets and increasing her physical activity over the years, but this has not been sustainable. Her past medical history includes hypertension, obstructive sleep apnoea on CPAP and pancreatitis secondary to gallstones. She had strong family history of obesity. The diagnosis of lymphoedema has also not helped with performing regular exercise. The only medication she takes is Ramipril. Examination did not show signs of endocrinopathy, and Bariatric blood screen was not significant including full blood counts, liver function, bone profile, folate, vitamin B12, vitamin D, Iron study, CRP, thyroid function, HbA1c, renal Function and lipid Profile.
Management
The most significant success to weight loss was achieved through lifestyle modification and also taking orlistat about 20 years ago when she manged to lose significant amount of weight but because of the gastrointestinal side effects she had in the past she never went back on orlistat again. Her recent weight was 237.6 kg with a height of 181.5 cm making a BMI of 72.1 kg/m^2. She has been advised to change her lifestyle again by reducing portion sizes, reducing the number of takeaways and restarted on Orlistat. She has also looked into online courses for increasing exercises but it was unaffordable for her. She has lost 10.2 kilogram in 6 weeks.
Discussion
This case illustrates significant weight reduction with lifestyle modification combined with orlistat. As currently there is national shortage of GLP1 agonists, therefore the option of orlistat should be considered as pharmacological option for weight management

DOI: 10.1530/endoabs.100.WG5.1

Workshop H: Miscellaneous endocrine and metabolic disorders

WH1.1

An interesting case of severe hypoglycaemia with neurological symptoms in a patient with no history of diabetes

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Case presentation
A 43 year old female patient presented to the Emergency Department (ED) after a seizure episode in which the patient was confused, with repetitive movements of her upper limbs touching the left side of her face. This episode lasted 5 minutes, and the patient was confused for 45 minutes following this. Her mother telephoned an ambulance, and on arrival of the paramedics, her capillary glucose was found to be 1.5 mmol/l. The severe hypoglycaemic episode was treated with intravenous 250 ml 10% glucose × 2, and the patient was brought to ED for assessment. The ED team referred her for endocrine review. A short synacthen test was performed which was normal with a time 0 cortisol of 325 and 30 minute cortisol 560. Three overnight fasting insulin C peptides were sent which showed mild hypoglycaemia each morning with inappropriately elevated insulin and C peptide, consistent with endogenous insulin excess. A CT abdomen was reported as normal appearances of the pancreas. An MRI head was normal. The patient was reviewed by the neurology team- seizure due to hypoglycaemia. An MRI pancreas subsequently revealed a pancreatic lesion and the patient was referred to the regional neuroendocrine Multidisciplinary Team (MDT) for review. She underwent an ultrasound guided biopsy of the pancreatic lesion which confirmed an insulinoma. The biopsy appears to have had a therapeutic benefit by removing some of the culprit cells because the patient's hypoglycaemic episodes have reduced following the biopsy. The patient has been referred to the pancreatic surgical team to consider surgical removal of the lesion or interventional radiology guided ablation. If her hypoglycaemic episodes re occur, she will be commenced on diazoxide pending definitive surgical or interventional radiology guided ablation management.
Learning point
This case demonstrates the importance of biochemical investigation for unexplained hypoglycaemia in patients without diabetes, as the initial CT imaging showed normal pancreatic appearances, but the raised insulin C peptide biochemical result confirmed endogenous insulin excess which prompted further imaging with an MRI pancreas. The MRI pancreas was able to identify a pancreatic lesion. The patient had a therapeutic benefit from the biopsy, and has been referred for definitive management with surgical excision of the pancreatic insulinoma or ablation. The patient had previous surgery for an incisional hernia repair, and therefore may opt for ablation due to increased technical difficulty of the surgery which is being discussed with the pancreatic surgical team.

DOI: 10.1530/endoabs.100.WH1.1

WH1.2

Unmasking the hidden culprit: a case report on hypoglycemia stemming from pancreatic insulinoma

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A 76 year-old male was admitted to hospital after an episode of dysarthria and right upper limb weakness. On initial assessment by the pre-hospital team, a capillary blood glucose of 2.9 mmol/l was found and symptoms and signs resolved upon correction with intravenous (IV) 10% dextrose. The patient reported a six month history of episodic episodes of tremors, diaphoresis and fatigue, without loss of consciousness. Occurring mostly late in the morning when he skips breakfast and resolves after eating. No weightloss. Past medical history includes ischemic heart disease, needing CABG 15 years ago, and dyslipidaemia. Drug history includes aspirin, atorvastatin and perindopril. No history of impaired glucose metabolism or diabetes mellitus from past medical visits or biochemical tests. No signs of hereditary endocrine disease in patient or relatives. On clinical assessment, the patient was hemodynamically stable with no abnormal systemic findings and a BMI of 27 kg/m^2. Initial blood test were all normal - including thyroid function tests, random morning cortisol (512 nmol/l), random glucose of 4.8 mmol/l and Hba1 c of 5.2%. CT brain was normal. The patient was kept as an inpatient for a fasting test giving the clinical history of Whipple's triad. 5 hours into the fast, the patient complained of lethargy and sweating, his capillary blood glucose was 2.5 mmol/l and urgent bloods during the hypoglycaemic episodes were taken - C-peptide, insulin, pro-insulin, Beta-hydroxybutyrate, plasma glucose, insulin antibodies and urine for sulphonylurea screen. Hypoglycaemia was corrected with oral agents and patient's symptoms resolved. Biochemical evaluation was in keeping with endogenous hyperinsulinemia (**Table 1**). A CT of the pancreas showed a 2.4 × 1.5 cm lesion at the body-tail junction of the pancreas with no signs of nodal involvement or metastasis. A 68-Ga-DOTA scan was also done, showing a focus of increased tracer uptake at the known pancreatic site, in keeping with a pancreatic neuroendocrine tumour (insulinoma). Chromogranin A was taken (108.38 ng/ml, normal <108). The patient underwent spleen-preserving distal pancreatectomy as curative intent. Histology showed a Grade II pancreatic endocrine tumour, R0, TNM: pT2 pNX with a Ki-67 index of 3%. He was doing well and with complete resolution of symptoms. A repeat CT scan 3 months post-op showed successful removal of the lesion with no signs of recurrency.

Table 1.

Symptoms of hypoglycaemia	Glucose (mmol/l)	Insulin (μU/ml)	Proinsulin (pmol/l)	C-peptide (nmol/l)	β-Hydroxybutyrate (mmol/l)	Antibodies to insulin	Sulphonylurea urine screen
Yes	2.17	37.5	139.0	1.2	0.06	Negative	Negative

DOI: 10.1530/endoabs.100.WH1.2

WH1.3

Unusual cause of confusion

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Non-Islet Cell Tumour Hypoglycaemia (NICTH) is a rare paraneoplastic phenomenon caused by aberrant production of pro-IGF-II from tumours, usually mesenchymal or epithelial in origin. Previous case studies report significant reduction in hypoglycaemia with tumour resection, while medical therapy with glucocorticoids and sometimes growth hormone has reduced the frequency of events in some cases. A 63 year old non-diabetic lady presented with a collapse and episodes of fatigue, disorientation and confusion. Her medical history included ulcerative colitis treated with colectomy, during which peritoneal nodules were noted and biopsy showed a fibrous tumour of uncertain malignant potential. On this occasion, transient ischaemic attack and possible early dementia were thought to have caused her presentation, but a thorough history by her GP prompted further investigation, which revealed a fasting hypoglycaemia of 1.6 mmol/l. Admission for a 72-hour fast was arranged and blood samples taken during a hypoglycaemic event revealed low insulin <10 pmol/l and C-peptide <94 pmol/l. Further analysis found a raised IGF-II:IGF-I ratio 26.3 (<10), consistent with a diagnosis of Non-Islet Cell Tumour Hypoglycaemia (NICTH). Imaging revealed a large pelvic mass, confirmed on biopsy as solitary fibrous tumour. A debulking procedure was planned. Meanwhile, she was taught to self-monitor and manage episodes of hypoglycaemia. These became less frequent with the addition of prednisolone 20 mg, but continued to occur even after surgery. Previous cases reports have shown little benefit from diazoxide or octreotide. Over the course of 3 years she developed progressive cognitive impairment, thought to be due to recurrent hypoglycaemic state. During her final admission she was unable to continue with oral intake and glucose was maintained with IV dextrose and IV hydrocortisone. A palliative approach was adopted as no further treatment options were available. Non-Islet Cell Tumour Hypoglycaemia is a rare paraneoplastic phenomenon caused by aberrant production of pro-IGF-II from tumours, usually mesenchymal or epithelial in origin. Previous case studies report significant reduction in hypoglycaemia with tumour resection, while medical therapy with glucocorticoids and sometimes growth hormone has reduced the frequency of events in some cases. This case demonstrates that it can be difficult to diagnose recurrent hypoglycaemia and NICTH as the vague symptoms can be misinterpreted as more common illnesses. Therefore it may be worth considering hypoglycaemia when investigating patients presenting with symptoms such as confusion or collapse.

DOI: 10.1530/endoabs.100.WH1.3

WH1.4

An unforeseen carcinoid crisis

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A 64-year old female presented to the emergency department with a three week history of worsening shortness of breath, palpitations and fatigue. In the preceding 5 years, she was reviewed by various specialists for diarrhoea, nausea, palpitations, shortness of breath, weight loss and fatigue. The colorectal team organised a CT chest abdomen pelvis (CTCAP) in 2020, which reported multiple mesenteric, para-aortic and mediastinal lymphadenopathy. No masses were

identified. Her chronic diarrhoea was thought to be attributed to bile acid malabsorption. She was referred to Haematology to investigate for a possible lymphoproliferative disorder. Immunophenotyping and bloods were generally unremarkable. Biopsy of a mesenteric lymph node was not successful. It was assumed that the lymphadenopathy was secondary to autoimmune disease as she is known to have Sjogren's disease. She recently underwent an aortic, mitral and tricuspid valve replacement for severe regurgitation and is on diuretics for heart failure. She also was diagnosed with recurrent atrial flutter. During this admission, she was in atrial flutter and had pitting oedema up to her sacrum. She was treated with rate control and a furosemide infusion. Echocardiogram showed reduced longitudinal function of the right ventricle but was otherwise unremarkable. A repeat CTCAP was performed due to ongoing weight loss. Multiple lymph nodes above and below the diaphragm were identified, similar to previous scans. However, a new finding of a soft tissue mass in the central mesentery was also reported. The mass was biopsied via ultrasound guidance. Shortly after the biopsy, the patient became unwell with vomiting, tremors, and went into hypotensive shock. She was transferred to ITU for inotropic support. CT angiogram did not identify any signs of active haemorrhage. However, the development of multiple nodules within the lung bilaterally concerning for pulmonary metastases was reported. Histology came as back as a grade 1 well differentiated neuroendocrine tumour. She was then started on an octreotide infusion, as well as dexamethasone and cyproheptadine. The 24-hour urine 5-HIAA result is pending. This case demonstrates that carcinoid syndrome should be considered in patients who have non-specific symptoms and valvular heart disease, as 50% of patients with carcinoid syndrome have carcinoid heart disease. Furthermore, if carcinoid is suspected by a raised urine 5-HIAA, treatment with somatostatin analogues prior to biopsy can help reduce to risk of precipitating a carcinoid crisis.

DOI: 10.1530/endoabs.100.WH1.4

WH2.1

A case of treatment refractory hypoglycaemia secondary to metastatic insulinoma with complicated course

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Insulinomas are functional pancreatic tumours which is mostly benign. Malignant disease is rare with variable course. Much remains unknown with regards to clinical trajectory as well as response to treatment to the commonly used agents between a benign or malignant disease. 70-year-old-man, very fit enthusiastic cyclist a month before initial presentation at another hospital with collapse, blood glucose of 2.4 and mild eosinophilia at which point Addison disease was explored. At his second visit with recurrent episodes of light-headedness and confusion especially during fasting, he was diagnosed with hyper-insulinemic hypoglycaemia and abdominal CT scan confirmed a large pancreatic mass in the body and tail with vascular infiltration, regional lymphadenopathy and numerous bilobar hepatic metastasis. He had a liver biopsy which was inconclusive and started on Diazoxide before discharge. He was only home a single night when he developed severe nausea and further severe hypoglycaemia and admitted to our hospital. He was initially managed with titrating dose of diazoxide, anti-emetics, Lanreotide, Acarbose in addition to repeating his biopsy. However, he developed significant fluid overload and electrolyte derangements thus diazoxide was stopped which precipitated further severe hypos despite the other agents. He was therefore restarted on diazoxide at lower dose and with glycaemic stabilisation, he was discharged. He was re-admitted a day after with seizures, severe electrolyte derangements, fluid overload and further severe hypos requiring ITU care. Diazoxide was discontinued and he was started on high dose dexamethasone and verapamil in addition to aforementioned agents and supportive care including IV Dextrose, NG feeding (unable to tolerate) and CGM (difficulty to manage) until hypos became manageable at the ward level with ongoing 6-8 episodes/day. The repeat biopsy confirmed Grade 2 neuroendocrine tumour which are MNF116, synaptophysin and chromogranin positive with Ki67 of 10%, liver MRI showed 15-20% parenchymal volume liver metastasis and delayed functional scan. He was subsequently started on Everolimus with short-lived partial response but still significant hypoglycaemia Dextrose dependent. Admission was also complicated by hospital acquired pneumonia, right arm DVT. Neuroendocrine MDT advised chemotherapy (CAPTEM) which led to significant metabolic control at about 6 weeks of starting and patient discharged after weaning Dextrose on weaning regimen of steroid and NG feeding. This patient has an extensive aggressive resistant insulinoma and despite being tried on multiple agents, sustained and significant metabolic control could not be achieved until chemotherapy was used. He developed multiple complications with significant impact on quality of life.

DOI: 10.1530/endoabs.100.WH2.1

WH2.2

A case of type 2 diabetes masked by insulinoma

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Introduction

Insulinomas are the most common functioning endocrine neoplasms of the pancreas. 53% of patients are diagnosed within five years of experiencing their first symptoms. Surgical resection is the primary treatment modality. However, patients awaiting surgery or who are not surgical candidates have achieved symptomatic relief from medical therapy. Cases of insulinoma masking diabetes has been described but are rare and diabetes often presents following surgery. Here, we describe a case of insulinoma diagnosed four years after symptom onset with unmasking of type 2 diabetes mellitus following initiation of medical treatment.

Clinical case

An 89-year-old woman presented with severe hypoglycaemia, having been found by relatives in bed with neuroglycopenic symptoms. Capillary blood glucose was 1.4 mmol/l. She was given intramuscular Glucagon by paramedics. Upon further questioning, the patient reported having one to two similar episodes of hypoglycaemia per month over the past four years, which she was self-correcting at home or by help of the ambulance service. Pituitary, liver and renal profiles were within normal limits. During the admission, the patient underwent a prolonged fasting test. Although nadir blood glucose achieved was 2.5 mmol/l due to significant symptom, hypoglycaemia screen revealed high level of C-peptide 2885 pmol/l (370-1470) though normal insulin (64 pmol/l) and beta-hydroxybutyrate levels (0.1 mmol/l) at hypoglycaemia episode. CT pancreas revealed a 14.5 mm enhancing nodule on the body of the pancreas consistent with a neuroendocrine tumour, which was confirmed by MRI imaging. After discussion at the MDT, the patient was started on diazoxide 50 mg TDS. A dotatate-PET scan was arranged, and she was listed for surgery. Blood glucose was in range after starting diazoxide. However, the patient was readmitted after one month with hyperglycaemia (37.1 mmol/l), fever, cough, and bilateral pitting oedema. Diazoxide was held and she was commenced on oral antihyperglycaemic agents, and then eventually switched to insulin management. Unfortunately, the patient deteriorated during the admission and passed away.

Discussion

Our case highlights the challenges with the diagnosis of insulinoma and how insulinoma can mask undiagnosed type 2 diabetes. This also highlights the importance of continuing glucose monitoring after starting medical management for insulinoma, even if stable glycaemia has been initially achieved.

DOI: 10.1530/endoabs.100.WH2.2

WH2.3

A case of non islet cell tumour hypoglycaemia

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Non-islet cell tumour hypoglycaemia (NICTH) is a relatively rare form of hypoglycaemia affecting patients with solid tumours originating from mesenchymal and epithelial cells. The hypoglycaemia is due to the excessive secretion by these tumours of high molecular weight insulin-like growth factor (IGF)-2 or pro IGF-2 which stimulate the insulin receptor and suppresses GH secretion by negative feedback mechanism, resulting in hypoglycaemia. The causative tumours may present with hypoglycaemia which may also present first and lead to the diagnosis of the tumour. The hypoglycaemic episodes may become more frequent and severe resulting in serious and detrimental effects on quality of life. Complete surgical removal of the causative tumour may be curative. Otherwise, high doses of long-term glucocorticoids may be required to prevent hypoglycaemia. We are presenting a 67-year-old male who presented to our emergency department in October 2023 with hypoglycaemia. He gave history of episodes of hypoglycaemia which started and increased in frequency over the preceding 4 to 5 weeks, associated with blurring of vision, sweating and confusion. In 2017 he was diagnosed with a jejunal gastrointestinal stromal tumour (GIST), with liver and omental metastases and treated with Imatinib till March 2023. Of late the disease progressed, but could not be started on Umatinib, a second line medication, due to his other associated illnesses of heart failure, chronic renal impairment (CKD3) and atrial fibrillation. Following infusion of high concentration dextrose, he was given intravenous hydrocortisone, then switched to oral prednisolone of which he was discharged on 60 mg per day, with a plan to gradually reduced to 40 mg to prevent hypoglycaemia.

Conclusion
Patients with GISTs, who show tendency to persistent hypoglycaemia, should be routinely evaluated for NICTH from the outset. Complete removal of the underlying tumour should be performed if possible. Otherwise, adequate dosing with glucocorticoids may be helpful.

DOI: 10.1530/endoabs.100.WH2.3

WH2.4

Mind your PJPs and coombs

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A previously fit and well 29-year-old male presented with an 8-month history of progressive facial and peripheral swelling, accompanied by generalised weakness, weight gain, nocturia and a 2 year history of left-sided abdominal pain. He was originally from Ghana and moved to the UK in 2022 with limited family support. On examination he was hypertensive (157/108 mmHg) with facial fullness, dry skin, proximal muscle weakness, conjunctival injection and haematomata at recent venepuncture sites. Abdominal examination revealed a palpable large left upper quadrant mass. Blood tests demonstrated profound hypokalaemia (2.7 mmol/l [3.5- 5.3]) with a metabolic alkalosis (pH 7.49 [7.32-7.43], bicarbonate 34.8 mmol/l [22-29]). He was also thrombocytopaenic (93 × 10^9/l [150-410], had an elevated AST (68 u/l [0-41]) and HbA1 c of 55 mmol/mol [20-41]. His free T4 was low (6.3 pmol/l [10.5-24.5]) with a TSH of 1.19 mU/l [0.27-4.2]. Serum cortisol levels taken at various time points, including midnight, ranged between 1971 and 2658 nmol/l. His ACTH was elevated at 184 ng/l [<50]. Cross-sectional imaging identified a 13 cm heterogenous mass arising from the tail of the pancreas, multiple liver lesions consistent with metastases and hyperplastic adrenal glands. A diagnosis of an ectopic ACTH-secreting pancreatic neuroendocrine tumour with liver metastases and associated nephrogenic diabetes, secondary to severe hypokalaemia, was made. He was commenced on metyrapone, which was uptitrated to 500/500/750 mg, and hydrocortisone 5 mg twice a day was later added. He was also treated with spironolactone and amiloride. Pancreatic biopsy confirmed a neuroendocrine tumour with a Ki-67 of <2%. His inpatient stay was complicated by acute respiratory failure secondary to pneumocystis jirovecii pneumonia (PJP), and treatment with co-trimoxazole resulted in a drug-induced acute haemolytic anaemia. This necessitated discontinuation of co-trimoxazole and a short course of high dose prednisolone. PJP treatment was completed with oral clindamycin and primaquine. Subsequent functional imaging confirmed FDG- and DOTATATE- avidity in the pancreatic tumour but most of the liver deposits were not DOTATATE-avid. His case was reviewed in the regional hepatobiliary multidisciplinary team meeting and the tumour was deemed inoperable with no suitable targets for ablation. He was commenced on monthly lanreotide alongside his block-and-replace regimen. He reports symptomatic improvement and his HbA1 c has normalised. Follow-up imaging will be arranged in due course.

DOI: 10.1530/endoabs.100.WH2.4

WH3.1

A case of insulinoma in a young adult man

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Background
An insulinoma is a rare pancreatic neuroendocrine tumour. The incidence is about four cases per million individuals per year. The most common presentation of insulinoma is fasting hypoglycaemia with associated neuroglycopenic symptoms. They are commonly sporadic, usually small in size and majority are benign in nature. A few cases have been associated with genetic mutations.
Clinical Case
A 26-year-old man presented to the endocrine clinic with episodes of symptomatic hypoglycaemia for the last two years. His hypoglycaemic symptoms consisted of intermittent pins and needles sensations in his limbs, blurred vision and occasionally change in behaviour. These episodes were relieved by intake of sugary drinks or snacks. He was not known to have any family history to suggest MEN1 syndrome. He attended emergency department on one occasion with severe hypoglycaemia and a laboratory glucose of 0.6 mol/l. His cortisol, bone, thyroid and renal profile were all within normal values. His systemic examination was unremarkable. Further evaluation of his biochemistry showed low fasting glucose (1.9 mmol/l), raised insulin (78 pmol/l), raised c-peptide (530 pmol/l), low beta-hydroxybutyrate (64 micromol/l), in keeping with insulin-mediated hypoglycaemia. His IGF-2 : IGF-I ratio was not in keeping with IGF-2 mediated hypoglycaemia. He had an initial CT triple phase scan done that showed a small hypervascular focus on the head of pancreas. A follow up MRI of his pancreas showed a 15 mm exophytic focus adjacent to the head of the pancreas which was consistent with a primitive neuroectodermal tumour (PNET). He had a DOTATATE PET CT which revealed increased DOTATATE avidity in the pancreatic head mass consistent with neuroendocrine tumour but no evidence of metastatic disease. EUS was suggestive of three lesions on the pancreatic head. He subsequently underwent surgical resection of the tumour (open Whipples's procedure). Histopathology confirmed the diagnosis of a Grade 1 insulinoma, a 22 mm well differentiated neuroendocrine tumour, pT2pN0, Ki-67 <1%, MMR proficient with no nodal metastasis. He had good post-operative recovery with resolution of symptoms.
Conclusion
Insulinomas are rare neuroendocrine tumours. The treatment of choice is usually that of surgical excision of the tumour. After surgical treatment, the majority of patients are cured from the disease. For patients who are not candidates for surgical resection, medical treatment could be explored as an alternative option. Clinicians should have a high index of suspicion in patients who present with recurrent episodes of symptomatic hypoglycaemia particularly if they are resolved after eating.

DOI: 10.1530/endoabs.100.WH3.1

WH3.2

From cardiology to endocrinology: decoding the mystery of insulinoma mimicking cardiac symptoms

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We present a case of a 45-year-old female referred from cardiology with a history of blackouts and palpitations. Initial investigations by GP revealed T-wave changes on ECG, prompting further evaluations, including 24-hour Holter ECG and echocardiogram. Despite extensive cardiac investigations, the patient's symptoms persisted, leading to referral to the endocrine clinic. The patient reported frequent episodes of hypoglycaemias-associated symptoms such as excessive eating, blackouts, and fainting. Endocrine evaluation revealed normal short synecthen Test and following that non-suppressed insulin levels with elevated C-peptide during a 72-hour fasting period. A contrast-enhanced CT scan of the pancreas unveiled an enhancing lesion, raising suspicion for insulinoma. The patient was promptly referred to the Neuroendocrine Multidisciplinary Team (MDT) for comprehensive evaluation. Additional tests, including gut hormone profiling and CA 19-9, along with urine metanephrines returned normal results, ruling out other endocrine causes. While awaiting an endoscopic ultrasound (EUS)-guided biopsy for lesion confirmation, the patient was initiated on Diazoxide to manage hypoglycaemias. The biopsy, following discussion in the MDT, confirmed the presence of a neuroendocrine tumor, specifically an insulinoma. The patient was subsequently scheduled for surgical intervention. This case underscores the importance of considering endocrine causes in patients with persistent symptoms despite thorough cardiac evaluations. The atypical presentation of insulinoma as cardiac symptoms highlights the importance of thorough history taking during initial assessment and consideration of hypoglycaemia as a differential diagnosis in patients with ECG changes presenting with such symptoms. In cases where hypoglycaemia is suspected, assessing insulin and C-peptide levels during fasting is crucial for diagnosis. Our experience emphasizes the value of a multidisciplinary approach, involving neuroendocrine specialists, for accurate diagnosis and timely management of insulinomas.

DOI: 10.1530/endoabs.100.WH3.2

WH3.3

Idiopathic ketotic hypoglycaemia in an adult male

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Idiopathic ketotic hypoglycaemia is cited as the most frequent cause of hypoglycaemia in childhood but is a rare phenomenon in adults. We present the case of a 72 year man without diabetes presenting to the emergency department with spontaneous symptomatic hypoglycaemia with a glucose of 2.2 mmol/l. On admission he had a normal pituitary profile, negative insulin antibodies, a normal short synacthen test, a negative urine and serum sulphonylurea screen and a normal IGF-II and IBF BP3. A collateral history revealed he had lost weight in the months preceding admission and frequently skipped meals. The day prior to admission he had eaten less than usual and gone on a long walk He underwent a 72 hour fast as an inpatient during which time his blood glucose dropped to 2.8 mmol/l after 48 hours with an appropriately suppressed insulin, C-peptide and pro-insulin. Interestingly his beta hydroxybutyrate level was undetectably high at >5 mmol/l. His blood glucose normalised with refeeding and he was discharged with a glucometer and education from a diabetes nurse specialist. Following discharge this gentleman went on to have a prolonged oral glucose tolerance test which revealed some mild post prandial hypoglycaemia which was also felt to be a contributing factor to his presentation. He was diagnosed as having idiopathic ketotic hypoglycaemia and mild reactive post prandial hypoglycaemia. He was followed for an 18 month period during which time he was advised to eat more frequent meals and avoid periods of prolonged starvation which lead to complete resolution of his hypos and he was subsequently discharged from clinic without issue.

DOI: 10.1530/endoabs.100.WH3.3

WH4.1

Insulinoma presenting with asymptomatic hypoglycemia

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Ms T. B. is a 72-year-old retired teacher referred with asymptomatic hypoglycemia found on screening for diabetes with fasting plasma glucose 1.8 mmol/l, HbA1 c 23 mmol/mol (4.3%). On repeated questioning, denies any symptoms of neuroglycopenia or autonomic activation even after prolonged fasting. Her only symptom is a 1.5 kg weight gain over the past 6 months.

Social

Ms. T.B. is a nonsmoker and nondrinker. She is divorced, with 2 children. On the basis of her own extensive research, she believes that she should not be vaccinated for COVID-19 and has, accordingly, not done so. Says she distrusts pharmaceutical industry and most doctors.

Drugs

Current medications: zopiclone and cannabis p.r.n. for insomnia. No drug adverse events reported.

Past medical history

Remote episode of nephrolithiasis tought to be due to primary hypercalciuria (Ca, PTH mid-range). No features suggestive of NET, MEN1 or diabetes.

Family

Nil significant. No NET, no MEN, no nephrolithiasis, no diabetes or family members in health care.

Physical examination

43 kg well-looking woman. No significant findings.

Laboratory investigations

Morning cortisol (0944): 205 nmol/l, short synacthen 305 $\rightarrow$891 nmol/l Fasting plasma glucose: 2.5 mmol/l Insulin: 31 (13-161) pmol/l C-peptide: 503 (298-2350) pmol/l Proinsulin: 83.8 ($<$18.8) pmol/l Plasma ß-OH-butyrate: 0.17 (0.00-0.42) mmol/l, urinary ketones -ve Sulphonylurea drug screen: not available

Imaging

Radiology recommended triphasic CT, declined by patient in favour of MRCP. 3.3 cm enhancing solid mass in the pancreatic tail and complex septated cyst in the pancreatic head, probably a sidebranch IPMN. Mild central intrahepatic and extrahepatic bile duct dilatation probably due to the mass effect of the cystic mass in the pancreatic head.

Surgery

Distal pancreatic resection with splenectomy. Declines more extensive surgery.

Pathology

3.3 cm G3 PNET (Ki67 27%) with 2 of 5 regional lymph nodes showing evidence of metastatic spread.

Follow up post op

HbA1 c risen from 23 (4.3%) to 38 mmol/mol (5.6%). Fasting glucose risen from 1.8, 2.5 to 6.0 mmol/l. Repeat MRI suggestive of numerous, small intra-heaptic metastases Declines further follow-up, investigation, or treatment.

DOI: 10.1530/endoabs.100.WH4.1

WH4.2

Insulin-dependent spontaneous hypoglycaemia: where is the lesion?

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Case report

A 47-year-old lady presented to the Emergency Department (ED) with an episode of dizziness, sweating and palpitations. On ambulance arrival CBG was low at 2.2 mmol/l, and symptoms resolved after treatment of hypoglycaemia. She had first noticed these symptoms eight years ago when fasting for Ramadan. However over the past two years she had experienced episodes multiple times per day, relieved by sugary food or drinks. She occasionally woke at night with symptoms but there was no specific correlation with time or meals. She had gained 20 kg weight unintentionally over the past two years. Systems review was unremarkable. Past medical history was significant for depression, treated with sertraline 50 mg. She took no other medications or supplements and denied insulin or sulphonylurea use. There was a strong family history of type 2 diabetes mellitus (father, paternal grandfather and uncle). She was unemployed and did not consume alcohol or recreational drugs. On arrival in ED observations were unremarkable with a CBG of 5 mmol/l. There were no clinical signs of endocrinopathy and examination was unremarkable. Further investigations showed a 9 AM cortisol of 568 nmol/l and HbA1 C 38 mmol/mol. Sertraline was stopped. An inpatient 72 hour fast elicited hypoglycaemia at 60 hours. Lab results confirmed hypoglycaemia (1.8 mmol/l) with inappropriately normal C-peptide 709 pmol/l (366-1465 pmol/l) and insulin 76 pmol/l (21-175 pmol/l). Urine sulphonylurea screen was negative. Diazoxide 100 mg t.d.s. was commenced. Freestyle LibreView 2 sensor was supplied and demonstrated improvement in hypoglycaemia, to a glucose range of 6-11 mmol/l. CT pancreas showed no pancreatic lesions. Gallium-68 DOTATATE scan showed no avid lesions. She is currently awaiting endoscopic ultrasound (EUS) for further work-up.

Discussion

The most likely diagnosis in this case is insulinoma, a rare but important condition. Diagnosis is frequently delayed, as in this case, due to the non-specific presenting symptoms. A careful history and investigation is required, with biochemical confirmation of inappropriate endogenous insulin secretion must be sought before proceeding to imaging. Biochemistry demonstrates raised or inappropriately normal C-peptide and insulin at the time of hypoglycaemia. Differential diagnoses of this biochemical picture including sulphonylurea intake, nesidioblastosis and insulin autoantibodies. Most cases are benign and surgical treatment is generally very effective, but this case highlights the challenges in localising a surgical target. CT pancreas has a sensitivity of around 54% (1) and even EUS only 81% (2). Arterial calcium stimulated venous sampling may be required in particularly elusive cases.

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DOI: 10.1530/endoabs.100.WH4.2

WH4.3

Recurrent severe hypoglycaemia: think about antibiotic choice

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A 64 year-old Caucasian woman was admitted with a five-week history of lethargy, sore throat and dyspnoea, and diarrhoea with intermittent rectal bleeding, with a collapse on the morning of admission. She presented to the Emergency Department via ambulance and was found to be profoundly unwell with cold sepsis. She had a background of rheumatoid arthritis treated with weekly methotrexate, with no history of diabetes or long-term steroid-use. Blood tests revealed pancytopaenia, secondary to methotrexate (stopped on admission), acute kidney injury and severe metabolic acidosis. CT angiogram demonstrated lung base ground-glass changes, the patient had been double-vaccinated for COVID-19 and all COVID swabs were negative. Despite receiving a course of intravenous Tazocin, respiratory symptoms worsened. On the advice of our local Respiratory and Infectious Diseases teams, treatment-dose co-trimoxazole (at 120 mg/kg/day in split doses) with a short course of prednisolone 30 mg daily was commenced for suspected Pneumocystis pneumonia from being immunocompromised. Over the next ten days she developed new-onset confusion, reduced appetite and a random blood glucose at midday was found to be 1.2 mmol/l. After

treatment, hypoglycaemia recurred and persisted despite repeated intravenous dextrose boluses and glucagon injection. Blood glucose improved only with continuous 10% dextrose infusion. Causes were explored – a normal 9 am cortisol ruled out adrenal insufficiency, and a recent CT scan showed no pancreatic or other intra-abdominal pathology. When serum glucose was 3.3 mmol/l, C-peptide measured was found to be inappropriately high (5175 pmol/l). A literature review revealed rarely Co-trimoxazole can cause hypoglycaemia at higher doses, hence this medication was stopped. Hypoglycaemia subsequently resolved and confusion improved within 48 hours. Co-trimoxazole is biochemically similar to sulfonylureas, mimicking their action on pancreatic beta-cells. Endogenous insulin hypersecretion resulted in raised C-peptide levels during the hypoglycaemic phase. As Co-trimoxazole is renally excreted, when renal function is impaired it accumulates further, with exacerbation of side effects such as protracted hypoglycaemia, especially at higher doses, as in our case. Hypoglycaemia will likely resolve after a 24-48 hour washout period, especially if renal function improves back to baseline. We recommend awareness of hypoglycaemia risk with high-dose co-trimoxazole treatment and blood glucose monitoring for inpatients especially in the setting of renal impairment.

DOI: 10.1530/endoabs.100.WH4.3

WH5.1

Symptomatic hypoglycaemia

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47 M Presented with increasingly frequent unresponsiveness and hypoglycaemia. Systemic review revealed a recent pattern of similar events, associated profuse sweating and uncharacteristic aggression. The patient had poor memory of the events but reported his symptoms improved by eating and he had gained weight. He also reported eating overnight. Past medical history included a Vasectomy and Haemorrhoids A 72 hour fast was terminated after symptomatic hypoglycaemia at 16 hours of 2.2 mmol/l on capillary blood glucose. Lab results at time as table. Hypoglycaemia was managed with Diazoxide 150 mg PO TDS and the patient was taught self-monitoring of blood glucose and administration of glucagon to allow further investigation as outpatient. Initial CT imaging found no evidence of a pancreatic malignancy or mass. Neuroendocrine MDT review recommended Octreotide scan and arterial phase CT. These were also negative. Endoscopic ultrasound was arranged followed by MRI pancreas which confirmed the lesion seen on ultrasound as a 1.9 cm exophytic mass arising from the posterior aspect of the pancreas adjacent to the splenic artery.

			range
Glucose	1.6	mmol/l	3 – 7.8
Insulin	9.4	mIU/l	<5 during Hypo
C-Peptide	1175.0	pmol/l	0-480
Beta-Hydroxybutyrate	110	umol/l	<300
Free Fatty Acid	640	umol/l	100 – 900
Sulphonylurea screen	Negative		
Insulin/Pro-insulin/ C-peptide	4145/616/690	pmol/l	All inappropriately high
Chromogranin A&B	Normal		

Curative surgical management was achieved with a distal pancreatectomy for insulinoma with a histologically well differentiated insulinoma grade 2 R0, 0/3 lymph nodes (pT2 pN0). Post operative course was complicated by duodenal obstruction requiring total parenteral nutrition. Post insulinoma symptomatic sensory and motor neuropathy with chronic fatigue are an ongoing problem. MEN1 testing negative.

DOI: 10.1530/endoabs.100.WH5.1

WH5.2

Ketogenic diet for weight loss revealed an underlying medical condition!!

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51 year male ex-professional hockey player, now works as a coach 2 years ago had knee injury and was less active. He gained 3 stone weight over 2 years and feels that he needs to eat more. Started ketogenic diet (PronoCal) for trying to lose weight. The day after starting this diet spent one hour in gym and whilst playing tennis developed double vision. Then he ate lunch at 12 pm mostly protein and vegetables. Che had conference call at work between 4-5 pm and his writing was illegible during that time. Then he had protein bar and went to sleep. Found by wife at 20:30 lying in bed, before becoming acutely confused at 01:00 in the morning. At that time patient was half off bed, bizarre behaviour, confused and slurred speech. Ambulance was called his blood glucose was found to be 2.2 mol/l and confusion improved when given glucogel. He was then admitted to hospital, denies any use of medication or supplement. He also mentions that his wife has noticed that he sweats a lot and will occasionally be tachypnoeic at night. On further questioning remembers having few episodes of feeling lightheaded last year, like he needs sugar. This usually occur in evening after meals and hasn't noticed similar symptoms in the mornings, but does feel like needs an early lunch sometimes. Brain imaging was nil significant. After prolonged fasting as inpatient while blood glucose was 2.1 mmol/l serum insulin 267 pmol/l and c-peptide high at 1015 pmol/l with negative sulphonylurea screen. CT pancreas showed 18 mm lesion arising from tail of pancreas. Endoscopic ultrasound showed 2.4 × 9.1 hypoechoic vascular mass inferior to pancreatic tail. NM Ga68 DOTATATE whole body PET CT showed no definite dotatate avid focus suspicious for insulinoma. He was discharged on diazoxide but couldn't tolerate due to side effects. Subsequently patient had distal pancreatectomy and splenectomy. Histology of the mass confirmed grade 2 well differentiated pancreatic linsulinoma with MIB-1,6-10%. Insulinomas, the most common cause of hypoglycemia related to endogenous hyperinsulinism, occur in 1-4 people per million of the general population. Delays in the diagnosis of insulinoma are common because the symptoms usually precede detection of a tumor and there may be misattribution of the symptoms to psychiatric, cardiac, or neurological disorders. Surgical resection is the treatment of choice for insulinomas and offers the only chance for cure.

Points for discussion

Medical therapy to control symptomatic hypoglycaemia Imaging modalities

DOI: 10.1530/endoabs.100.WH5.2

WH5.3

Exploring metformin and GLP-1 analogues as therapeutic approaches for reactive hypoglycaemia in roux-en-y gastric bypass patients

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Background

Reactive hypoglycaemia following Roux-en-Y gastric bypass (RYGB) surgery poses unique challenges in diagnosis and management. This abstract explores the utility of Metformin and GLP-1 analogues in two distinct cases.

Case 1- LH

LH, a post-RYGB patient, presented with recurrent hypoglycaemic episodes, intriguingly manifesting primarily at night; after a long day at work in a fasted state followed by a carbohydrate heavy meal. LH experienced hypoglycaemic episode-related seizures, precipitating emergency department admissions. Mixed meal testing confirmed a significant drop in blood sugars (baseline 6.8 mmol/l, rising to 9 mmol/l and then dipping to 2.7 mmol/l, at 2 hours post-mixed meal), coupled with elevated insulin (2180 pmol/l from <10 pmol/l) and C-peptide levels (6625 pmol/l from 393 pmol/l), confirming reactive hypoglycaemia. Metformin, an off-label choice, successfully settled symptoms. Gradual dose escalation resulted in sustained improvement over three months, highlighting the potential for metformin in preventing post-prandial hypoglycaemia in this group of patients.

Case 2- LS

LS had a history of diabetes and Roux-en-Y gastric bypass, presented with sweats and light-headedness. Mixed meal test noted glucose fluctuation (baseline 5 mmol/l, peaking at 12.5 mmol/l in 30 minutes, then gradually dropping to 4.2-4.4 mmol/l, over the next two hours), suggestive of reactive hypoglycaemia. Metformin at 500 mg bd induced symptomatic relief, and modest weight loss. However, LS continued to experience late morning symptoms, prompting consideration of GLP-1 analogue therapy. The initiation and optimisation of GLP-1 did settle her symptoms. This case underlines the intricate balance between insulin excess and insulin resistance.

Conclusion

These cases illuminate potential roles for Metformin and GLP-1 analogue, in managing post-RYGB reactive hypoglycaemia. Tailoring interventions to the unique presentations of these patients underscores the need for personalised approach, in post-bariatric reactive hypoglycaemia management. Further research is warranted to establish the broader applicability and safety of these interventions, offering hope for enhanced patient outcomes in this challenging context.

Reference
https://www.frontiersin.org/articles/10.3389/fendo.2024.1332702#:~:text= These%20findings%20highlight%20the%20potential,and%20flash%20glucose%20monitoring%20technology

DOI: 10.1530/endoabs.100.WH5.3

WH5.4

Metformin- a novel approach to managing reactive hypoglycaemia in patients with pre-diabetes and diabetes

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A 70-year old gentleman was referred to the endocrine clinic by the Cardiology team following an admission with blackouts- three in three years, two causing road traffic accidents. During one of the accidents, his capillary blood glucose reading dropped below 3 mmol/l. The patient reported dizzy spells, accompanied by hot flushes, sweats, tremor, change in colour- "looking grey", feeling hungry and nausea, alleviated by sugary snacks. These episodes were linked to missing meals and consuming sweet snacks following a meal. Despite extensive investigations- 24-hour ECG, echocardiogram and implantable loop recorder, a cardiac cause could not be identified. He was also known to have pancreatic insufficiency. His HbA1 c was in keeping with pre-diabetes. Glucose monitoring at home revealed capillary readings ranging from 4.8- 7.4 mmol/l, and peaking at 10-13.5 mmol/l after meals. Investigations; urinary metanephrines and cortisol were within range. HbA1 c indicated pre-diabetes (46 mmol/mol). Mixed meal test showed significant glucose variability of >7 mmol/l, an exaggerated insulin response (C-peptide 1687 pmol/l, insulin 317 pmol/l) and hyperglycaemia (blood glucose 12.2 mmol/l). He was diagnosed with reactive hypoglycaemia. He was advised to adopt a low glycaemic index diet and Metformin initiated, titrated to maximum dose, aiming to improve insulin sensitivity, and prevent recurrence of hypoglycaemia. Remarkably, he did not experience recurrence of symptoms. This case underscores the potential role of metformin as an effective treatment strategy for managing reactive hypoglycaemia in patients with pre-diabetes.

Reference
https://www.frontiersin.org/articles/10.3389/fendo.2024.1332702#:~:text= These%20findings%20highlight%20the%20potential,and%20flash%20glucose%20monitoring%20technology

DOI: 10.1530/endoabs.100.WH5.4

WH5.5

Managing post-bariatric surgery reactive hypoglycaemia: a dual approach with metformin and GLP-1 receptor agonist

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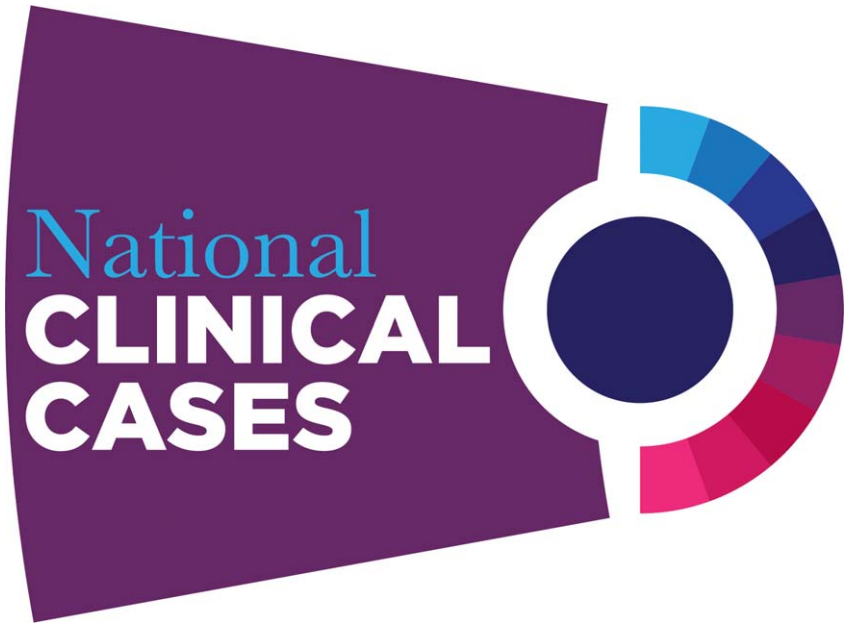
A 61-year old woman, referred to the endocrine clinic, post Roux-en-Y gastric bypass, exhibited symptoms of dizziness, weakness, light-headedness and sweating. These symptoms were associated with light meal following prolonged fast. A clinical diagnosis of reactive hypoglycaemia was made. She was advised to make lifestyle modification and adopted a low glycaemic index diet. Baseline bloods including cortisol, IGF-1 and urinary metanephrine were within reference range. Mixed meal test revealed rapid fluctuations in blood glucose; exaggerated insulin(545 pmol/l) and C peptide (2316 pmol/l) response, at blood glucose of 11.6 mmol/l. This glucose fluctuation seemed to precipitate symptoms. CT pancreas revealed no evidence of pancreatic lesion. Metformin was initiated in March 2018, titrated to the maximum dose. She was in remission from diabetes after bariatric surgery. Her BMI was 42.4 kg/m^2. Her frequency of symptoms improved with metformin, but she occasionally experienced hypoglycaemia in the morning, thus a trial of weekly GLP-1 receptor agonist was commenced resulting in resolution of symptoms. This case suggests potential efficacy of dual therapy with metformin and GLP1 receptor agonist in managing reactive hypoglycaemia post- bariatric surgery.

Reference
https://www.frontiersin.org/articles/10.3389/fendo.2024.1332702#:~:text= These%20findings%20highlight%20the%20potential,and%20flash%20glucose%20monitoring%20technology

DOI: 10.1530/endoabs.100.WH5.5



Society for Endocrinology National Clinical Cases 2024

Endocrine Abstracts

Volume 100
May 2024

Society for Endocrinology National Clinical Cases 2024

Friday 24 May 2024, Royal Society of Medicine
London, United Kingdom

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Oral Communications

OC1

Making scents of hemi-anosmia in a woman presenting with secondary amenorrhoea

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Case history

A 25-year-old woman presented with secondary amenorrhoea present since aged 18yrs. She had spontaneous albeit late menarche aged 16yrs and five menstrual periods over the subsequent two-years, before complete menstrual cessation. She denied other medical history, psychological stress, excessive exercise, or regular medications. Notably, she reported normal sense of smell via her right nostril, but anosmia via her left nostril. Family history included a diagnosis of Kallmann syndrome (heterozygous for FGFR1-variant) in both her mother and sister, having presented with primary amenorrhea and anosmia. Her mother required ovulation induction to conceive. On examination, her BMI was 23.7 kg/m^2 and she had normal secondary sexual characteristics.

Investigations

Unilateral left-sided anosmia was confirmed with a validated smell-test (UPSIT) and MRI-brain revealed absent left olfactory nerve, bulb, and sulcus. Hormonal assays revealed undetectable oestradiol ($<$100 pmol/l), and low LH (0.2 IU/l) and FSH (0.4 IU/l) consistent with hypogonadotrophic hypogonadism. Pelvic-ultrasound demonstrated thin endometrium (3 mm). Whole-exome sequencing identified heterozygous *FGFR1* and *IL17RD* variants, consistent with congenital hypogonadotrophic hypogonadism (CHH). GnRH testing (100 mg) induced an LH-rise of 24.8 IU/l indicating preserved pituitary function. An intravenous bolus of kisspeptin-54 (9.8 nmol/kg) elicited a subnormal early LH rise (3.4 IU/l), greater than typically seen in CHH, but earlier and smaller than observed in healthy women. Intranasal kisspeptin-54 (12.8 nmol/kg) delivered to the right nostril induced a small rise in LH (0.5 IU/l), whereas kisspeptin-54 to the left nostril didn't induce any LH-rise.

Conclusions

CHH typically presents with primary amenorrhoea, and isn't usually considered in patients with secondary amenorrhoea. This lady had a family history of Kallmann syndrome (KS), raising the possibility, however this may not always be present. KS is CHH with anosmia and usually indicates defective GnRH-neuronal migration. KS is typically associated with bilaterally reduced (microsmia) or absent (anosmia) sense of smell. Unilaterally hypoplastic or absent olfactory structures on MRI are reported, although smell disturbance is typically bilateral. Patients with KS can have partial forms, which are difficult to detect, or even spontaneous reversal of their condition. Reversal of CHH/KS is less commonly reported in women. Kisspeptin stimulates hypothalamic GnRH-neurons and can be used to assess hypothalamic function. Endocrine responses to kisspeptin are usually minimal in CHH. This patient had a subnormal response to kisspeptin, greater than typically observed in CHH but less than in a healthy woman. Given her spontaneous puberty and unilateral anosmia, she appears to have a partial/unilateral form of KS, not previously reported in the literature.

DOI: 10.1530/endoabs.100.OC1

OC2

Non-islet cell tumour hypoglycaemia in adrenocortical carcinoma responding to combined growth hormone and corticosteroid therapy

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Case History

A 26-year-old woman with known metastatic adrenocortical carcinoma (ACC) was transferred to our department with recurrent severe hypoglycaemic episodes. Her ACC was diagnosed in 2018 and a 175 $\times$ 130 $\times$ 89 mm 1200 g mass was surgically resected (ENS@T stage-II, Weiss score-5, Ki-67 20%, Helsinki score-28). Her disease progressed despite adjuvant radiotherapy, mitotane and three chemotherapy regimens. In January 2023, she began experiencing episodes of profound hypoglycaemia, associated with hypokalaemia. She had loss of hypoglycaemic awareness and had prolonged hospitalisations for collapse and seizures.

Investigations and method

Her diagnostic work up centred on serum samples taken during a hypoglycaemic episode, including c-peptide, insulin, growth hormone (GH), insulin-like growth factor (IGF)-1 and sulphonylurea screen. Subsequent IGF-I and IGF-II assays were done before and after initiating treatment.

Results and treatment

Test	Value
Fasting plasma glucose (3.5-6 mmol/l)	1.4
Potassium(3.5-5.3 mmol/l)	2.4
C-peptide(370-1470 pmol/l)	$<$50
Insulin(2.6-24.9 mU/l)	$<$1.0
Beta-hydroxybutyrate(mmol/l)	0.02
Urine sulphonylurea screen	negative
Growth Hormone (mg/l)	0.60
IGF-1 (103.3-328.4 mg/l)	39

The raised IGF-I:IGF-II ratio (30.3, normal $<$10) confirmed non-islet cell tumour hypoglycaemia (NICTH). A trial of GH (somatropin 1.2 mg OD subcutaneously) and corticosteroids (dexamethasone 1 mg OD) was started. Her hypoglycaemia and hypokalaemia resolved within days and her IGF-I:IGF-II ratio improved. Unfortunately, her ACC progressed and she died in February 2024.

Test	February-23	April-23	May-23	November-23
IGF-I(11.2-54.5 nmol/l)	2.3	*GH and corticosteroids started*	11.3	11.2
IGF-II(nmol/l)	69.7		139.4	85.5
IGF-II:IGF-I ratio($<$10)	30.3		12.3	7.6

Conclusions

ACCs are rare; although 50-60% are functional they typically produce glucocorticoids and/or mineralocorticoids and/or or androgens. Although many ACCs are associated with overexpression of IGF-II, aberrant expression of the immature form of IGF-II believed to be important in the mechanism of NICTH is very rare. NICTH can be suspected in the context of malignancy with recurrent hypoglycaemia, exclusion of the presence of endogenous/exogenous insulin and is supported by a raised serum IGF-I:IGF-II ratio. After initial stabilisation with glucagon and glucose, management can be surgical or with medical therapy. Treatment options include GH and/or corticosteroids. Somatostatin analogues have been used with varying effect. This is a very rare case of metastatic ACC secreting pro-IGF-II causing NICTH. The hypoglycaemic episodes responded well to combination treatment with corticosteroids and GH. The use of GH in this setting is a risk-benefit decision; the theoretical mitogenic effects of GH on the ACC were offset by the need to treat life-threatening hypoglycaemia.

DOI: 10.1530/endoabs.100.OC2

OC3

Endocrine complexity in a case of MEN2A

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Case History

A 53-year-old female with MEN2A (C634P mutation) and localised medullary thyroid cancer (MTC) was noted to have an adrenal nodule that was presumed by referring centre to be a phaeochromocytoma, given symptoms of anxiety and palpitations. There were also concerns about possible Cushing's syndrome, as she reported fatigued, weight gain and a recent diagnosis of type 2 diabetes mellitus. Furthermore, she suffered a tibial plateau fracture which had been managed conservatively given concerns about her endocrine issues. The initial plan was for an adrenalectomy prior to thyroidectomy for her MTC.

Investigations

CT scan showed a 5 cm heterogeneous nodule in the left lobe of the thyroid, and a right adrenal 8 mm nodule that remained indeterminate on MRI evaluation. On ultrasound, the thyroid nodule was graded as U4. Plasma metanephrines were within normal range (metadrenaline 303 pmol/l, normetadrenaline 480 pmol/l, 3-methoxytyramine $<$85 pmol/l). Cortisol level failed to suppress following an overnight dexamethasone suppression test (177 nmol/l) with ACTH level of 29.1 ng/l. Random serum cortisol was 364 nmol/l and 24-hour urinary cortisol was within normal limits (152 nmol/day). Raised level of CEA (620 mg/l) and calcitonin (6240 ng/l) were in keeping with MTC. Her HbA1c was 53 mmol/mol.

Results and treatment

Functioning phaeochromocytoma was extremely unlikely given normal plasma metanephrines; hence treatment of malignant MTC was prioritised before

reassessing cortisol secretion. Her overall cortisol levels were deemed satisfactory for her to proceed with total thyroidectomy for her MTC without cortisol lowering therapy. Reduced CEA (4 mg/l) and calcitonin (90.7 ng/l) levels following the operation demonstrated successful treatment of her MTC. Repeat overnight dexamethasone suppression test post-operatively showed suppression of cortisol to <28 nmol/l and reduced ACTH level (7.9 ng/l). Her HbA1c also improved to 47 mmol/mol. This confirmed that her Cushing's syndrome was secondary to ectopic ACTH secretion from her localised MTC.

Conclusion and points for discussion:

Differentials considered for Cushing's syndrome included ectopic ACTH from a phaeochromocytoma or the MTC, a cortisol-secreting adrenal adenoma or pituitary dependent Cushing's incidental to her MEN2A. Although ectopic ACTH is usually seen in advanced MTC, it can be seen in localised disease. Importantly, although phaeochromocytomas are associated with MEN2A, this cannot be assumed for all adrenal nodules identified. Therefore, adrenal nodules in patients with MEN2A still warrant full clinical and biochemical evaluation to determine underlying aetiology, ensure correct sequencing of treatment and avoid unnecessary delays to treating the malignant pathology.

DOI: 10.1530/endoabs.100.OC3

OC4

Peritoneal strumosis – balancing the management and preservation of fertility

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Section 1: Case history

A 20-year-old Bangladeshi female presented to her GP with an 18-month history of nonspecific abdominal pain. She is nulligravida, not sexually active and reports no intermenstrual bleeding, dysmenorrhoea, menorrhagia or dysuria. Past medical history includes obesity, OSA and anosmia.

Section 2: Investigations

The patient underwent a TVUS which demonstrated a large (158 × 84 × 156 mm) multiloculated lesion with a solid vascular component (55 × 29 × 17 mm). Subsequent MRI pelvis confirmed a complex loculated right ovarian mass and excluded any malignant features. Ca125 18 units/ml; Ca19.9 60.5 units/ml; CEA 2.6 units/ml. The patient underwent a laparoscopic ovarian cystectomy. There was multiple cyst rupture during surgery with both solid and fluid components, as well as omental samples, sent for cyto- and histopathology. Left ovary was of normal appearance.

Section 3: Results and treatment

Histopathological examination demonstrated an ovarian teratoma containing a thyroid tissue predominance, struma ovarii, with evidence of peritoneal dissemination, termed peritoneal strumosis. Thyroid function tests were within normal range (T4 15.2 pmol/l; TSH 1.15 mU/l). Ultrasound neck demonstrated mild generalised increase in thyroid parenchymal volume with some underlying colloid micronodular change. The patient underwent a total thyroidectomy to facilitate the probable need for conventional dose radioiodine ablation and therapy, guided by thyroglobulin, to target the ectopic thyroid tissue. Post-thyroidectomy I-123 uptake scan demonstrated residual thyroidal tissue in the central compartment of the neck as well as a 30 mm right sided intensely iodine avid ovarian mass consistent with a struma ovarii. The left ovary also demonstrated iodine uptake which may or may not be physiological. Repeat surgery on the right ovary was opted against due to the subsequent predicted increase in radioiodine uptake by the left ovary during radioiodine ablation. To preserve fertility options, the patient underwent oocyte storage prior to I-131 ablation. This is the extent of management at time of submission.

Section 4: Conclusions and points for discussion

Struma ovarii is a very rare ovarian pathology which comprises <5% of all ovarian teratomas. In exceptionally rare cases, histologically benign appearing struma ovarii exhibits peritoneal dissemination, termed peritoneal strumosis. It is thought that peritoneal strumosis may represent metastasis from a high differentiated follicular carcinoma arising in struma ovarii. The rarity of this case inherently limits the evidence base for its management, which is further nuanced by the patient's desire to preserve future fertility options and discussion remains about the best option for ongoing care.

DOI: 10.1530/endoabs.100.OC4

OC5

Young onset diabetes in non-obese individuals with fatty liver should be investigated for partial lipodystrophy

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Background

Monogenic familial Partial Lipodystrophy, a rare but clinically important cause of severe insulin resistance, is often underdiagnosed.

Case

A 33 years' lady was referred to the diabetes clinic for sub-optimal glycaemic control. She was diagnosed with diabetes at 22 years of age, insidious in onset, and was managed as Type 2 diabetes for 10 years until presentation. She had a h/o oligomenorrhoea and was diagnosed with PCOS. She also had history of biopsy confirmed fatty liver, diagnosed due to elevated liver enzymes. She had a family history of diabetes as well. She was commenced on Metformin at diagnosis of diabetes, and Dapagliflozin was added later. At presentation in clinic, she had a BMI of 29, severe acanthosis nigricans, with loss of fat on extremities. Biochemically, HbA1c was 81 mmol/mol, with triglycerides 4 mol/l, and a plasma C-peptide of 3274 pmol/l. This, in the absence of obesity, suggested severe insulin resistance. She underwent genetic testing which was positive for PPARG gene (p. (Pro454LeufsTer14) mutation. Diagnosis of autosomal dominant familial partial lipodystrophy (FLPD2) was thus confirmed, which explained her diabetes, PCOS, as well as fatty liver. She was commenced on a low-fat diet and managed with insulin and Metformin as part of preconception planning. HbA1c is now 53 mmol/mol.

Conclusion

Non-obese patients with history of early onset diabetes and fatty liver should raise suspicion of insulin resistance syndrome and be investigated for partial lipodystrophy.

DOI: 10.1530/endoabs.100.OC5

OC6

Case of recurrence olfactory neuroblastoma presented with ACTH dependent Cushing syndrome

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A-49-year-old female with previous history of Olfactory neuroblastoma treated surgically in 2003 and no adjuvant treatment was given. She has a past medical history of depression, bilateral sensory neural hearing loss which is thought to be genetic. In Feb 2023 presented with uncontrol hypertension associated with hypokalaemia. Clinical examination showed BMI of 48.4, uncontrol high blood pressure despite using multiple antihypertensive medication. The initial assessment for the in Feb 2023 showed:

Test	Value	Normal range
Aldosterone	<55 pmol/l	100-850
Renin	<0.02 nmol/lH	0.5-3.5
TSH	0.10 miu/l	2.0-4.0
T4	15.9 pmol/l	10-20
T3	1.1 nmol/l	0.9-2.5
Prolactin	249 mu/l	<600
IGF-1	4.5 nmol/l	6.9-28.0
GH	<0.1 mg/l	
DHA sulphate	14.6 umol/l	1.3-8.5
LH	<0.3 iu/l	
FSH	<0.3 iu/l	
Androstenedione	31.7 nmol/l	1.1-5.7
Overnight dexamethasone suppression test	2728 nmol/l	<50
Morning Cortisol	1984 nmol/l	
ACTH	572 ng/l	<47
Potassium	2.8 mmol/l	3.5-5.3
HBa1c	38 mmol/mol	20-41

After the biochemical confirmation of ACTH dependent Cushing, she underwent Pituitary MRI which revealed extensive midline skull base enhancing tumour with suprasellar extension, more on the left with elevation of the left side of the chiasm.There is encasement of the carotid arteries bilaterally. She was started on metyrapone and was booked for the Transpheniodal surgery for debulking. She underwent the surgery in May 2023. The Histopathology confirmed the diagnosis of Recurrent olfactory Neuroblastoma. Immunostaining was positive for Synaptophysin, Ki67 very high (>30%), P53 20%, and it was negative to AE1/3, ACTH, EMA, GH, LH, MNF, Prolactin, S100. She had hydrocortisone post op and metyrapone was continued. She then received radical radiotherapy which was completed on 06.11.2023. Three months after the surgery, BMI was 41, her blood pressure well controlled. ACTH was 59 ng/l (<47) and the mean

cortisol in Cortisol Day Curve was 143 nmol/l. MRI pituitary after the surgery showed a good anterior tumour debulk. With prominent posterior tumoral remnant within the suprasellar cistern with persistent although slightly reduced, chiasmatic tenting and ongoing envelopment of the left internal carotid artery within the cavernous sinus She remains on the hydrocortisone and the metyrapone.

Conclusion

This case highlights the rare association between olfactory neuroblastoma and ACTH dependent Cushing syndrome. The significant improvement after the transsphenoidal surgery make the focus of this lady's Cushing's does seem to be the olfactory neuroblastoma despite not having ACTH staining.

DOI: 10.1530/endoabs.100.OC6

OC7

Managing endocrine neoplasia in mccune albright syndrome

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Case history

This 27 year female was first seen at GSTT in 2012, having had treatment for acromegaly due to a presumed GH-secreting adenoma in 2007 (Trans-sphenoidal surgery × 2, EBRT (2007), pegvisomant (2007-2012 (discontinued due to adverse effects)), & GammaKnife SRS (2011). GH and IGF-1 remained elevated and further treatment with pegvisomant/ SSA was declined. Abnormal bone growth with jaw and skull asymmetry was evident from age 10 years and final height was 182 cm. Imaging confirmed extensive polyostotic fibrous dysplasia. Café-au-lait pigmentation was present resulting in a clinical diagnosis of McCune Albright Syndrome (MAS). In 2014 genetic testing of blood lymphocytes did not confirm GNAS1 mutation. The acromegaly remained uncontrolled (average IGF-1 ~75 nmol/l) with SSA used for a brief period in 2016 with little biochemical response.

Investigations

Spinal imaging was performed in 2016 and demonstrated a left adrenal mass (4.4 cm, characterised as an adenoma). ACTH was undetectable with elevated cortisol (UFC 1023 nmol/24hrs) confirming autonomous cortisol secretion, which has only rarely been reported in adults with MAS. Laparoscopic adrenalectomy was performed in 2017 and post-operatively there was cortisol insufficiency (which has persisted to 2024). Although clinical features of Cushing's syndrome were thought to be mild pre-adrenalectomy, post-operatively there was weight loss and reduction in facial fullness and reduced abdominal adiposity. Despite no GH-directed treatment the IGF-1 fell into the age-matched reference range following the adrenalectomy, suggesting cross-talk between the adrenal adenoma and pituitary GH secretion, possibly by production of GHRH (unproven). In 2017 analysis of bone obtained from TSS demonstrated low-level mosaicism for the GNAS c.601C>T pathogenic sequence variant confirming MAS. The patient is currently 38 years of age and clinically well. Bone turnover markers are non-elevated. Bisphosphonate therapy has not been used. Pregnancy is being considered.

Conclusions

MAS is rare, affecting 1:100000 to 1:1000000 people. The disorder is characterized by the classic triad of polyostotic fibrous dysplasia (POFD), cafe-au-lait skin pigmentation, and peripheral precocious puberty. MAS is clinically heterogeneous and may include thyrotoxicosis, pituitary gigantism, and Cushing's syndrome (usually in neonates with bilateral adrenal disease). Our case highlights the MAS is a clinical diagnosis and routine peripheral blood mutation testing may fail to demonstrate a mutation. This patients experience emphasizes the need for long-term surveillance and vigilance for development of endocrine neoplasia and associated hormone excess in MAS.

DOI: 10.1530/endoabs.100.OC7

OC8

Dexamethasone-suppressed PET CT, using an 18F-ligand ('CETO'), allows non-invasive diagnosis of unilateral aldosterone-producing adenoma, and prediction of complete clinical cure after adrenalectomy

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Case History

A 57-year-old lady was referred with a 6-year history of hypertension and hypokalaemia necessitating hospital admission. Her medical background included breast cancer managed with chemotherapy, radiotherapy and surgery. She required Eplerenone 50 mg OD and Amlodipine 5 mg to control her hypertension, and Sando-K 2 tablets TDS to maintain normokalaemia. The patient was enrolled into the MATCH trial comparing adrenal vein sampling (AVS) with [^{11}C]-metomidate PET-CT(MTO) in predicting outcome from adrenalectomy in Primary Aldosteronism (PA). An extension to the trial investigated whether para-chloro-2-[^{18}F]fluoroethyletomidate PET-CT(CETO) is interchangeable with MTO. The selectivity of both ligands for aldosterone-synthase is achieved by 72-hour pre-treatment with dexamethasone 0.5 mg QDS. CETO has a longer T1/2 compared with MTO (110 vs 20 minutes) and has reduced non-specific liver uptake, making it a more attractive and widely available radiotracer.

Investigations

The diagnosis of PA was evidenced by her spontaneous hypokalaemia, suppressed renin activity (0.4 nmol/l/hr), and aldosterone 1400 pmol/l (normal <550 pmol/l). Adrenal CT demonstrated a 2.5 cm right adrenal nodule with Hounsfield units typical of a benign adenoma. AVS results were as follows: right adrenal vein aldosterone 396,000 pmol/l and cortisol 10,084 nmol/l; selectivity index 12.96. Left adrenal vein aldosterone 6,670 pmol/l and cortisol 7,638 nmol/l; selectivity index 9.82. Lateralisation index 44.97 on the right, contralateral suppression index zero on the left. MTO vs CETO: tumour SUVmax 72.3 vs 57.8; left adrenal SUVmax 21.5 vs 15.6; lateralisation ratio 3.36 vs 3.71; liver SUVmax 14.4 vs 2.5. Despite the 72-hour dexamethasone suppression and ACTH <5 ng/l, her cortisol was 144 nmol/l.

Results and Treatment

The patient lateralised on both AVS and PETCT and proceeded to right adrenalectomy. 6 months post-operatively her BP was 110/75 mmHg off medication, renin 2.2 mmol/l/hr and aldosterone 209 pmol/l. Sequencing of tumour DNA revealed a *KCNJ5* p.Gly151Arg mutation.

Conclusions and points for discussion

The case highlights recent developments in the management of PA:

1. Radioligands targeting aldosterone-synthase offer a non-invasive alternative to AVS. 18F-CETO, is demonstrated in this, and 30 other patients, to be comparable to MTO, enabling PETCT to be undertaken in any hospital already performing 18F-FDG.
2. A complete biochemical and clinical cure was observed, as per PASO criteria. The clinical presentation and response to treatment was typical of the KCNJ5 mutation.
3. The pre-operative clue to this genotype was the failure of dexamethasone to suppress her cortisol. This failure is observed in ~50% of our patients with KCNJ5 mutations, without other biochemical or clinical features of cortisol excess.

DOI: 10.1530/endoabs.100.OC8

OC9

Mediastinal ectopic parathyroid in pregnancy

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A 26-year-old primigravida woman presented with hypercalcaemia at 8-weeks gestation. Initial symptoms included nausea, vomiting and palpitations, with an admission serum adjusted calcium of 3.8 mmol/l. A biochemical diagnosis of primary hyperparathyroidism (PHPT) was supported by a raised PTH and a 24-hour urinary calcium-creatinine ratio of 2.0 mmol/ mmol, excluding familial hypocalciuric hypercalcaemia. Initial management with intravenous fluids and antiemetics was unable to control the hypercalcaemia, resulting in multiple hospital admissions. A multidisciplinary team comprising a Consultant Obstetrician, Endocrinologist and Endocrine Surgeon discussed management options available, including conservative measures, cinacalcet (currently unlicensed) and surgery. Investigations were limited due to radiation exposure in pregnancy. An ultrasound identified a 7 mm lesion on the right, suggestive of a parathyroid adenoma. Comprehensive counselling was undertaken on the risks of hypercalcaemia to both the mother and foetus, highlighting the potential foetal risk reaching up to 40% at term. Maternal complications include hyperemesis, nephrolithiasis, pancreatitis and hypercalcaemic crisis. Neonatal complications included hypocalcaemia, tetany, preterm delivery, low birth weight and foetal death. After detailed consent, a bilateral neck exploration was performed in the second trimester. Four normal parathyroid glands were identified, with no ectopic parathyroid seen in excised thymic tissue. Intraoperative PTH levels remained elevated. Postoperatively, calcium levels remained elevated at 2.95 mmol/l and low-dose cinacalcet was initiated. Discharge after 7 days with calcium levels between 2.65-2.75 mmol/l. At 24 weeks and 3 days gestation, 17 days

postoperatively, she presented with an adjusted calcium of 3.2 mmol/l and 24-hours of vaginal discharge in the surgical clinic. Cinacalcet dose was increased. Premature labour occurred. Despite successful delivery, the neonate developed sepsis and regrettably died 7 days later. Postnatally, despite improvement in hyperemesis, calcium and PTH levels remained elevated. Genetic screening was negative. Postpartum, a 99Tc-MIBI SPECT/CT scan was reported as negative for localising an ectopic parathyroid gland. A PET-Choline CT scan and Four-dimensional parathyroid CT scan suspected a 10 mm isodense, enhancing nodule in the mediastinal left thymus, likely to represent a parathyroid adenoma. A radiology review confirmed the lesion on all imaging. A robotic thoracoscopic resection of her left mediastinal thymus was performed, successfully removing a histologically confirmed 8 mm parathyroid adenoma. The patient is now cured, normocalcemic, and has since given birth to a baby girl. PHPT is relatively uncommon during pregnancy. However, it carries significant maternal and foetal risks. Early recognition and management are imperative for the safety of both mother and foetus. The role of cinacalcet is still under discussion.

DOI: 10.1530/endoabs.100.OC9

OC10

Autoimmune hypothalamitis and hypophysitis due to SLE manifesting as arginine vasopressin deficiency and hypothalamic hyperphagia

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Clinical Case

A 30-year-old female was referred with subfertility and hypogonadotropic hypogonadism. She had systemic lupus erythematosus (SLE) and was on maintenance 5 mg prednisolone, having received intermittent high doses since her diagnosis in 2018. She reported 12 months of amenorrhea and reduced libido without galactorrhoea, despite regular menses since menarche aged13. This coincided with a rapid weight gain of 20 kg. On examination, her BMI was 36.8 kg/m^2, presenting with acanthosis nigricans, an intrascapular fat pad, centripetal obesity, and violaceous striae, without proximal myopathy or visual field deficits. As her SLE was presumed quiescent and following discussion with her rheumatologist, prednisolone was discontinued to allow assessment of her hypothalamic-pituitary-adrenal axis off glucocorticoids. However, she continued to gain a further 10 kg in weight over the following 8 months. Upon further inquiry, she reported compulsive eating, polydipsia with polyuria, and worsening cognition, predating discontinuation of glucocorticoids.

Investigations

Her initial 0900 hours pituitary profile off glucocorticoids while amenorrhoeic revealed: oestradiol 91 nmol/l, LH 4.1 u/l, FSH 6.4 u/l, prolactin 568 (0-495 mU/l), ACTH 20 (< 50 ng/l), cortisol 198 nmol/l, free T4 14.2 pmol/l, TSH 1.94 mU/l.

Results and Treatment

At follow-up, she was also hypernatremic (153 mmol/l; reference range: 135–145 mmol/l) with hyperosmolar serum (309 mmol/kg; reference range: 275–295 mmol/kg) and dilute urine (149 mmol/kg; reference range: 50-1200 mmol/kg). She maintained normocalcemia and euglycemia. Self-recorded fluid balance averaged 7000 ml intake and 6000 ml output. Oral desmopressin titrated to 200 mg twice daily controlled polyuria, and pituitary MRI reported absence of the posterior pituitary bright spot. She was subsequently diagnosed with arginine vasopressin deficiency (AVP-D) presumed due to autoimmune hypophysitis (AH) . Cortisol of 11 nmol/l following 48 hr low-dose dexamethasone testing excluded endogenous Cushing's syndrome driving weight gain and cognitive decline. Moreover, an MRI head showed changes consistent with hypothalamitis, likely contributing to her cognitive impairment and hyperphagia. She received pulsed intravenous methylprednisolone under the guidance of the neurologists. A multidisciplinary team discussion concluded that both her hypothalamitis and AH were likely due to SLE. Other differentials such as sarcoidosis and other neuro-inflammatory conditions were excluded.

Discussion

The co-existence of autoimmune hypothalamitis (ATA) and AH due to SLE, presenting with AVP-D and hypothalamic hyperphagia, is rare. Glucocorticoids are first-line therapy; while radiological improvement is described, endocrine recovery is not assured, and cognitive outcomes vary. Occasionally, biologics such as Rituximab are necessary to prevent progression and/or achieve remission. Currently, our patient is on weaning prednisolone, desmopressin, and hormone replacement therapy, awaiting re-evaluation of radiology, cognition, and pituitary function under multidisciplinary care.

DOI: 10.1530/endoabs.100.OC10

Poster Presentations

P1

Acute intestinal pseudo-obstruction as a rare complication of pheochromocytoma

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Pheochromocytoma is an uncommon tumour found in the adrenal gland medulla. It is identified by the excessive release of catecholamines. The typical symptoms include paroxysms of high blood pressure and adrenergic symptoms like headaches, sweating, breathlessness, and palpitation. In severe instances, patients may experience hypertensive crises and cardiomyopathy. We describe a case where intestinal pseudo-obstruction, a rare complication of pheochromocytoma, was only resolved through surgical removal of the tumour. A 76-year-old woman presented to the Emergency Department with worsening shortness of breath, chest discomfort, and collapsing after starting a new beta blocker medication. Initial evaluation showed tachypnoea, low oxygen saturation, and high blood pressure. A CT pulmonary angiogram ruled out a pulmonary embolism but unexpectedly detected an 8-centimeter lesion on her right adrenal gland, highly suggestive of pheochromocytoma. Additional imaging with CT scans of the chest, abdomen, and pelvis, along with elevated urinary metanephrines, confirmed the diagnosis of non-metastatic pheochromocytoma. During her hospital stay, the dosage of Doxazosin was gradually increased to the maximum amount, yet her blood pressure remained uncontrolled, and she began experiencing symptoms of bowel obstruction. A CT scan of the abdomen revealed a non-mechanical small bowel obstruction, confirming a diagnosis of paralytic ileus. She was placed on nothing by mouth (NBM) and transferred to the Intensive Care Unit (ICU) for intravenous Phentolamine infusion, but her paralytic ileus continued to worsen. Consequently, she underwent an urgent laparoscopic right adrenalectomy, which successfully resolved the paralytic ileus and allowed for a gradual discontinuation of her antihypertensive medications. In conclusion, this case highlights the uncommon complications of pheochromocytoma, such as intestinal pseudo-obstruction, which should be considered during acute presentations. Early recognition and appropriate management are crucial in addressing these rare complications effectively.

DOI: 10.1530/endoabs.100.P1

P2

An unusual case of severe hypercalcemia

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A 59 year old female patient presented with fall and Syncopal episode to Emergency Department. She had a few days history of increasing thirst, polyuria and diffuse abdominal discomfort. These symptoms were ongoing for weeks prior to her syncopal episode. Her past medical history of Endometriosis, Type 2 diabetes mellitus, epilepsy, ex-IVDU user with hep B in remission and self-neglect. She suffered with frequent episodes of heart burns and self-treated this with over counter Rennie tablets. She had been taking almost 100 Rennie tablets per day and this over few weeks. On admission our patient was found to be very confused and dehydrated. she had an adjusted calcium level of 4.55, Phosphate levels of 0.85, Suppressed PTH levels and acute kidney injury. Her Vitamin D levels on admission was 34 with urea of 16.9 and creatinine of 334. She had ECG changes related to the severe hypercalcemia. CT head performed for her syncopal episode and this was reported as n abnormalities found. Bence jones proteins, electrophoresis and ACE levels were within normal range. A CT Thorax, Abdomen and Pelvis was reported a 25 mm exophytic low density lesion over the upper pole of the right kidney. Following this an ultrasound was performed and this resulted in simple cyst as the lesion found on the upper pole of the kidney. Her Calcium levels responded well to aggressive Intravenous fluid resuscitations. Her latest calcium levels and renal function are within normal range and she was also imitated on vitamin D therapy.

Conclusion

Her Acute kidney injury, metabolic alkalosis and severe hypercalcaemia was a result of Milk Alkali syndrome secondary to over counter antacid tablets-Rennies. Our patient was taking upto hundred tablets on daily basis for two to three weeks prior to her acute admission. We would like to emphasise the importance of considering over counter antacids treatment as iatrogenic cause of hypercalcemia, especially severe hypercalcemia like our patients. Milk Alkali syndrome is rare nowadays, given new treatment modalities for indigestion and peptic ulcers. However, with this case we would conclude Milk Alkali syndrome should also be included as part of differential diagnosis of Hypercalcaemia.

DOI: 10.1530/endoabs.100.P2

P3

An interesting case of hypothyroidism: hypothyroidism with bilateral foot drop

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Here we present a 49 year-old-male patient with known T1DM, hypothyroidism on Levothyroxine, with previous history of poor compliance with his Levothyroxine. He was admitted with 3 days history of bilateral feet swelling and foot droop. Following the improvement of his leg swellings, his bilateral foot droop became more prominent. He was diagnosed with Hashimoto hypothyroidism with anti TPO ab levels of 279 IU/Ml (reference range: $<$34 IU/ml) in 2012. His regular medications were Levothyroxine 150 mg OD, Novorapid and Lantus. Our patient complained of bilateral leg swelling and foot droop, which progressed and rapidly deteriorated over a course of three days. This prior to his admission. He was found to have acute kidney injury on admission, this due to the cause of rhabdomyolysis.

These were his initial admission investigations:

Aspartate transaminase	1042 U/l ($<$ 40 U/l)
Creatine Kinase	56600 U/l (40-320 U/l)
Lactate dehydrogenase	2381 U/l ($<$ 250 U/l)
TSH	$>$100 mU/l (0.27-4.20 mU/l)
Free T4	0.7 pmol/l (11-25 pmol/l)
Hba1c	90 mmol/mol ($<$48 mmol/mol)
eGFR	52 ml/min/1.73m^2
0900 hours Cortisol levels	480 nmol/l ($>$ 420 nmol/l)

Following these investigations his hepatitis screen was reported as negative. Radiological investigations such as Ultrasound abdomen were reported normal. MRI spine were reported as degenerative changes of the L4/l5 vertebral disc with impingement of L4 nerve bilaterally. However, there were no evidence of significant cord compression. Vasculitis screening such as ANA, ANCA, DsDNA an Anti-GBM were also negative. During his stay in hospital, he was reviewed by neurology and Orthopaedic team. Nerve conduction study indicated peroneal nerve paresis secondary to anterior compartment syndrome. The neurological features were keeping with a peripheral neuropathy secondary to compartment syndrome. This following acute swelling of his lower legs associated with myxoedema and rhabdomyolysis. With Levothyroxine 200 mg once daily and appropriate instruction given to take his Thyroxine, this in order to improve the absorptions in the most effective way, his thyroid function improved rapidly. His TSH levels improved over the next 2 to 3 months.

Conclusion

To conclude, we would like to emphasise the importance of recognising Anterior compartment syndrome associated with Rhabdomyolysis and hypothyroid myopathy. As, Rhabdomyolysis are rare complications of hypothyroid myopathy. Anterior compartment syndrome is most commonly unilateral. However, bilateral involvement has been reported in literature in the past. Bilateral anterior compartment syndrome is rare.

DOI: 10.1530/endoabs.100.P3

P4

A rare case of AVP deficiency secondary to Chloroma

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Case

60 year old male presented to his GP with symptoms of polydipsia, polyuria, reduced appetite and weight loss of about 1 stone over 6-7 weeks. Routine bloods showed abnormal blood film with left shift in neutrophils, moderate thrombocytopenia (61), basophilia and occasional blasts (1%). Morphology was suggestive of Chronic Myeloid Leukaemia (CML). He was referred to haematology for further management and had specialist bloods and a bone marrow examination. Due to ongoing symptoms of polyuria and polydipsia, repeat bloods were taken - increasing sodium (153 mmol/l), high serum osmolality (320 mmol/kg) and low urine osmolality (171 mmol/l). Review by Endocrine Consultant suggested a clinical diagnosis of AVP deficiency and he was treated with Desmopressin (DDAVP) 100 mg PO nocte. On DDAVP, the sodium rapidly normalised. MRI pituitary showed absent posterior pituitary high signal and a small lesion at the base of the pituitary stalk: differential diagnosis included a proteinaceous or midline inclusion cyst, hamartoma or possibly low-grade glioma. Haematology results confirmed a Philadelphia chromosome with final diagnosis being chronic phase CML, treated with oral Dasatinib (tyrosine kinase inhibitor). From a CML point of view- he had a normal Full Blood Count within 2 months and was in a Major Molecular Remission 4 months after starting Dasatinib. MRI at 3 months showed remission of the hypothalamic enhancing

lesion and still showed an absent posterior pituitary bright spot. His Haematology Consultant suggested that the lesion could have been a chloroma related to the CML, which had responded to the Dasatinib treatment. A repeat MRI at 9 months showed normal appearances of the infundibulum, hypothalamus and posterior pituitary bright spot.

Discussion

Chloroma also known as Myeloid sarcoma (MS) is a rare condition characterized by the presence of solitary or multiple tumours consisting of immature myeloid cells, at an extra medullary site. Most commonly, it occurs concurrently with acute myeloid leukaemia, myeloproliferative disorders or myelodysplastic syndrome. Symptoms usually occur as result of mass effect or organ damage.

Conclusion

AVP deficiency secondary to chloroma is very rare (6 case reports in the literature). This case shows an early presentation with AVP deficiency concurrently with the diagnosis of CML, with Dasatinib treatment resulting in resolution of the presumed hypothalamic chloroma and subsequent reappearance of the posterior pituitary bright spot. In this case the principle of 'Occam's razor' resulted in a unifying diagnosis in a patient presenting with two seemingly unrelated rare medical conditions.

DOI: 10.1530/endoabs.100.P4

P5

Pancreatic neuroendocrine tumor presenting with recurrent confusion and recent posterior circulation stroke

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83-year-old lady presented to emergency department with intermittent confusion. Detailed history revealed that she had a background of recent posterior circulation ischemic stroke 3 weeks prior. She was then referred from her rehabilitation center to us for episodic unresponsiveness with associated low capillary glucose, improving with intravenous dextrose. Prior to her stroke, she had episodes of intermittent dizziness, usually mid-morning, which resolved with snacks. Past medical history was unremarkable apart from previously treated meningioma, and recent ischemic stroke. No h/o alcohol consumption. No history similar problems in her family. Capillary glucose monitoring showed intermittent hypoglycemia during her stay, confirmed with venous glucose. She fulfilled Whipple's triad, warranting further tests. Routine biochemistry, liver and renal function were normal. Sulfonylurea screen was negative. Plasma C-peptide levels were significantly raised, with low paired plasma glucose. CT abdomen showed a cystic lesion in the uncinate process of the pancreas. Octreotide scan confirmed the diagnosis of an insulinoma at the same site. Looking back, it was likely recent stroke was precipitated by a severe hypoglycemia episode, given preceding symptoms. Ideally, surgical resection is the mainstay of treatment. However, given her age, and frailty post-stroke, the multi-disciplinary team meeting, and patient, favored conservative medical management. She was commenced on long-acting somatostatin analogue and provided a continuous glucose monitoring sensor. On review, there were no further hypoglycemia episodes and her glucose levels remained above 4 mmol/l on long-acting somatostatin analogue.

DOI: 10.1530/endoabs.100.P5

P6

Terlipressin induced SIADH

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Case History

An 83-year-old male patient was admitted with coffee ground vomiting. He had no associated melaena, abdominal pain or previous episodes of vomiting. He was on apixaban and bisoprolol for his hypertension and atrial fibrillation. He did not smoke and only drank alcohol occasionally. The patient underwent endoscopy and was found to have variceal bleeding and had band ligation. He was started on terlipressin and pantoprazole. He was referred to endocrine for ongoing persistent hyponatraemia (122 mmol/mol) with fluctuating confusion.

Investigations

His sodium level on admission was 136 mmol/mol. When examined, he was alert and oriented, and did not appear to be confused. He was euvolaemic on examination with BP of 126/81 mmHg and no postural drop. He was eating and drinking well. He was passing sufficient amount of urine (0.5 ml/kg/hour). He had no ascites or peripheral oedema. He had a normal chest X-ray. Hypothyroidism and adrenal insufficiency were excluded. His paired serum osmolality and urine osmolality were 248 mOsml/kg and 540 mOsmol/Kk respectively. His urinary sodium was 70 mmol/l.

Results and Treatment

In this instant, medications were the first potential reason causing his hyponatraemia. We replaced his IV pantoprazole with oral famotidine after discussing with his endoscopist. Fluid restriction to 1.5l was advised. However, his hyponatraemia continued to worsen (114 mmol/mol) (Table 1). Due to his recent variceal bleeding, terlipressin was not discontinued initially. Terlipressin can be given up to 5 days after oesophageal bleeding. However, in view of his persistent hyponatraemia, it was stopped after discussing with his team. Consequently, this led to a gradual improvement in his sodium levels to 132 mmol/mol.

Table 1.

Time scale	Na+ (mmol/mol)
On admission	136
Day 2 on Terlipressin	122
Day 4 on Terlipressin	114
Terlipressin stopped	114
Day 1 after stopping Terlipressin	117
Day 3 after stopping Terlipressin	122
Day 5 after stopping Terlipressin	132

Conclusions and points for discussion

Apart from V1 receptors, Terlipressin has substantial affinity for V2 receptors which can lead to increased water reabsorption in the renal collecting tubules leading to dilutional hyponatraemia. I think this case would have been particularly challenging if the patient already had underlying hypervolaemic hyponatraemia because of decompensated liver cirrhosis and in addition required terlipressin treatment for his variceal bleeding. As a result of this, monitoring of sodium is required when patients are treated with terlipressin.

DOI: 10.1530/endoabs.100.P6

P7

Occult thyrotropinoma unmasked in a woman preconception: diagnostic and treatment challenges

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Case History

A 39 year old female who was trying to conceive was referred with a raised T4 and non-suppressed TSH, on a background of a miscarriage after embryo transfer one month earlier. She reported no symptoms, however, on specific questioning she had palpitations, a mild tremor and later showed mild tachycardia on holter monitoring. There were no childhood features of Resistance to Thyroid Hormone β (RTHb). There was a family history of primary hypothyroidism only.

Investigations

Centaur TSH 5.89 mU/l (RR 0.35-5.5), FT4 30.9 pmol/l (10.5-21), FT3 11.3 pmol/l (3.5-6.5). Detailed biochemical analyses excluded assay interference testing. Additional results were conflicting: some were consistent with an underlying diagnosis of RTHb (SHBG 158 nmol/l, RR 10-180 nmol/l; MRI pituitary with contrast reported as normal), however, others were in keeping with thyrotropinoma (a subunit, aSU, 1.52 mU/l, RR <1 mU/l; two fold increase in TSH following TRH stimulation: 0 min TSH 5.12 mU/l, 30 mins TSH 10.28 mU/l; absence of *THRB* mutation on sequencing). Response to somatostatin receptor ligand (SRL) therapy (autogel lanreotide 90 mg every 28/7) showed a fall in TSH (4.01 to 1.4 mU/l) and both FT4 (41.8 to 17 pmol/l) and FT3 (9.3 to 3.69 pmol/l).

Results and Treatment

Following analysis of SRL response, images from the MRI pituitary were re-examined and a 5 mm left sided pituitary mass, typical of an adenoma, was identified. Trans-sphenoidal surgery was performed, and histology was consistent with a thyrotropinoma. Post-operative TSH suppression ensued, with associated mild transient central hypothyroidism, with later restoration of normal TSH, FT4, FT3 levels. Menses continued as expected and post-operative short synachten testing was normal.

Conclusion and Points for Discussion

This case highlights the (i) clinical challenges in diagnosing microthyrotropinomas and (ii) management of microthyrotropinomas prior to planned conception.

(i) Tests to differentiate RTHb from thyrotropinomas are less sensitive and specific in patients with small tumours (10% RTHb have pituitary incidentalomas/negative *THRB* sequencing/no affected family members, small tumours may not lead to aSU or SHBG rise). Analysis of biochemical response to SRL therapy can be a very helpful diagnostic and therapeutic manoeuvre. (ii) Untreated thyrotropinoma presents potential risks in pregnancy (due to thyroxicosis and presence of pituitary adenoma). Ongoing SRL therapy is an option, but is not licensed in pregnancy and there are risks (tachyphylaxis, development of SRL resistance, tumour growth). Surgery is the ideal treatment, given a high rate of cure in experienced hands (~90%) and low rate of complications.

DOI: 10.1530/endoabs.100.P7

P8

A case of connshing syndrome in northern ireland

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Section 1: Case History
A case of 51 year old female who was referred to us by GP due to increase in size of previously known adrenal adenoma that was picked up on the abdominal ultrasound requested by GP for her deranged liver function test. She had previous investigations in 2017 by endocrinologist in another hospital for a left benign adrenal incidentiloma and it was found non-functional at that stage. She had hypertension 3 years ago and was started on Ramipril by GP. She also takes Bisoprolol 1.25 mg twice a day for palpitations, which was thought to be anxiety driven and also sertraline, Lamotrigine and Lurasidone as she had hx of bipolar disorder. She has no history of hypokalaemia. She had no overt signs of Cushings' but had high BMI and BP was 139/86. She said she put on weight during pandemic.
Section 2: Investigations
Her Ramipril was switched over to doxazosin for 2 weeks prior blood investigations. Aldosterone 818 pmol/l, renin was 3.75 Miu/ml giving a ratio of 218(reference <35). Saline suppression test with a basal aldosterone of 552 pmol/l and the result at the end of the test of 248 nmol/l (ref <150). Renin correspondingly was 4.5 and 3.15 Miu/ml. Overnight dexamethasone suppression test was 92 nmol/l 24 hours urine metanephrines were normal. Her CT scan showing a left adrenal adenoma measuring 3.8 cm in diameter slightly increased from 3.5 cm in 2015 but with low density in keeping with an adrenal adenoma. She was referred to the tertiary hospital in Belfast for consideration of adrenal vein sampling. Results were surprisingly pointing that hyperaldosteronism was from right adrenal gland which adenoma was only on left side as cortisol was very high on left side making aldosterone/cortisol ratio lower.
Results of adrenal vein sampling are as under:

	Right	left	Periphery
Aldosterone	44900	19000	1400
Cortisol	8923	>17500	2037
A/C	5	1.09	0.69

Section 3 Results and Treatment
MDM decision was to do 8 mg overnight dexamethasone suppression test to evaluate extent of burden of autonomous cortisol secretion. Results was 90 nmol/l. DHEAS was 0.96 UMol/l (normal range 0.96-6.95) ACTH with undetectable levels. Result confirmed clinically significant autonomous cortisol secretion so decision for left adrenalectomy was made while continuing to treat her aldosteronism medically as it appears to be coming from right adrenal.
Section 4 Conclusion
This is a Connshing (Conn's/Cushing's) syndrome where both hormones are being secreted from contralateral side.

DOI: 10.1530/endoabs.100.P8

P9

Atypical presentation of pseudo-acromegaly in a patient with a history of adrenalectomy

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Case History
We present a case of a 52-year-old female with a history of right adrenalectomy at age 30, insulin-dependent Type 2 diabetes, and atypical clinical manifestations mimicking acromegaly. The patient presented with a five-year history of worsening facial appearance, blurry vision, and a noticeable hunch in the back. Notably, she had undergone right adrenalectomy for an adenoma in the past and had never received steroid therapy post-surgery. Despite presenting with features suggestive of acromegaly, including insulin resistance evidenced by a markedly elevated HbA1c of 99, comprehensive diagnostic evaluations were pursued.
Investigations
Pituitary profile hormones including TSH and Magnetic Resonance Imaging (MRI) Pituitary revealed no abnormalities, and the oral glucose tolerance test (OGTT) demonstrated normal glucose metabolism with appropriate suppression of insulin-like growth factor 1 (IGF-1) and growth hormone. Additionally, the Dexamethasone suppression test and 24-hour urinary free cortisol was normal, effectively excluding Cushing syndrome.
Results and Treatment
Given the absence of biochemical evidence of acromegaly and other related disorders, the patient was diagnosed with pseudo-acromegaly. The emphasis shifted towards addressing the underlying insulin resistance due to features of obesity and acanthosis nigricans with biochemical confirmation of raised C peptide and Insulin levels, and lifestyle modifications were recommended, particularly weight loss, to improve glycaemic control.
Conclusion and Points for discussion
Pseudo- acromegaly is a rare condition characterized by acromegalic features without the associated growth hormone excess seen in true acromegaly. This case underscores the importance of considering pseudo-acromegaly in patients presenting with acromegalic features, especially in those with a history of adrenalectomy and atypical clinical manifestations. Timely and thorough diagnostic evaluations are crucial to exclude underlying endocrine disorders and guide appropriate management strategies, emphasizing the significance of addressing insulin resistance in the absence of growth hormone excess.

DOI: 10.1530/endoabs.100.P9

P10

Primary adrenal lymphoma – a rare but lethal disease

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Case History
A 73-year-old gentleman with no prior comorbidities, presented with 2-month history of decreased appetite, weight loss and lethargy. He denied experiencing paroxysmal symptoms of headache/sweating/palpitations, abdominal pain, fever, night sweats or chronic cough. Clinically, he was cachexic, dehydrated (blood pressure 98/82 mmHg; heart rate 125 beats per minute) with a vague mass palpable over the right lumbar. There were no palpable lymphadenopathy or features suggestive of Cushing's syndrome.
Investigations
Biochemical analysis revealed non-parathyroid hormone (PTH) dependent severe hypercalcemia [corrected calcium 3.67 mmol/l (N 2.2-2.6); phosphate 1.13 mmol/l (N 0.78-1.65); PTH 0.1 pmol/l (N 1.4-6.8)] with acute kidney injury [creatinine 157 umol/l (N 54-97); urea 16.3 mmol/l (N 3.2-8.2)], elevated lactate dehydrogenase 941 U/l (N 120-246) and anaemia [haemoglobin 100 g/l (N 130-170); white blood cell 10×10^9/l (N 4-10); platelet 417×10^9/l (N 150-400); iron 3.5 umol/l (N 11.6-31.3); transferrin saturation 10% (N 20-45)]. A random serum cortisol was appropriately elevated for his ill condition, at 1169 nmol/l (N 145-619). 24hour urine metanephrines and 24hour urine cortisol were within normal limits. CT imaging showed bilateral adrenal lesions with heterogenous enhancement. The right lesion ($12.4 \times 9.0 \times 12.6$ cm) encased the right renal artery and vein with infiltration of the right kidney while the left lesion measured $4.0 \times 4.2 \times 4.3$ cm.
Results/Treatment
In addition to saline diuresis, he received subcutaneous (S/C) calcitonin 200 IU TDS for 3 days and a dose of S/C Denosumab 60 mg. He showed marked improvement clinically and biochemically (Table 1). CT-guided adrenal biopsy was performed and histopathology of the biopsy established the diagnosis of diffuse large B-cell lymphoma (DLBCL) with high Ki-67 (>90%). Staging done via FDG PET-CT showed extensive disease involving both supra and infra-diaphragmatic lymph nodes, spleen, lung and brain. Treatment with intravenous dexamethasone and pre-phase cyclophosphamide was initiated. Unfortunately, he succumbed after developing sepsis post-treatment.
Table 1

Date	**17.7.23**	**18.7.23**	**19.7.23**	**20.7.23**	**22.7.23**
Corrected Calcium mmol/l (N 2.2-2.6)	3.67	3.44	3.11	2.88	2.69

Conclusion/Discussion Points
This case highlights primary adrenal lymphoma (PAL) as a rare but lethal cause of bilateral adrenal lesions. PAL accounts for <1% of non-Hodgkin lymphomas and CT-guided adrenal biopsy is the gold standard to establish the diagnosis. R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone) chemotherapy regime remains the mainstay of treatment, though the long-term prognosis remains guarded with reported median survival time of 14 months (based on a study of 136 patients with PAL). Besides hypercalcemia, a more prevalent endocrine complication in these patients is adrenal insufficiency, which requires prompt intervention if present.

DOI: 10.1530/endoabs.100.P10

P11

Persistent adrenal insufficiency post-unilateral adrenalectomy for cushing's syndrome

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Case History
A 56-year-old woman initially sought evaluation at an endocrine clinic in 2018 due to the discovery of an adrenal incidentaloma (AI). She complained of chest pain and underwent coronary computed tomography angiography, which revealed no significant coronary artery disease but incidentally detected a lung nodule. Subsequent interval assessment of the lung nodule via HRCT unveiled a well-defined 25 × 20 mm left adrenal mass. Further examination indicated a 30 Hounsfield unit (HU) density and 75% washout, consistent with a benign adrenal adenoma. The patient had well-controlled, relatively recent onset hypertension, weight gain (BMI 38) and easy bruising, but no proximal myopathy or pathognomonic striae.
Investigations
Additional assessments of the adrenal incidentaloma revealed normal 24-hour urine metanephrines and serum renin: aldosterone ratio. However, she exhibited elevated 24-hour urinary free cortisol levels on 3 occasions (189, 175 and 246 nmol/24 hours -normal range: 0-165), increased midnight salivary cortisol on 2 occasions (suggesting loss of circadian rhythm of cortisol secretion -9.4 and 6.7 nmol/l, normal: <2 nmol/l). There was failure to suppress cortisol during two overnight dexamethasone suppression tests (cortisol 397 and 385 nmol/l, <50 is considered normal), and during a low-dose dexamethasone suppression test (Cortisol 371, <50 is considered normal with low adrenocorticotropic hormone (ACTH) level (<5 ng/l). These findings were in summary strongly suggestive of Cushing's syndrome stemming from the Left adrenal gland.
Treatment and Follow-up Outcome
Following multidisciplinary discussion, she underwent laparoscopic left adrenalectomy with peri-operative steroid cover in October 2019. Histopathological analysis of the resected adrenal gland revealed fibro-fatty tissue consistent with an encapsulated adrenocortical adenoma. Her 24-hour urinary cortisol levels normalized postoperatively; she lost all excess weight gained in the years prior to the diagnosis; her hypertension resolved indicating recovery from Cushing's disease. However, despite more than four years since the operation, her remaining adrenal gland has repeatedly failed to adequately produce cortisol, in keeping with profound adrenal insufficiency. Subsequent stimulation tests performed in February, July, and December 2020, as well as yearly thereafter, consistently demonstrated inadequate cortisol production. However, her pituitary hormone levels, including insulin-like growth factor 1 (IGF-1), thyroid function tests (thyroid-stimulating hormone [TSH] and free thyroxine [FT4]), prolactin, and sex hormones, remained within normal ranges. She is currently receiving hydrocortisone replacement therapy and had a couple of hypoadrenal crises requiring medical intervention.
Conclusion and points for discussion
Adrenal hypercortisolism is independent of ACTH regulation and results in Hypothalamic-pituitary-adrenal axis suppression, with varying degrees of severity. Surgical removal of the culprit adrenal mass often leads to post-operative adrenal insufficiency, necessitating glucocorticoid replacement therapy perioperatively and for a variable period thereafter which in turn depends on the duration and severity of hypercortisolism and tumour size. A longer follow-up of these patients is often necessary to ensure resolution of Cushing's syndrome and to assess recovery of the contralateral adrenal gland.

DOI: 10.1530/endoabs.100.P11

P12

Thyrotoxicosis-induced valvular regurgitation and biventricular dysfunction

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Introduction
Thyrotoxicosis, characterized by excessive production of thyroid hormones, can precipitate a spectrum of cardiovascular complications, including heart failure and valvulopathy. This case study highlights a case where effective management of thyrotoxicosis precipitated the reversal of heart failure and valvulopathy.
Case Presentation
A 44-year-old woman presented at the emergency department with complaints of dyspnea, palpitations, and fatigue. She reported a recent history of weight loss, heat intolerance, and tremors. Physical examination unveiled signs of perspiration, tachycardia, and a distinct systolic murmur audible at the apex. Furthermore, bilateral lower limb edema was noted.
Investigations
Thyroid function tests indicated markedly elevated levels of serum free thyroxine (T4) and triiodothyronine (T3), and suppressed thyroid-stimulating hormone (TSH) in conjunction with positive TRAB levels confirming a diagnosis of Graves' disease. Echocardiography revealed biventr icular failure with reduced ejection fraction, accompanied by moderate mitral and tricuspid regurgitation, and mild pulmonary regurgitation, suggestive of valvulopathy secondary to thyrotoxicosis. Atrial fibrillation was detected by ECG.
Results and Treatment
Treatment initiation involved the administration of antithyroid medications (Carbimazole) and beta-blockers to address Atrial fibrillation. Additionally, standard heart failure therapy, including diuretics, was instituted. Regular monitoring of thyroid function and echocardiography ensued to evaluate treatment efficacy.
Outcome
With aggressive management directed at thyrotoxicosis, the patient's symptoms exhibited gradual amelioration. Subsequent echocardiography displayed notable enhancement in ventricular function, with ejection fraction restoration to normal levels and resolution of pulmonary, mitral and tricuspid regurgitation. Consequently, manifestations of heart failure resolved, precluding the necessity for diuretic therapy. Subsequent ECGs confirmed the resolution of atrial fibrillation.
Discussion
This case underscores the intricate nexus between thyroid dysfunction and cardiovascular sequelae, underscoring the imperative of promptly identifying and managing thyrotoxicosis in individuals concurrently presenting with heart failure and valvulopathy. Effective management of thyrotoxicosis holds the potential for reversing cardiac abnormalities and ameliorating symptoms.
Conclusion
In conclusion, this case serves as a testament to the successful management of heart failure and valvulopathy secondary to thyrotoxicosis through timely recognition and intervention targeting thyroid dysfunction. It accentuates the potential for holistic cardiac recovery with judicious medical intervention, advocating for a collaborative, multidisciplinary approach in addressing such clinical scenarios. Early recognition and management of thyrotoxicosis emerge as pivotal in mitigating cardiovascular complications in patients with heart failure and valvular abnormalities.

DOI: 10.1530/endoabs.100.P12

P13

Ketosis-prone diabetes (KPD): a mystery yet to be elucidated?

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KPD remains poorly understood. It is characterised by unprovoked hyperglycaemia with ketoacidosis at diagnosis, in the context of brief history of hyperosmolar symptoms and weight loss in individuals with no prior history of diabetes. The initiation of insulin therapy in these patients is accompanied by insulin-free periods, during which oral hypoglycaemic medications and diet achieve normoglycaemia. KPD has been reported predominantly in Africans, African Americans, Hispanics and, less commonly, Asians.
Case presentation
29-year-old Zimbabwean lady (BMI of 49 kg/m^2) presented to the A&E with a one-month history of osmotic symptoms and weight loss. She reported persistent vomiting of a week duration, and systemic reviews were unremarkable. Her Father and grandfather had type 2 diabetes, and her grandmother has type 1 diabetes. She has a history of polycystic ovarian syndrome and takes no regular medication. The Patient was dehydrated at presentation, and systemic examinations were unremarkable. She had a blood glucose of 23 mmol/l, PH of 7.249, bicarbonate of 10 mmol/l and ketone of >7 mmol/l. Other investigations showed sodium of 132 mmol/l, potassium of 4.0 mm/l, Urea of 2.5 mmol/l and Creatinine of 59 mmol/l. HBA1c was 116 mmol/mol, and there was no evidence of chest or urine infection. She was commenced on insulin infusion and then

discharged home on basal-bolus (Lantus 20 units, Novorapid 8 units TDS) following the resolution of her DKA. She was followed up at the outpatient clinic within a month, during which she reported resolution of osmotic symptoms and weight gain, and SMBG revealed optimal glycaemic control with some episodes of symptomatic hypoglycaemia. GAD65 and Islet cell antibodies were negative, C-peptide was 2241 pmol per litre and urine ACR was 7.22 mg/g. Novorapid was stopped, Lantus was reduced to 10 units, and She was commenced on metformin and Ramipril. Her insulin was discontinued during further follow-up within three months, and HBA1c was 42 mmol/mol. The Patient remained well on oral hypoglycaemic agent with optimal glycaemic control. The classification of this heterogeneous condition still poses great challenge, though the recent Aβ classification gave some clarity to four different phenotypes ($A^+\beta^-$, $A^-\beta^-$, $A^+\beta^+$, and $A^-\beta^+$) with recognisable limitations. Moreover, the aetiopathogenesis of DKA remains largely debated; proposed mechanisms include prolonged glucotoxicity, increased oxidative stress, high glucagon levels and viral-induced insulin resistance with secretory defect. It is hoped that guidelines for the long-term management of this condition will be established by relevant authorities as the incidence of KPD in the UK is likely to increase.

DOI: 10.1530/endoabs.100.P13

P14

Jaw woe: delayed osteonecrosis post-zoledronate treatment

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Case history
A 67-year-old-lady was first seen in the endocrinology clinic in December 2015 for management of her osteoporosis- deemed to be secondary to menopause with alcohol excess as an additive factor. This had been confirmed on the bone densitometry scan. She had previously been on Alendronate from July 2012 to April 2015, but discontinued this due to intolerance. Considering her latest bone mineral densitometry (BMD) values (in g/cm^2) of 0.766 (T-score of -2.6) at the lumbar spine and 0.704 (T-score of -1.9) at the left hip, it was deemed that the best way forwards would be cutting down on alcohol, calcium and Vitamin-D supplementation and intravenous (IV) Zolendronate. She received the first dose of IV Zolendronate in January 2016, and received the 3rd dose of IV Zolendronate in February 2018. Her post-Zolendronate BMD values (in g/cm^2) were 0.817 (T-score of -2.0) at the lumbar spine and 0.701 (T-score of -2.0). She had not reported any new fractures on this drug nor did she develop any complications secondary to the Zolendronate and hence she was kept on a drug-holiday with a plan to monitor her progress and BMD. The endocrinology team had last reviewed her in early December 2022. Around late December 2022, she started experiencing pain in the LR6 tooth, and underwent a dental extraction in January 2023. Following this, intense pain started developing at the site and hence she was referred to the maxillofacial team, who diagnosed her with Osteonecrosis of the jaw (ONJ), for which she required 3 months of Doxycycline.
Discussion
Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is defined as the exposure of the bone in the maxillofacial region for more than 8 weeks, in patients who are under bisphosphonate treatment without any radiation treatment, and who have undergone dental surgery including dental implant placement. For those receiving IV bisphosphonates, the incidence of BRONJ ranges from 5-20%. Amongst the bisphosphonates, Zolendronate is the most potent drug in causing BRONJ because of its high potency in slowing down bone turnover. The mean time for development of BRONJ after Zolendronate can be as long as 84 months, especially in those with underlying cancer. In our patient, the BRONJ developed 84 months after receiving the first dose of Zolendronate, with a long latent period of 59 months between the last dose and the development of BRONJ. To the best of our knowledge, this is the longest latent period reported.

DOI: 10.1530/endoabs.100.P14

P15

Finding the culprit – a case of multifactorial hypercalcaemia

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Case history
We present the case of a 59-year-old gentleman admitted to our hospital in February 2023 with severe hypercalcaemia. He had a background of mild intermittent hypercalcaemia since 2018 (highest 2.73 mmol/l), chronic kidney disease, hypertension, and a recently climbing prostate-specific antigen that had warranted a 2-week-wait Urology referral. On admission, his only symptom was constipation, without weight loss or constitutional symptoms. His parathyroid hormone (PTH) level was inappropriately high at 17.9 pmol/l with adjusted serum calcium of 3.43 mmol/l, 25-hydroxyvitamin D was 51 nmol/l. He was started on intravenous fluids and cinacalcet for hypercalcaemia presumed secondary to primary hyperparathyroidism. However, his chest X-ray (CXR) revealed bulky bilateral hilar lymphadenopathy. His calcium levels improved with this treatment, and he was discharged on cinacalcet with outpatient endocrinology follow up. He subsequently required re-admission on four separate occasions between March and July 2023 with hypercalcaemia.
Investigations
During this time, he had an ultrasound of his neck and technetium-99 m sestamibi scan which confirmed a right inferior parathyroid adenoma. In view of the hilar lymphadenopathy found on CXR, computed tomography was arranged and revealed extensive symmetrical mediastinal and hilar lymphadenopathy, peribronchial nodules and splenomegaly, raising the possibility of sarcoidosis or lymphoma. His endobronchial ultrasound-guided biopsy showed non-necrotising granulomas consistent with sarcoidosis. He had magnetic resonance imaging and biopsy of his prostate which confirmed low grade adenocarcinoma. No skeletal metastases were found on his bone isotope scan, thus excluding this as a contributor to his hypercalcaemia.
Results and treatment
He was initially treated with intravenous fluids, bisphosphonates and cinacalcet with short-lived improvement in his calcium levels. On confirmation of his diagnosis of sarcoidosis, he was commenced on a weaning regime of oral prednisolone. He underwent a right superior and inferior parathyroidectomy in August 2023, with excellent response in his PTH levels postoperatively. However, he developed recurrent severe hypercalcaemia shortly after and oral steroids were restarted, with subsequent normalisation in his calcium levels since. He currently remains under both respiratory and endocrine follow up and under active surveillance for prostate cancer.
Conclusion and points for discussion
The outcome raises the question to what extent, in hindsight, the parathyroid surgery was necessary. Our case illustrates that PTH-dependent hypercalcaemia can present concomitantly with multiple PTH-independent causes. In such instances, it can be difficult to establish the main driver for the symptoms and a systematic approach to addressing each aetiology is key to achieving a successful outcome.

DOI: 10.1530/endoabs.100.P15

P16

Pregnancy perspectives: navigating hypopituitarism and cranial diabetes insipidus management

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Case history
A 31-year-old-lady was referred to the antenatal clinic at 6 weeks gestation. She had a background of a Craniopharyngioma and underwent transsphenoidal surgery (TSS) at age 9 years. She subsequently developed post-operative hypopituitarism which required supplementation with Growth hormone (GH), Levothyroxine and hormone replacement therapy (HRT). She also developed cranial diabetes insipidus (CDI) requiring supplementation with desmopressin. She had never been steroid deficient and only transiently required hydrocortisone following TSS. Over the years, there were multiple alterations of her hormonal therapy. She had primary amenorrhea as TSS had been done prior to puberty. Using ovulation induction treatment and a HCG trigger, she conceived. On review, she was on subcutaneous GH 1 mg daily, 125 mg OD Levothyroxine and Desmopressin 0.2 mg PO in the morning, 0.1 mg PO in the afternoon and 0.3 mg PO in the evening. She was however advised to cease the GH injections. Her dose of Levothyroxine had been empirically increased to 125 mg PO OD post conception. She was experiencing increased osmotic symptoms thus Desmopressin dose was increased. She continued to be monitored on a 4-weekly basis, with her Levothyroxine dose being increased further, aiming for her FT4 to be in the upper third of the normal range. This case highlights the challenges of complexities and challenges of managing hypopituitarism and CDI in pregnancy.
Discussion
Fertility can be subnormal in women with hypopituitarism with affliction of the reproductive hormone axis, but also when other pituitary hormones are affected. Women often require assisted reproduction techniques to conceive. However there are reported cases of spontaneous conception. Simple regression analysis for hypopituitarism in pregnancy identified only maternal age and depression as predictors of pregnancy outcomes whereas multiple regression analysis found a

trend, albeit non-statistically significant for worse pregnancy outcomes in women with childhood onset disease. DI is associated with increased complications of pregnancy that include including preeclampsia. With pulsatile GnRH treatment, the pregnancy rates are comparable to the normal population. The supplementation of GH in pregnancy is controversial as the placenta is known to produce GH, thereby suppressing pituitary GH production. Keeping this in mind, we omitted the GH supplementation in our patient. Owing to altered water homeostasis, and the effect of placental vasopressinase, the dose of Desmopressin may need to be increase, as was seen with our patient

DOI: 10.1530/endoabs.100.P16

P17

'Don't forget the eye when seeing thyroid!'

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Case History with Investigations
A 65-year-old female, with no previous thyroid abnormalities, was originally referred to ENT with goitre. She was clinically and biochemically euthyroid, and following ultrasound with fine needle aspiration for right-sided nodules with benign cytology, was discharged. She was subsequently referred to Endocrinology with persistent lethargy and hair loss despite normal thyroid function. She described gritty eyes and swollen eyelids for 2 years, with mild proptosis for 5 years. She was noted to have evidence of thyroid eye disease (TED) with slight left eye exophthalmos, bilateral eyelid inflammation and mild injection of the sclera. There was no ophthalmoplegia and visual acuity was normal. TSH receptor antibody (TRAB) was positive at 2.2 IU/l. Prompt review in the Thyroid Eye Disease multi-disciplinary clinic (oxTED) confirmed mildly active and mildly severe TED (CAS 1, VISA 2). Orbital MRI confirmed bilateral thyroid eye disease. At TED 4-month clinic follow up, left exophthalmos was more pronounced, and she reported new intermittent diplopia with left ocular pain. CAS score was 4, VISA score 3, and TRAB increased to 3.6 IU/l with persistently normal thyroid profile.
Results and Treatment
She received treatment for thyroid eye disease with low dose Rituximab (100 mg) infusion and single dose iv methylprednisolone (100 mg). Symptomatic improvement was noted at 6-month review, with fall in TRAB (2.5 IU/l) as well as CAS score 1 and VISA score 1. To date, she remains biochemically euthyroid.
Discussion
Euthyroid Graves' Disease is a challenging diagnosis, due to its atypical clinical manifestations and absence of abnormal thyroid function. Typically, thyroid ophthalmopathy is associated with thyrotoxicosis and positive thyrotropin receptor antibodies (TRAB). However, minority of patients remain euthyroid[1], presenting with milder ophthalmopathy. The above case highlights the importance of remaining vigilant for screening for thyroid eye disease in Graves' disease even if patients remain biochemically euthyroid. A recent systematic review reported that the global prevalence of TED in euthyroid patients 7.9% [1]. Whilst most of historical reports suggest mild disease, the reported case above demonstrates TED may be active and warrant immunotherapy. Although it is usual to note a dysthyroid lab profile prior to ophthalmopathy (80% of cases) or follow it within 2 years of presentation (20%) [2], this patient has remained biochemically euthyroid for almost 9 years from first description of symptoms. This emphasizes the importance of long-term follow-up in the management of euthyroid Graves' patients and signposting TED symptoms.

DOI: 10.1530/endoabs.100.P17

P18

Thyrotoxicosis with multi organ failure precipitated by iodinated contrast in grave's patient

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Case History
49 year old female presented to emergency with severe shortness of breath with non-productive cough, of 5 days duration. There was no h/o flu like symptoms nor GI symptoms. She did not have a significant past medical history but consumed alcohol in excess and was a heavy smoker. On examination, the patient was of normal build, with blood pressure of 150/90 mm Hg and pulse rate of 160/min, irregular. There were fine hand tremors, with sweaty palms and forearms. There was no proptosis, and no palpable goitre. Her respiratory examination revealed bibasal crackles and cardiovascular examination showed pan systolic murmur. Her abdominal and neurological examinations were normal. Her Burch Wartofsky scale for thyrotoxicosis was 65. Soon after admission, she was posted for CTPA to rule out pulmonary embolism for her acute shortness of breath. Patient deteriorated rapidly following CTPA and was intubated and transferred to ITU for ventilation and vasopressor support
Investigations
Her TSH was <0.001 with T3 – >30.4 pmol/l (2.9-4.9 pmol/l) & T4 >64 pmol/l (9-19 pmol/l) markedly elevated. Her anti TPO antibodies was positive and Anti-TSH Receptor antibodies level was 20.11 IU/l (0-2 IU/l). US Neck showed features suggestive of Grave's disease. Her US abdomen showed portal venous flow demonstrated with marked pulsatility and distended hepatic veins suggestive of right-sided heart failure with ECHO showing features of elevated right atrio-ventricular pressures. Her CTPA was Negative for pulmonary embolus with appearances suggesting significantly raised right sided pressures and small right pleural effusion.
Results and Treatment
She was treated for multi organ failure due to possible potentiation of thyrotoxicosis by iodine based contrast. She received high dose carbimazole 30 mg once daily along with bisoprolol 10 mg once daily followed by fluids and vasopressors for treatment for heart failure. She recovered after prolonged intensive treatment and was stepped down to ward based care. On discharge, she had been followed in the endocrinology clinic and her TFT results improved with subsequent visit.
Conclusion & point of discussion
Iodine mediated contrast can aggravate or precipitate thyrotoxicosis in patients of hyperthyroidism especially Grave's disease, multinodular goitre, and patients living in iodine deficient areas. This can precipitate life threatening complications such as arrhythmias, heart failure and venous thromboembolism. Iodinated contrast mediated acute deterioration of thyrotoxicosis due to Jode-Basedow effect is an important complication and judicious use of such investigations is essential.

DOI: 10.1530/endoabs.100.P18

P19

Adult-onset clinical presentation of ABCD1 gene mutations and X-Linked adrenoleukodystrophy: a case report and review of the literature

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Case history
We discuss a 40-year-old man with an unusual presentation of newly diagnosed Adrenoleukodystrophy following a family genetic screening test that was performed when his nephew aged 8 years was diagnosed with the same condition. He was struggling to articulate his thoughts and occasionally developed slurring of speech and these changes were noted over a period of 3 years preceding the diagnosis. The patient also reported symptoms of fatigue, clumsy gait and muscle stiffness. In contrast, his nephew developed features of the condition at a much younger age, initially presenting with a language development disorder which later rapidly progressed to recurrent falls and eventually to profound immobility.
Investigations and results
Genetic screening confirmed he was positive for ABCD1 gene alteration linked to X-linked Adrenoleukodystrophy (Hemizygous for ABCD1:c.901-5 C$>$A). 0900 hours cortisol level was low normal at 237 nmol/l, with a failed short Synacthen test demonstrating unsatisfactory cortisol response (0-minute: 74 nmol/l and 30-minute cortisol values of 308 nmol/l). MRI Brain and Spine did not reveal any gross sinister abnormalities.
Treatment
Hydrocortisone treatment was initiated, and subsequently his symptoms improved significantly, namely fatigue and muscle weakness.
Conclusion and discussion
Adrenoleukodystrophy (X-ALD) is an X-linked recessive disorder caused by mutations of the ABCD1 gene which codes for the adrenoleukodystrophy protein (ALDP). ALDP helps in the transport of very long chain fatty acids (VLCFA) to the peroxisomes for oxidative degradation. Due to the pathogenic variants and mutations of the ABCD1 gene, peroxisomes cannot oxidise VLCFA. It is

characterised by the accumulation of VLCFA in the plasma and tissues, predominantly the adrenal gland, nervous system, and testes. Those affected with this mutation do not usually show signs or symptoms at birth, but males affected may develop adrenal insufficiency and spastic paraparesis. Previously, it was thought that females could only present as asymptomatic carriers as the condition is X-linked recessive. Despite this, more recent data show that heterozygous females can eventually develop signs of myelopathy. The three major phenotypes are cerebral adrenoleukodystrophy (CALD), primary adrenal insufficiency and adrenomyeloneuropathy (AMN). CALD is the most severe presentation of X-ALD resulting in demyelination within the cerebral white matter. It is characterised by a progressive and potentially fatal neurological decline, manifesting as seizures, paralysis and dysarthria. AMN typically presents in adulthood with a combination of myelopathy and peripheral neuropathy, with a more insidious course. In routine clinical practice, the implications of the ABCD1 mutation are well-recognised but less commonly perceived.

DOI: 10.1530/endoabs.100.P19

P20

Hypercalcaemia in the third trimester: a difficult case of primary hyperparathyroidism

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Case history
A 30-year-old female was investigated and treated for hypercalcaemia during the third trimester of pregnancy. She has a background of rheumatoid arthritis on hydroxychloroquine and was reviewed by the rheumatologists during her pregnancy due to worsening limb and back pain. She had multiple calcium levels monitored during her pregnancy. Her calcium had been elevated since 2022 but had increased further during the pregnancy and it wasn't until she was referred to the obstetricians during the third trimester that it was investigated further. She had significant symptoms of hypercalcaemia including bone pain, constipation, thirst and polyuria.
Investigations
Blood tests confirmed an adjusted calcium level of 2.99 mmol/l; a parathyroid hormone level of 12.4 pmol/l; a vitamin D level of 23 nmol/l; and normal thyroid function. A calcium creatine excretion ratio was 0.04. An ultrasound confirmed an enlarged lower left parathyroid gland. Genetic screening identified no genetic cause for hyperparathyroidism. Plasma metanephrines were normal. The results confirmed a diagnosis of primary hyperparathyroidism.
Results and treatment
She was admitted to the central delivery suite for intravenous fluids, and she was commenced on high dose vitamin D treatment. She was discussed in multidisciplinary team meetings with the regional maternal medicine network and endocrine surgeons. The limited evidence available for managing obstetric primary hyperparathyroidism suggests that parathyroidectomy should be considered in the second trimester. A decision was made to use the best medical approach. She developed proteinuria and was monitored for pre-eclampsia. Intravenous fluids were given cautiously. She was commenced on calcitonin. A caesarean section was performed at 37 weeks with no immediate complications. However, baby subsequently developed hypocalcaemia requiring paediatric input.
Points for discussion
This case questions whether similar cases are being missed if clinicians are unfamiliar with the importance of early detection of hypercalcaemia during pregnancy, and whether greater education is needed in order to avoid delayed presentations. Perhaps screening calcium levels in pregnant women during the initial ante-natal visits would be beneficial. Managing primary hyperparathyroidism in pregnancy is difficult, particularly if diagnosed in the third trimester. There is limited evidence with how to manage such cases and the evidence is primarily based on case reports. The complication of proteinuria made intravenous fluids difficult but there is limited evidence with regards to medications such as calcitonin and timing of delivery. Detailed guidelines for the management of primary hyperparathyroidism during pregnancy and postnatally would be helpful.

DOI: 10.1530/endoabs.100.P20

P21

Reversal of congenital hypogonadotrophic hypogonadism (CHH) in a woman with a heterozygous inactivating variant in GnRHR gene

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Case history
Our patient presented with primary amenorrhoea and incomplete puberty aged 15 yrs. Based on BMI >40 kg/m^2 from early adolescence, clinical hyperandrogenism, family history of polycystic ovary syndrome (PCOS), and insulin resistance, she was diagnosed with PCOS and commenced on a combined oral contraceptive (COC), achieving breast development. Aged 21yrs, she was reassessed for amenorrhoea of COC. Biochemical assessment revealed hypogonadotrophic hypogonadism (HH): LH 0.2 IU/l, FSH 0.3 IU/l, oestradiol <92 pmol/l. She had a normal sense of smell and Tanner 4 breasts; MRI demonstrated normal olfactory bulbs and pituitary. The diagnosis was therefore revised to congenital HH (CHH) and COC was restarted, later changed to HRT due to hypertension. A 22-gene CHH panel (R148) identified a heterozygous pathogenic variant c.3171$>$Gp in *GNRHR*. At reassessment of HRT aged 32yrs, she remained amenorrhoeic. Ultrasound showed normal ovarian morphology, antral follicle count 17 and endometrial thickness 5.8 mm; hormonal assays: LH 5.0 IU/l, FSH 8.3 U/l, oestradiol 162 pmol/l, AMH 12.2 pmol/l, testosterone 1.6 nmol/l (RR <2.0), SHBG 35 nmol/l (RR 30-100 nmol/l). She then achieved ~20 kg weight loss (BMI 41.8 to 35.2 kg/m^2) on GLP-1-agonist. GnRH test (Gonadorelin 100 mg) incremented LH from 5.16 to 44.46 IU/l and FSH from 6.47 to 15.27 IU/l at 60 mins. After an intravenous kisspeptin (9.6 nmol/kg) bolus, LH rose from 5.05 to 29.99 IU/l, FSH from 6.68 to 13.91 IU/l. Off HRT, she began having regular cycles (oestradiol 800 pmol/l).
Conclusion and discussion
CHH was diagnosed based on primary amenorrhoea, HH and pathogenic *GnRHR* variant that would not, however, be expected to result in a productive phenotype in the absence of a second deleterious allele (oligogenicity occurs in ~20% of CHH), so whole exome sequencing is awaited. Kisspeptin is a potent stimulator of hypothalamic GnRH neurons and can be used to interrogate hypothalamic function. Typically, gonadotrophin responses to kisspeptin are minimal in CHH. Thus, her kisspeptin response was not consistent with CHH at time of assessment, indicating reversal of CHH (seen in 20% of CHH, particularly with *GnRHR* variants). However, CHH reversal is far less commonly reported in women. Notably, her kisspeptin response was higher than in healthy women, consistent with decreased hypothalamic function and potentially a 'Female Obesity-Related Hypogonadism'. Our case highlights the value of interrogating hypothalamic function using kisspeptin, both for the diagnosis of CHH, to identify alternate pathology and to identify recovery of reproductive function in CHH reversal.

DOI: 10.1530/endoabs.100.P21

P22

Biliopancreatic diversion bariatric surgery as a cause of non-hepatic hyperammonaemic encephalopathy

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The case describes a 49-year-old woman with a history of previous biliopancreatic diversion and duodenal switch procedure carried out in 2010. She was known to the local bariatric service with multiple micronutrient deficiencies and had no prior history of liver disease. She was admitted to hospital in 2023 with a widespread rash, proximal myopathy, multiple nutrient deficiencies, acute kidney injury, and spontaneous bleeding into the psoas muscle. She was seen by a dietitian and weight management physician early during the admission and her relatives disclosed poor compliance with supplements. One week into the admission she became acutely confused, and due to an acute drop in GCS required intubation and admission to the intensive care unit. Bloods showed an albumin of 25 g/l (25-50), ALT 54 U/l (10-40), zinc 3.8 umol/l (10-20), and normal bilirubin and ALP. A CT head showed normal intracranial appearances and a sepsis screen and cerebrospinal fluid analysis were normal. Electroencephalogram confirmed severe encephalopathy. Ammonia and glutamine levels were markedly elevated: 199 umol/l (<50) and 1566 umol/l (544-836) respectively. An ultrasound of the liver showed moderate diffuse fatty change with no evidence of cirrhosis. Her case was discussed with the local Biochemistry and Hepatology teams, and it was felt that the results were in

keeping with non-hepatic hyperammonaemic encephalopathy. There was no evidence of an underlying inherited metabolic disorder. She was started on lactulose and rifaximin with normalisation of ammonia levels. She also received ongoing dietetic input to minimise protein catabolism and manage her electrolyte and micronutrient abnormalities. Her encephalopathy resolved and she made a full recovery. Non-hepatic hyperammonaemic encephalopathy following malabsorptive bariatric surgery is a rare complication which is associated with a high mortality rate and can occur at any stage post-surgery. Most reports have been in women with previous Roux-en-Y Gastric Bypass surgery, but it has also been described in individuals with biliopancreatic diversion procedures, which are associated with a higher risk of nutritional deficiencies. Accumulation of ammonia is thought to occur due to increased protein catabolism and functional inhibition of urea cycle enzymes involved in its clearance. Zinc and essential amino acid deficiencies are thought to be major contributors to the pathophysiology. This case highlights the need to counsel patients post bariatric surgery about the risks of non-compliance with nutritional supplements. Ammonia levels should also be checked in any patient with a history of bariatric surgery presenting with acute confusion and nutrient deficiencies regardless of liver function.

DOI: 10.1530/endoabs.100.P22

P23

The adrenal puzzle: cure in primary aldosteronism

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Section 1: Case history
A 42-year-old man was referred with a five-year history of hypertension and multiple hospital admissions for hypokalaemia. His blood pressure was 164/104 mmHg on three drugs.
Section 2: Investigations
A diagnosis of primary aldosteronism (PA) was confirmed on a saline suppression test: aldosterone 554 pmol/l at baseline, 240 pmol/l post saline infusion (normal $<$170). A CT adrenal revealed a 13 mm left-sided adrenal nodule. The right adrenal appeared normal. Adrenal vein sampling (AVS) indicated left-sided lateralisation (L:R ratio 42.5:1) with contralateral aldosterone secretion suppressed to 20% of peripheral. A [11C]metomidate PET-CT (MTO), undertaken as part of the MATCH study, showed high MTO tracer activity in the left adrenal nodule (SUVmax Ratio 1.86). After spironolactone 50/100 mg for 4 weeks, BP fell by only 15/3 mmHg, to 148/101 mmHg.
Section 3: Results and treatment
Following a left adrenalectomy, hypokalaemia resolved and quality of life improved (baseline Physical Component Summary (PCS) 21.75 and Mental Component Summary (MCS) 28.79; post treatment PCS 49.73, MCS 48.35). Markers of cardiac damage also improved: BNP reduced from 354 ng/l at baseline to 209 ng/l at 6 months, LVEDV on CMR reduced from 283 mls to 263 mls. Other measures were mixed. He remained hypertensive (BP 175/117 at 6 months, off treatment). Aldosterone/renin ratio reduced from 1010 (normal $<$1000) to 164 at 6 months, indicating biochemical success by PA Surgical Outcomes ('PASO') criteria, but levels of individual hormones at 6, 12 and 24 months suggested early recurrence of aldosterone excess (aldosterone 312 pmol/l at 6 months, 747 pmol/l at 12 months,725 pmol/l at 24 months). Immunohistochemistry and RNA sequencing of the adenoma were strongly positive for aldosterone synthase, as predicted by the *in vivo* 11C-metomidate binding, and revealed a novel somatic mutation, of *DPYSL2*. This abundantly expressed adrenocortical gene traffics calcium channels to the plasma membrane, and the adenoma transcriptome indeed resembled the pattern seen in *CACNA1D*-mutant adenomas.
Section 4: Conclusions and points for discussion
Despite convincing lateralisation, adrenalectomy achieved only partial success. The patient illustrates the MATCH trial's finding that the strongest predictors of complete clinical success are a systolic BP on spironolactone of $<$135 mmHg and somatic genotype (*KCNJ5*). By contrast, 0/20 patients with a calcium-channel (*CACNA1D*) mutation were completely cured. This patient's unique somatic genotype mimics impact of a *CACNA1D* mutation, both on cell function and clinical outcome. He also illustrates that reductions in plasma aldosterone and BP can under-estimate surgical impact on cardiovascular health and quality of life.

DOI: 10.1530/endoabs.100.P23

P24

Doctor, my hands are getting bigger! - a classical case of acromegaly

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A 40 year old male presented to his general practitioner with numbness in his fingertips, especially at night. Since his screening for peripheral neuropathy was unremarkable, he was called in for an in-person appointment to look for carpel tunnel syndrome. At the surgery he was noticed to have enlarged hands but he did not have any other complaints at that time. He missed his further appointments, until after 2 years when he presented with dental problems, protrusion of his lower jaw, with jaw pain. On further exploration he admitted increase in his shoe size along with increase in the size of both hands, coarsening of facial features, headache and occasional sweating. His IGF-1 was found to be raised and he was referred to endocrinology clinic for further evaluation. In clinic we noted a recent diagnosis of hypertension with atrial fibrillations. He also admitted the use of anabolic steroids in the past for body building, but was not sure about the use of growth hormone. He exhibited typical features of growth hormone excess including frontal bossing, frontal burrow, prominent nasolabial folds, prognathism, interdental separation and acral enlargement. His growth hormone levels and anterior pituitary functions were assessed and an oral Glucose tolerance test was arranged, which demonstrated failure to suppress growth hormone. This was followed by an MRI of his pituitary gland which showed a pituitary adenoma on the right measuring 17 mm with no chiasmal displacement or extension into the cavernous sinus. His case was discussed in a multidisciplinary meeting and he was planned to have trans-sphenoidal resection of pituitary adenoma after pre-surgical optimisation. Post operatively he was commenced on hydrocortisone replacement and day 3 Growth Hormone levels came back normal. His hypertension also improved and required reduced dose of anti-hypertensive. Specimen histology demonstrated a sparsely granulated somatotroph cell pituitary neuroendocrine tumour (pitNET)/adenoma. He was discharged with a planned follow up after 3 months. Normalizing mortality to the level in general population is the key aim in the management of acromegaly. Biochemical goal to control mortality is a GH less than 2.5 ng/ml or a normal age and sex-adjusted IGF-I levels. Co-morbidities such as hypertension, diabetes and cardiac diseases should be managed appropriately.

DOI: 10.1530/endoabs.100.P24

P25

MDT approach towards thyrotoxicosis and carbimazole induced hepatitis

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A 54 year old gentleman with a background of treated B cell lymphoma presented to his practitioner with symptoms of thyrotoxicosis. His thyroid work up confirmed positive thyroid receptor antibodies, and hence treated as Graves' disease. He was started on carbimazole by his practitioner. After two weeks of initiation of treatment with carbimazole, he presented to his GP with yellowish discoloration of skin, nausea, vomiting and passing dark coloured urine. He was found to have remarkably deranged liver function tests indicating acute liver injury warranting urgent MRCP. MRCP ruled out any obstructive pathology. Non Invasive Liver Screening was unremarkable. Carbimazole was stopped. Patient was started on high dose propranolol and cholestyramine to optimise the symptoms of thyrotoxicosis. Gastroenterology team was consulted and the patient was started on ursodeoxycholic acid with a trial to improve the Liver Functions

and reduce the level of bilirubin. Liver function tests were monitored regularly which showed sluggish improvement in weeks. Liver biopsy showed acute cholangitis and cholestatic hepatitis suggesting likely drug induced liver injury. He was started on Enteral feeding to support nutrition during the phase of acute liver injury. Team of gastroenterologists, endocrinologists and dietitians were involved to devise a holistic management plan of the patient to further facilitate the eligibility of the patient to have thyroidectomy eventually. Hepatitis is one of the rarely reported side effects of carbimazole with almost all the reported cases consistent with intrahepatic cholestasis. In the index case, the hepatic injury is reported with a relatively lower dose of carbimazole and within 2 weeks of initiation of carbimazole treatment as compared to other reported cases where the liver damage is evident after months of carbimazole intake and on increasing the dose. So, it is unclear if the hepatic injury is more common with higher doses and longer duration of treatment with carbimazole. Hepatitis being an uncommon side effect of carbimazole, early histological diagnosis is essential for the prompt management of both thyrotoxicosis and liver injury by seeking valuable contribution from endocrinologists, hepatologists and nutrition specialists.

DOI: 10.1530/endoabs.100.P25

P26

Pheochromocytoma presenting as acute coronary syndrome

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A 63 year old male presented with sudden onset severe chest pain which clinically seemed cardiac in nature. A diagnosis of Non-ST Elevation MI was made and was managed conservatively. Later, after 6 months he again presented with chest pain. On this occasion, CT aorta and CT Thorax, Abdomen and Pelvis was done to rule out aortic aneurysmal rupture, and to look for post-infarct changes in the myocardium, cardiac MRI was done. Cardiac MRI and CTTAP both showed an incidental finding of left adrenal lesion measuring 4.8 cm highly suspicious of adrenal pheochromocytoma. On further exploration, he expressed having headache, sweating, palpitations and persistently raised blood pressure along with chest pain for past 6 months. Radiologists' opinion was sought for further characterization of the mass. The lesion was suggested to have high vascularity due to rich capillary network, arterial phase enhancement and significant washout on PV phase. Investigations showed high levels of urinary and plasma metanephrines. Low-dose dexamethasone suppression test and overnight dexamethasone suppression test showed unsuppressed cortisol levels supporting possibility of co-secreting cortisol. Renin activity and aldosterone levels were normal. He was given adequate alpha blockade with increasing dose of doxazosin and was planned to have elective laparoscopic adrenalectomy. As an intraoperative complication, he developed grade 2 splenic rupture followed by a litre of blood loss due to which spleen was removed. Having sensitivity of 97% and specificity of 93%, the compelling evidence suggests using plasma free metanephrines as primary test of excessive catecholamines for diagnosis of Pheochromocytoma and Paragangliomas (PPGL). Computed Tomography is the first line investigation to confirm the location. PPGL should be ruled out in patients presenting with chest pain and persistently high blood pressure. Our patient did not have a family history of PPGL and the syndromes associated with it. However, one third of patients with PPGL have germline mutations and PPGL may often be a part of hereditary syndromes, so genetic testing is advisable for all the patients diagnosed with PPGL. The incidence of persistently low blood pressure after PPGL removal varies between 20-77% which is attributed to downregulation of alpha and beta receptors. Our patient developed persistent hypotension after the tumor removal which was managed with vasopressors in Intensive care.

DOI: 10.1530/endoabs.100.P26

P27

Myxoedema coma - practical considerations

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Section 1: History
Myxoedema coma is a rare, emergency presentation of extreme hypothyroidism, but without robust evidence to base management recommendations on. We present the case of a woman in her seventies who was admitted following a fall. Collateral history revealed five days of worsening mobility, drowsiness, and confusion with poor oral intake. This progressed to slurred, incoherent speech, and brief vacant episodes. Her background included glaucoma, mastectomy, and iron deficiency anaemia. No recent illnesses prior to this admission was reported.
Section 2: Investigations
On examination, she was bradycardic and hypothermic, with a depressed sensorium. Initial blood tests demonstrated hyponatraemia (115 mmol/l) and raised Creatine Kinase (11236 U/l). Inflammatory markers were within normal range. CT head excluded intracranial haemorrhage. TSH was elevated at 88 mU/l, with depressed free thyroxine <5.5 pmol/l and free T3 2.2 pmol/l, supporting the diagnosis of myxoedema coma. Cortisol was 808 nmol/l. No obvious precipitating event was identified on work up.
Section 3: Results and Treatment
Endocrinology input was sought and they initially recommended intravenous (IV) loading doses of both T3 (liothyronine) and T4 (levothyroxine), followed by a maintenance prescription. However, IV formulation of T4 was not available immediately, therefore a nasogastric feeding tube was placed. T3 was delivered intravenously and T4 was administered enterally. Under this regimen and supportive measures, remarkable clinical improvement was observed. In 72 hours, serum T3 normalised, and the TSH reduced to 16.9 mU/l. T3 subsequently discontinued. Follow up for hypothyroidism was arranged as an outpatient.
Section 4: Conclusion and Points for Discussion
Myxoedema coma has a high mortality rate and controversy exists as to the optimum regimen for thyroid hormone replacement. Recommendations are largely based on case reports and expert opinion. There is debate as to whether to employ purely T4 or use it in combination with T3. Concerns also exist about safety in those with arrhythmias and coronary artery disease. There is also potentially impaired enteral absorption in this situation. However, there are multiple case reports of enteral routes being utilised to deliver thyroid hormone treatment in this setting. In our patient, the choice of replacement was influenced by both the clinical status and the immediate availability of drugs. Endocrinologists are encouraged to make themselves aware of the local availability patterns to prevent delays in an emergency situation. The decisions regarding replacement strategies are guided by a case-by-case approach.

DOI: 10.1530/endoabs.100.P27

P28

Don't forget hypogonadism in obesity

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Case History
Patient 1: A 44 years old gentleman with BMI of 44.7 was referred to the weight management clinic for the management of obesity. His weight was in obesity range since childhood and he reported excessive tiredness and lethargy. He also had history of anxiety and depression. Examination showed lack of body hair, reduced muscle mass and small testes. Patient 2: A 48 years old lady was referred to the endocrinology clinic for incidental adrenal adenoma. She reported gradual weight gain over years. She had central obesity with BMI at 53.4 and history revealed amenorrhoea since the age of 20 years.
Investigations
Patient 1: Pituitary tests performed in view of clinical findings, showed low Testosterone at 6.1 nmol/l, FSH 1.8 IU/l, LH 5 IU/l with normal TFTs, IGF-1, low cortisol but SST showed an adequate response. MR pituitary was normal. USS testes demonstrated reduced vascularity but normal testicles. Patient 2: Biochemical investigations for adrenal adenoma were negative Pituitary function test showed low gonadotrophins (FSH - 3.2, LH - <0.3 IU/l), elevated Prolactin at 171030 mu/l with normal IGF1, cortisol and TFT. MR pituitary showed large macroadenoma.
Results and Treatment
Patient 1: Results suggested hypogonadism secondary to obesity; His energy levels, exercise capacity and muscle mass improved with testosterone replacement. He achieved weight loss with liraglutide (Saxenda) with latest BMI at 35.3. Patient 2: Results suggested secondary hypogonadism caused by prolactinoma. She showed good response to treatment with dopamine agonist. Her weight did not reduce as she is likely to have developed hypothalamic obesity.
Conclusions and points of discussion
Obesity is a largest and fastest growing public health problem with a prevalence of ~27% in England. Concomitant hormonal diseases can be present in obesity, so it is important to work up with detailed history, examination and investigations to exclude hormonal pathology. It is a common practice to investigate for Cushing's as a cause for obesity but other hormonal causes are usually overlooked. There is a bidirectional relationship between obesity and hypogonadism in men, so the presence of either condition could lead to the other. Our second patient did not have typical symptoms of prolactinoma like headache, visual defects or

galactorrhoea despite the presence of large pituitary adenoma, so it is important to be aware that clinical features can be subtle. We present our patients to highlight the importance of addressing hypogonadism, as an aid to the management of unexplained obesity.

DOI: 10.1530/endoabs.100.P28

P29

Hyperthyroxinaemia with normal TSH: a diagnostic conundrum

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Case History
A 49 year old man was referred from primary care with clinical features of thyrotoxicosis, including weight loss, anxiety and palpitations, over the previous four months. The patient had a 20 year history of abnormal thyroid function, characterised by elevated fT3 and fT4 with normal TSH. He had been previously assessed by the regional thyroid service 12 years prior and diagnosed with thyroid hormone resistance syndrome (RTH). This was based on clinical and biochemical assessment including TRH stimulation test, demonstrating an exaggerated response (TSH rising from 1.36 mIU/l to 14.1 mIU/l at 60 minutes) and a non-elevated alfa-subunit. Previous pituitary imaging was reported as normal. There was no family history of RTH and genetic tests failed to identify a mutation of the thyroid hormone receptor beta-gene.
Investigation & Results
On review in clinic, he appeared euthyroid, with no goitre present. Carbimazole (30 mg) had been commenced in primary care. TFTs showed: TSH 7.06 mIU/l, fT4 17.9 pmol/l. Carbimazole was then stopped and TFTs repeated: TSH 5.21 mIU/l, fT4 27.3 pmol/l, fT3 8.5 pmol/l. Pituitary MRI showed a normal sized pituitary with a possible sub-centimetre left sided pituitary lesion.
TSHoma was suspected and the patient was given a 3 month trial of somatostatin analogue (SA).

	Baseline	On treatment
TSH (mIU/l)	15.84	0.92
FT4 (pmol/l)	26.2	22
FT3 (pmol/l)	12.8	7.8

There was improvement, but no normalisation of TFTs. SA was initially stopped, but then recommenced, demonstrating biochemical normalisation and symptomatic improvement.

	Baseline	On treatment
TSH (mIU/l)	1.86	0.95
FT4 (pmol/l)	25.3	23.5
FT3 (pmol/l)	9.8	5.7

Methionine PET-CT was performed (off SA) which demonstrated a skew of tracer towards the left inferior paramedian aspect of the gland. Repeat Methionine PET-CT (on SA) showed a loss of this asymmetry, in-keeping with a small thyrotroph tumour.
Treatment
The patient proceeded to transsphenoidal surgery for resection of the presumed TSHoma. Histology confirmed TSH immune-positive pituitary adenoma. SA was discontinued and post-operative TFTs have remained normal (TSH 1.61 mIU/l, FT4 15.7 pmol/l, FT3 4.3 pmol/l). The patient is well and is undergoing T3 suppression test to assess cure of the TSH-oma.
Conclusion and Points for Discussion
This case shows a patient, originally misdiagnosed with thyroid hormone resistance, but subsequently found to have TSH-oma 20 years later. It is unusual for a TSH-microadenoma to be resected after such a prolonged period. The case illustrates the effective use of both somatostatin analogues and Methionine PET in the diagnosis of TSHoma.

DOI: 10.1530/endoabs.100.P29

P30

A rare case of ovarian carcinoid presenting with heart failure and trivalvular disease

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Case History
We present the case of a 77 year old female, who presented to the cardiology team with progressive shortness of breath and signs of heart failure. Echocardiogram showed pulmonary hypertension, tricuspid, pulmonary and aortic regurgitation and atrial septal defect with a bidirectional shunt. She also reported a 5 year long history of diarrhoea, flushing and wheezing. The Echocardiographic features together with the chronic symptoms raised suspicion for carcinoid syndrome and carcinoid heart disease (CHD). Abdominal computed tomography showed a 6 cm left adnexal mass without hepatic metastasis suspicious of ovarian carcinoid.
Results and Treatments
24 H Urine 5HIAA level was elevated at 781 umol/l (0-50 umol/l). A Gallium 68-DOTATATE Scan demonstrated high SSTR expression in the left adnexal mass, consistent with ovarian carcinoid and no features of hepatic or distant metastases. Short acting somatostatin analogue therapy (Octreotide 100 mg three times a day subcutaneously) was commenced while awaiting cardiac surgery and intravenous Octreotide as a bolus followed by a continuous infusion was given perioperatively in line with our local guidance. She underwent multivalve replacement (tricuspid, aortic and pulmonary), repair of the septal defect and a pacemaker insertion. Histopathology confirmed features in keeping with CHD. Post operatively, long acting subcutaneous somatostatin analogue therapy (Lanreotide 120 mg every 28 days) was started. Three months later, she underwent a laparoscopic total abdominal hysterectomy and bilateral salpingo-oophorectomy. Histopathology and post operative 24H Urine 5 HIAA levels are awaited.
Conclusion and Point of Discussion
CHD can occur as a complication of carcinoid syndrome, which is typically associated with carcinoid tumour of gastrointestinal tract(GIT)with hepatic metastasis. GIT carcinoids secrete large amount of vasoactive peptides such as serotonins which are metabolised by the liver before entering into the systemic circulation. Ovarian carcinoids are rare accounting for $<0.1\%$ of ovarian cancers and only 1% of carcinoid tumours. CHD caused by ovarian carcinoids without liver metastasis is a rare form of CHD. In ovarian carcinoid, the drainage of the ovary bypasses the liver on route to the inferior vena cava allowing vasoactive peptides to be secreted into the circulation. Left sided valve disease in this case is likely due to the ASD. The case is a rare case of CHD due to ovarian carcinoid with both right and left sided valvular disease who has been successfully managed through curative cardiac and gynecological surgery

DOI: 10.1530/endoabs.100.P30

P31

Acute severe hypocalcaemia after initiation of a selective ret inhibitor in medullary thyroid cancer

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Case history
A 64-year-old man was diagnosed with sporadic medullary thyroid cancer in 2018 after presenting with diarrhoea and a neck mass. He underwent a total thyroidectomy, neck dissection and post-operative radiotherapy, for extensive T4N1bM0 disease involving the tracheal wall and oesophagus. He was left with hypoparathyroidism, taking 1-alfacalcidol 1 mg OD. He also had T2DM on Gliclazide. In 2023 his calcitonin had risen to 12,220 pmol/l, with recurrent severe diarrhoea, and a change in voice with stridor. CT showed residual tumour invading the trachea, nodal disease in the mediastinum and multiple lung nodules. He was referred to our centre for further management. He had a somatic Met918Thr RET mutation. MDT discussion confirmed need to start systemic therapy and given the risk of fistulation with potent VEGF inhibitors such as Cabozantinib, Selpercatinib was started at an initial dose of 120 mg twice daily.
Investigations
Immediately prior to starting Selpercatinib the corrected calcium was 2.02 mmol/l (NR 2.1 to 2.5) with a phosphate of 1.34 mmol/l on a stable dose of 1-alfacalcidol only. 2 weeks after starting treatment, he was tolerating treatment well with significant improvement in his diarrhoea. However corrected calcium had fallen to 1.4 mmol/l and phosphate increased to 2.22 mmol/l. PTH was 2.1 pmol/l (0.8 to

5.7) and Vitamin D was 65 nmol/l. ECG showed a QTc of 489 mS. He retrospectively reported tingling in his hand for 24 hours.
Results and Treatment
He was admitted to a monitored bed and commenced on an intravenous Calcium Gluconate infusion, alfacalcidol was increased to 1 mg BD and he was started on Calcium Carbonate 4.5 g TDS. Corrected calcium improved over 48 hours to 1.9 mmol/l and phosphate fell to 1.58 mmol/l.
Conclusions and points for discussion
Despite a considerable rapid improvement in systemic symptoms and diarrhoea, severe hypocalcaemia developed within 2 weeks of treatment with Selpercatinib, on a background of previously well controlled post-operative hypoparathyroidism. Acute admission and prolonged intravenous Calcium were required. Selpercatinib, a selective RET inhibitor, had shown significant efficacy in RET mutated metastatic medullary thyroid cancer. In the phase 3 trial [1], hypocalcaemia was reported in 10.4% of patients (Grade 3 or higher in 1%). This was lower than in the control group (treated with either Cabozantinib or Vandetanib) where 25.8% had hypocalcaemia (Grade 3 or higher in 7.2%). Despite this, clinicians need to be aware of the risk of severe hypocalcaemia with Selpercatinib, the mechanism of which is currently unclear.
[1] Hadoux *et al*. NEJM 2023 389:1851-61
DOI: 10.1530/endoabs.100.P31

P32

Gestational diabetes insidious
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Introduction
Gestational diabetes insipidus (GDI) is a rare complication of pregnancy thought to be due to increased vasopressin produced by the placenta. It usually occurs at the end of the second or in the third trimester.
Case Description
We report the case of a 28-year-old female patient, a primigravida with a previous history of Right hemi-anomalous pulmonary venous drainage into IVC with an initial baffle operation in October 2019. She had diet-controlled gestational diabetes mellitus and was not on any medications. During the 34th gestational week, she was admitted to the hospital with a 6-week history of polyuria and polydipsia associated with haematuria. On the admission day urine output over 12 hours was 7740 ml. Initial investigation showed:

HB	110 g/l	115-160
Urea	2.2 mmol/l	2.5-7.8
Creatinine	66 mL/min/1.73 m^2	
Sodium	144 mmol/l	
Potassium	4.4 mmol/l	
Urine osmolality	51 mosmol/kg	
Serum osmolality	295 mosmol/kg	275-295
Adjusted calcium	2.26 mmol/l	2.20-2.60
Cortisol	537 nmol/l	
IGF-1	11.6 nmol/l	10.9-33.7
LH	$<$0.3 iu/l	
FSH	$<$0.3 iu/l	
TSH	1.8 miu/l	2.0-4.0
HBa1c	34 mmol/mol	20-41
ALT	13 iu/l	$<$40

MRI Pituitary: No pituitary or infundibula abnormality. Minor focal T2 signal dropout around the hypothalamus may represent an old area of microhaemorrhage but does not appear acute. Urine input per 24 hours was more than 10000 ml. She underwent the water deprivation test two days after the admission. She remained polyuric throughout the test with a weight loss of approximately 3 Kg. She was unable to concentrate urine throughout the test with urine osmolality not rising $>$30 mosm/kg. Urine osmo improved after DDAVP 1 mg s/c stat (108 – $>$ 288 mosm/kg). She was started with sublingual Desmopressin 50 mg twice a day which improved the urine output. Her Sodium remained within the normal range. She was discharged from the hospital on Desmopressin 100 mg once daily. She delivered a healthy baby with no complications. She was reviewed 8 weeks post-delivery, and she remains polyuric despite taking sublingual Desmopressin 100 mg at bedtime.
Conclusion
Polyuria is often dismissed as a normal symptom in pregnancy; however, it is important to recognize that it may indicate pregnancy-related DI, as this condition may lead to serious consequences for both the patient and the fetus.
DOI: 10.1530/endoabs.100.P32

P33

Exploring divergent outcomes in transient thyroiditis: lessons from two post-parathyroidectomy cases
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Background
Transient thyroiditis following parathyroidectomy, although uncommonly documented, can arise from various etiologies such as autoimmune disorder, infections and other post inflammatory states, commonly with Immunotherapy. Post-surgical thyroiditis, including cases post-parathyroidectomy, is not fully elucidated in terms of its mechanisms. Herein, we present two cases of transient thyroiditis post-parathyroidectomy, highlighting the divergent outcomes and thereby the need for specialist monitoring.
Case Report
Patient A, who underwent right inferior parathyroidectomy, developed sudden onset palpitations diagnosed as Fast Atrial Fibrillation, accompanied by a paired TSH and T4 of 0.05 and 41, respectively (Normal Values: TSH: 0.27 - 4.5 mU/l, T4: 11 – 23 pmol/l), a week after surgery. Patient B, who underwent inferior parathyroidectomy with total thymectomy, experienced worsening loose stools and palpitations, revealing a paired TSH and T4 of 0.03 and 31.5, respectively. After ruling out autoimmune factors, both cases were attributed to post-parathyroidectomy transient thyroiditis, illustrating the variable clinical presentations and outcomes of this condition. Subsequent symptomatic treatment for transient thyroiditis led to symptom resolution, with thyroid function tests (TFTs) revealing improved FT4 levels. Consequently, anti-thyroid medications were gradually reduced for both patients and eventually stopped. Patient A achieved complete recovery with stable TFTs. However, patient B developed symptomatic hypothyroidism (TSH 6.6, FT4 10.3) despite discontinuation of anti-thyroid medications six weeks earlier, with positive TRAb(TSH Receptor Antibody), that was initially negative. Consequently, Levothyroxine was initiated for management. This emphasizes the importance of continuous monitoring and personalized intervention in post-parathyroidectomy thyroiditis to address the variable outcomes.
Discussion and Conclusion:
Transient thyroiditis following parathyroidectomy presents with contrasting clinical outcomes, underscores the complexity of its management. While autoimmune factors were ruled out in our cases, the pathogenesis of post-parathyroidectomy thyroiditis remains unclear. Inflammation related to palpation and mobilisation intraoperatively are thought to mediate these changes. Similar cases of post-parathyroidectomy transient thyroiditis are scarcely documented online, reflecting the rarity of this condition. Given the potential for variable outcomes, close follow-up and individualized management are imperative.
DOI: 10.1530/endoabs.100.P33

P34

A rare case of hypoxia and metastatic multifocal paraganglioma
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A 48-year-old woman with complex cyanotic congenital heart disease due to dextrocardia was found to have a urachal remnant during routine ultrasound as part of her cardiac monitoring. Unexpected, excision via partial cystectomy without any hypertensive crisis identified 12 mm bladder paraganglioma [PGL], with local metastases to bladder (distinct from primary lesion) and lymph nodes (pT2b N1). Post operatively (following histopathology diagnosis), biochemistry demonstrated marked catecholamine excess (plasma normetadrenaline 7072 pmol/l ($<$1180 pmol/l), metadrenaline 485 pmol/l, plasma 3-methoxytyramine $<$120 pmol/l) and she was commenced on doxazocin 4 mg BD. Subsequent functional imaging (Dotatate PET) identified multiple avid lesions including bilateral neck PGLs, a 3 cm mediastinal PGL, and a small PGL between pulmonary artery and aorta. Retrospective review showed evidence of these masses on earlier scans as far back as 2012, with gradual but progressive enlargement of thoracic PGLs. Resection was considered; however, the mortality risk for thoracic surgery was estimated at 10% and instead she was initiated on monthly Lanreotide injections (current dose 120 mg). She remains clinically and biochemically stable; and radiologically all PGL have remained stable on annual MRI and cardiac CT over last 3 years. Hypoxia is an important driver of tumorogeneses; however, many tumours demonstrate hypoxia-associated changes (e.g., HIF pathway activation, angiogenesis, and the Warburg metabolic effect) without hypoxia being present, which phenotype is termed pseudohypoxia. The role of pseudohypoxia in PPGL is well-recognised, with PPGL-associated

germline mutations identified in multiple respiratory-associated genes (e.g. *SDHx*) and HIF pathway genes (e.g., *EPAS, EGLN2*). Conversely, PPGLs are more common in individuals living in high altitudes, smokers, and individuals with cyanotic heart disease. In particular, recent studies have found evidence of somatic *EPAS1* mutations in multiple cases of pheochromocytoma and PGL. The current individual has chronic hypoxia, with polycythaemia (Hb 165-183 g/l; Haematocrit 0.531- 0.580; SDHB immunohistochemistry was positive, excluding SDHx mutations; and panel germline genetic testing (14 genes) did not identify pathogenic variants in pseudohypoxia genes, nor any other PPGL-associated genes. Sequencing of EPAS1 hotspot regions in archived resected tumour tissue and germline DNA was undertaken; however, this did not identify any pathogenic variants. Nonetheless, the clinical picture suggests that lifelong hypoxaemia may be driving development of multiple PPGLs in this patient. This case suggests potential new gene discovery driving hypoxia associated PPGL, requiring further research.

DOI: 10.1530/endoabs.100.P34

P35

A case of an adrenal incidentaloma leading to a diagnosis of pituitary cushing's!

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Case history
A 41-year-old female presenting with abdominal pain and melaena, was found to have a left adrenal incidentaloma on her abdominal CT. Her past medical history included polycystic ovaries, menstrual irregularity, fibromyalgia and gallstones. Medications on presentation were lansoprazole and dihydrocodeine only. On further questioning, she was experiencing hair loss, proximal muscle weakness, bruising and striae, weight changes and low mood.
Investigations
Under the endocrine team, she went on to have an adrenal MRI which confirmed an 11 mm benign adenoma. Additionally, she had a normal aldosterone/renin ratio of 40.0 pmol/mU (0-91), with normal urinary metanephrines: normetadrenaline 0.64 umol/d (0-3), metadrenaline 0.3 umol/d (0-1.4) and 3-Methyoxytyramine 0.85 umol/d (057-2.39). Somewhat unexpectedly, however, she had an elevated morning serum cortisol of 622 nmol/l (<50) following an overnight dexamethasone suppression test (DST). A further low dose DST also resulted in high serum cortisol of 225 nmol/l on day 2, with an ACTH of 40 ng/l (0-46). These results confirmed that the source of her hypercortisolaemia was not the adrenal incidentaloma. The primary differential was now pituitary Cushing's disease, a far stretch away from the initial indication for having a CT abdomen and investigating an adrenal lesion.
Results and treatment
The patient went on to have further tests supportive of this, including a high-dose DST with >50% serum cortisol suppression recorded (day 0: 963 nmol/l; day 2: 345 nmol/l) and a dynamic MRI, revealing a 3 mm left-sided pituitary microadenoma with medialisation of the cavernous carotid artery. Inferior petrosal sinus sampling confirmed pituitary driven Cushing's with left lateralisation. After discussion about the increased risk of surgery, she subsequently opted for a surgical resection of her pituitary tumour and commenced hydrocortisone replacement for low day 3 post-op cortisol. Histology showed a sparsely granulated lactotroph adenoma with low Ki67 but further histology review is awaited. Reassuringly, a short synacthen test performed 3 weeks post-operatively confirmed adequate adrenal response to ACTH stimulation, and the ongoing plan is to wean hydrocortisone, and reassess for hypercortisolaemia.
Conclusions and points for discussion
In conclusion, this is a remarkable case of a patient being diagnosed with pituitary Cushing's after discovering an adrenal incidentaloma on CT, performed for an unrelated presenting complaint of melaena. It demonstrates the value of detailed history taking and stepwise testing for hypercortisolism.

DOI: 10.1530/endoabs.100.P35

P36

New nail growth after four decades in an amputated nail bed following cabergoline treatment for prolactinoma: a curious clinical outcome and review of the literature

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Case history
Dopamine agonists are effective and safe first line therapy for prolactinomas. We report an intriguing effect of dopamine agonist therapy in a 68-year-old man commenced on cabergoline treatment for a macroprolactinoma. At review, he reported new nail growth on the tip of a previously partially amputated finger which had been devoid of a fingernail for over four decades. This patient was incidentally diagnosed with a pituitary tumour on a CT brain scan performed for acute delirium during an admission with pneumonia.
Investigations
This was later confirmed on a contrast-enhanced pituitary MRI scan as a 1.9 cm × 1.9 cm × 1.6 cm adenoma extending to the left cavernous sinus and inferiorly to the sphenoid sinus. Pituitary profile showed prolactin of >21,200 mIU/l (63-262), testosterone level low at 6.2 nmol/l (6.51-23.74); other anterior pituitary hormones were normal. He had no symptoms of hyperprolactinaemia, or visual compromise.
Results and treatment
Cabergoline was initiated at a dose of 0.25 mg once weekly after explaining the side effects, increased to twice weekly. He was subsequently seen in out-patient clinic, where he reported no new concerns. To his delight, he had noticed new nail growing on a fingertip that had lost nail following an accident several decades ago. He confirmed that facial hair was growing thicker and faster. The testosterone had normalised to 11.1 nmol/l. The prolactin improved to 18,587 mIU/l, and to 13,409 mIU/l with further dose increase, anticipating further reductions with dose titration.
Conclusion and discussion
Cabergoline, a synthetic ergot derivative, exerts potent and selective inhibition on prolactin secretion by targeting dopamine receptors within pituitary lactotroph cells. Nail growth is dependent on vascular supply. Endothelium-derived relaxing factor plays a key role in blood supply, predominantly endothelial nitric oxide (eNOS). eNOS is inhibited by prolactin; stimulated by oestrogen. Furthermore, keratinocytes essential for nail growth are thought to be activated by oestrogen. Prolactin reduction and consequent reversal of hypogonadism appears to have caused this serendipitous new nail growth in the inactive nail bed of an amputated finger after several decades. The authors propose that the higher testosterone resulting from prolactin suppression by cabergoline led to increased oestrogen by aromatisation, which could account for this phenomenon. To our knowledge, there are no case reports of dopamine agonists stimulating nail growth. There is a case of levodopa-induced nail growth published over 50 years ago, describing accelerated nail growth during Parkinson's disease treatment. We will monitor this fascinating development with recent dose increments of Cabergoline.

DOI: 10.1530/endoabs.100.P36

P37

PET CT and ultrasound-guided endoscopic radiofrequency ablation: almost a one-stop, minimally-invasive cure for hypertension due to an aldosterone-producing adenoma

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Case history
A 39-year-old gentleman was referred to the Endocrine clinic with a 5-year history of hypertension and intermittent hypokalaemia. He had been seen in the hypertension clinic, screened for secondary causes, and found to have an aldosterone of 604 pmol/l, renin <0.2 nmol/l/hr and potassium 3.7 mmo/l (off interfering medication), in-keeping with a diagnosis of Primary Aldosteronism (PA). His blood pressure was 126/82 mmHg on Ramipril 10 mg, Amlodipine 5 mg OD and Spironolactone 25 mg OD. There was no family history of hypertension and on examination he had long-standing vitiligo. Although initially preferring indefinite medical therapy to surgery, he subsequently enquired about less invasive options than total adrenalectomy. He met the eligibility criteria for the FABULAS trial (Feasibility study of RadioFrequency endoscopic Ablation with Ultrasound guidance as a non-surgical, Adrenal Sparing treatment for aldosterone-producing adenomas).
Investigations
Prior to radiofrequency ablation (RFA), [^{11}C]-metomidate PET-CT (MTO) was performed to confirm that the nodule on CT was the sole site of aldosterone production. A post-ablation MTO was performed to assess radiographic response to treatment.
Results and treatment
CT adrenal demonstrated a left adrenal lesion with HU<0 and no contralateral nodules. The pre-ablation MTO demonstrated: a 22 × 17 mm nodule, TOF

SUVmax right 9.7 and left 18.6, to give a ratio of 1.92 (>1.25 confirms lateralisation). Prior to ablation, he was alpha- and beta-blocked (with doxazosin and bisoprolol) for 2 weeks, in case of peri-procedural adrenomedullary excitation. In a 10-minute procedure under deep sedation, the tumour was viewed under endoscopic ultrasound guidance and ablated at 8 places using a 10 mm Starmed RFA probe at 30 W. There were no haemodynamic changes during the RFA, and no abnormalities on the post-RFA safety CT. The patient was able to resume normal activities the next day, and all antihypertensives were stopped post-procedure. 6-month post-ablation results: aldosterone 131 pmol/l, renin 0.2 nmol/hr and potassium 4.7 mmol/l. PET CT demonstrated: a mainly cold, shrunken 21 × 12 mm nodule on CT, SUVmax right 13.3, left 12.2 to give a ratio of 0.92 vs the contralateral adrenal. His blood pressure is now 116/72 mmHg off medication.

Conclusions and points for discussion

This case, and others in FABULAS, provide proof-of-concept for a short, minimally-invasive procedure to replace adrenalectomy on the left side as a complete cure for PA. Multiple short-distance burns visualised in real-time render endoscopic RFA safe and potentially effective. It is now being compared with surgery in a randomised controlled trial (WAVE).

DOI: 10.1530/endoabs.100.P37

P38

Non-classical presentation of primary aldosteronism in patient presenting with normotensive refractory hypokalaemia leading to delayed diagnosis

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Primary aldosteronism (PA) is a highly prevalent syndrome which is often missed even in those that present classically due to poor awareness. The commonest initial presentation is varied degree of hypertension with hypokalaemia in only 37%. The presence of hypokalaemia could be a good pointer to the diagnosis of PA but it is not a common initial presentation in normotensive patients. We present a 22-year-old man who presented initially with refractory normotensive hypokalaemic metabolic alkalosis after recurrent episodes of vomiting. It was initially felt that hypokalaemia was likely due to vomiting, however, the vomiting settled relatively quickly, but there was persistent refractory hypokalaemia despite large amounts of potassium supplementations on admission. Oesophago-gastroduodenoscopy showed oesophageal reflux. There is no any medical history, no regular medication, no abuse of diuretic or laxatives, or liquorice but significant history of hypertension and stroke in father with mortality at age 45. The initial investigations include nadir potassium of 2.6, pH of 7.44, bicarbonate 30.3 and base excess of +9.1, high renal potassium level of 92.2 mmol/l, normal plasma and urinary Magnesium and calcium, negative porphyria screen. He was referred to Endocrine clinic due to high ARR of 413.9 (<91) with normal Blood Pressure (BP). Consequently, he had saline suppression test which showed basal suppressed renin (2.0 mU/l), raised aldosterone (1320 pmol/l with failure of complete suppression of aldosterone after saline infusion (819 pmol/l) and overnight Dexamethasone suppression test (Cortisol 33). The initial adrenal CT was inconclusive and thus had an adrenal MRI which showed 15 mm adenoma. 24hr BP was normal with overall mean of 132/81 and the case was discussed at the regional Neuroendocrine MDT. The diagnosis of Conn's disease could not be made due to normal BP and possibility of renal tubulopathy (Gitelman's) was suggested. Eplerenone was started which maintained the potassium in the relatively normal range. This was continued for 2 years until high Blood pressure was picked up on home BP machine despite being on 150 mg of Eplerenone daily. This was optimised with further titration of Eplerenone and amlodipine. He was thereafter referred to a national expert who agreed with the diagnosis of PA and recommended genetic testing for a familial aldosteronism (type 1) before proceeding to surgery which eventually came back negative. This case illustrates the potential dilemma and delays that could further be encountered in diagnosis and management of PA with non-classical presentation.

DOI: 10.1530/endoabs.100.P38

P39

Falling phosphate - finding the cause

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Background

Phosphate plays an important role in bone mineralisation. Hypophosphataemia is a common electrolyte abnormality which can result from poor intestinal absorption, increased renal loses (secondary to renal disease, alcohol abuse or drugs) or intracellular phosphate shift (often secondary to septicaemia or glucose or insulin treatment). This case showcases the importance of identifying the underlying cause of hypophosphataemia to guide subsequent treatment.

Case History

We present a case of a 41-year-old Afro-Caribbean woman referred to the inpatient endocrinology team with severe hypophosphataemia. She had been admitted a month prior, presenting with a life-threatening asthma exacerbation. Her medical history included brittle asthma with frequent exacerbations managed with steroids, Ehlers-Danlos Syndrome, type 2 diabetes mellitus, osteopenia and thalassaemia trait. During her prolonged admission, the patient was managed for her asthma exacerbation (with aminophylline infusions, intravenous hydrocortisone, nebulisers) and anaemia (with intravenous ferric carboxymaltose).

Investigations

The patient's admission bone profile was normal. Phosphate levels became abnormal three weeks into the admission and reached a nadir of 0.25 mmol/l (normal rage 0.8-1.5). At this time, the patient was also symptomatic with weakness and muscle cramps. Investigations showed a persistently elevated PTH level (23.6 pmol/l, normal 1.6 - 6.9) and a raised 24-hour urinary phosphate output (56.2 mmol/24 hour, normal 15 – 50), with a reduced 24-hour urinary calcium output (2.3 mmol/24hour, normal 2.5–7.5). Other investigations, including renal and liver function, serum vitamin D, metanephrines and gut hormones, were normal. A DEXA scan post-discharge showed generalised osteopenia.

Results and treatment

This patient had several risk factors for developing serum hypophosphataemia secondary to increased urinary phosphate excretion, inducing frequent corticosteroid use and treatment with ferric carboxymaltose. As the phosphate level was normal for several weeks after admission despite treatment with hydrocortisone and its nadir happened seven days after intravenous ferric carboxymaltose administration, it was deemed that this was the likely precipitant. The patient was commenced on a 12-week course of oral phosphate replacement. Subsequent blood tests revealed a normal phosphate level, even once oral supplementation was completed.

Conclusions and points for discussion

This is not the only documented case of severe hypophosphataemia secondary to ferric carboxymaltose. A recent analysis showed ferric carboxymaltose is associated with over 50 times increased risk of hypophosphataemia than other intravenous iron preparations. It is thought that ferric carboxymaltose leads to an increase of biologically active FGF23 levels, subsequently inducing pathophysiological renal phosphate wasting and secondary hyperparathyroidism, leading to hypophosphataemia.

DOI: 10.1530/endoabs.100.P39

P40

A case of an ectopic ACTH-secreting pancreatic neuoroendocrine tumour (p-NET)

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Case History

A 60-year-old female presented to the outpatient clinic with lethargy and proximal muscle weakness. She had a recent hospital admission with osmotic symptoms leading to a diagnosis of ketosis-prone diabetes and was started on insulin. Eight months prior, she was diagnosed with a pancreatic neuroendocrine tumour (p-NET) with hepatic metastases; immunopositivity staining strongly for synaptophysin, focal chromogranin and patchy CD56, with low Ki-67 index of <1%. Given the intense octreotide avidity of the tumour, she was receiving monthly treatment with somatostatin analogue therapy (octreotide-LAR).

Investigations and Results

On presentation, she had severe hypokalaemia (2.2 mmol/l), which prompted admission for further investigations. Paired cortisol and ACTH levels following an overnight dexamethasone suppression test (DST) were 2497 nmol/l and 162 mU/l, respectively. There was no suppression of cortisol with either a low-dose DST (cortisol-2346 nmol/l) or high-dose DST (cortisol-2334 nmol/l). There was only a 24% rise of ACTH, and no discernible rise in Cortisol at 60 minutes following CRH testing. CT-TAP showed marginal progression of her pancreatic mass compared to her scan eight months prior, no new metastases and bulky adrenal glands. Initial biopsy slides of the pancreatic mass were stained retrospectively and were positive for ACTH in keeping with an ectopic ACTH-secreting tumour.

Treatment

She was commenced on a block-and-replace regime initially with metyrapone and ketoconazole. Oncology treatment was started simultaneously with streptozotocin and 5-fluorouracil chemotherapy. Following 8 days of ketoconazole/metyrapone

therapy, her cortisol level was 193 nmol/l and hydrocortisone was added/replaced. The doses continued to be titrated in the outpatient setting based on 9 a.m. cortisol levels. Despite alterations to her chemotherapy regime, she had significant side effects and continued to deteriorate. She developed marked skin hyperpigmentation, acne and hirsutism with orthostatic symptoms and eventually opted for palliative management and died eleven months later.
Conclusions and Points for Discussion
The prevalence of Cushing Syndrome secondary to ACTH-secreting p-NET is low and only a few cases have been reported. They are usually aggressive, with a high ki-67 index, concomitant hepatic metastases and associated with high mortality. This case was unlike previous cases in the literature, as the disease showed rapid progression despite the initial low ki-67. The block-and-replace regime with metyrapone/ketoconazole and hydrocortisone provided good suppression of cortisol production. Given their aggressive nature, p-NETs should ideally be stained for ACTH as it can lead to earlier treatment decisions by the multidisciplinary team.

DOI: 10.1530/endoabs.100.P40

P41

Unusual presentation of a large lactosomatotroph adenoma masquerading as a chordoma

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Case history
A 64-year-old male was admitted to our hospital in January 2024 following a road traffic accident. The patient was not wearing a seatbelt, and airbags did not deploy due to low speed, resulting in the patient's head hitting the windscreen. A subsequent CT trauma series showed a large destructive expansile lesion within the clivus and sphenoid bone extending superiorly into the hypothalamus with findings typical of a chordoma. Appearance on non-contrast MRI was also consistent with a chordoma. Imaging was reviewed by the local Neurosurgical centre and a pituitary profile requested, which unexpectedly showed a prolactin level of $>100{,}000$ munit/l and an elevated IGF-1 level of 78.6 nmol/l. Symptoms and features of acromegaly (macroglossia, increase in hand and foot size) and low testosterone (erectile dysfunction and low libido) became apparent following review by the Endocrine team.
Investigations
Due to patient claustrophobia initial MRI scans of the brain and whole spine were performed without contrast, but these showed no other spinal pathology other than a $50 \times 40 \times 76$ mm lesion centred on the clivus. A CT chest, abdomen and pelvis was normal, showing no solid organ, lung or bony mass lesions (concern that clival lesion may be a metastasis). Visual field testing showed a possible left inferior arcuate defect (no bitemporal hemianopia). Pituitary function testing revealed normal thyroid and cortisol axes, and hypogonadotrophic hypogonadism consistent with hyperprolactinaemia. An oral glucose tolerance test (OGTT) confirmed acromegaly with failure to suppress growth hormone.
Results and treatment
The patient was initially treated with cabergoline 250 mg twice weekly and showed good biochemical (prolactin reduced to 98,510 munit/l) and radiological response (reduction in tumour size on repeat MRI) but discontinued therapy after three weeks due to an acute change in mood with depression, poor sleep and dark thoughts. The patient was not keen to restart cabergoline, and so testosterone replacement was commenced to try to ameliorate some of these psychological symptoms. Lanreotide was commenced once acromegaly was confirmed by OGTT. Despite concerns, there was no evidence of any CSF leak, and the current plan is to assess tumour response to medical therapy prior to surgical intervention. Surgical treatment and definitive diagnostic biopsy results are awaited.
Conclusions and points for discussion
Ectopic pituitary adenomas (in this case a lactosomatotroph adenoma) are a rare entity and can be mistaken for a chordoma. A definitive histopathologic diagnosis is awaited in this case.

DOI: 10.1530/endoabs.100.P41

P42

An interesting and rare case of a TSH-GH co-secreting pituitary macroadenoma

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We present a 43 year old gentleman of Bangladeshi origin, who was referred to us by his GP with increased sweating, palpitations and anxiety for the last few years and abnormal thyroid functions. He complained of headaches, tremors, weight loss, increased appetite and sleep disturbances in addition to the above symptoms. He had no other significant past, family or social history. On examination in the clinic, he was found to have a raised blood pressure. He had phenotypical features of acromegaly such as coarse orbital ridges, prognathism with dental malocclusion, broad nose and large sweaty hands with tremors. He did not have a visible goitre. His initial blood tests showed a high free T3 (27.1 pmol/l), a high free T4 (55.0 pmol/l) with a raised TSH (5.93 mIU/l). His GH (15.1 mg/l), and IGF-1 (402 ng/ml) were also raised. To distinguish from Thyroid hormone resistance, his α-subunit, and SHBG were checked, and both of these were raised at 18.7 IU/l and 129 nmol/l respectively. He underwent an OGTT which failed to suppress his Growth hormone. His Pituitary MRI revealed a 4 cm macroadenoma with displacement of optic chiasm and carotid arteries. He was referred to the local tertiary pituitary MDT and commencement of Lanreotide and surgery was recommended. The patient was reluctant for surgery at this point, he was hence started on carbimazole, propranolol and Lanreotide 120 mg SC every four weeks. Five months into the above intervention, a marked reduction in the size of the pituitary macroadenoma was noted on a repeat MRI. There was a significant improvement in his TFTs (fT3 pmol/l, fT4 29 pmol/l, TSH 1.56 mIU/l), SHBG (49.6 nmol/l). His IGF1 though showed only marginal improvement (352 ng/ml). He was rediscussed in the Pituitary MDT and continuation of Lanreotide and a repeat surgical offer was recommended. A TSH-GH co-secreting pituitary macroadenoma is a rare tumor. The prevalence of a TSHoma is estimated to be less than 1 per million general population. Of these $<30\%$ of are plurihormonal, with GH being the most commonly co-secreted hormone. It is essential to correctly identify and address the co-secretion to avoid incomplete management of such plurihormonal adenomas.
Discussion
- The use of Carbimazole is controversial in a TSHoma.
- Awareness of the possibility of co-secreting pituitary tumors is essential to identify such tumours.
- Surgery remains mainstay of treatment, somatostatin analogs can be used in the interim.

DOI: 10.1530/endoabs.100.P42

P43

Managing cushing's disease in a patient with learning difficulties presents significant challenges

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A 52-year-old woman presented in 1998 at age 26 with hirsutism, obesity, and purple striae. She had history of learning difficulties and hyperphagia since age7. Physical examination revealed a supraclavicular pad of fat and hypertension. Biochemical analysis indicated a non-suppressed low-dose dexamethasone suppression test and an ACTH level of 55 ng/l, with all other pituitary hormones normal. MRI findings showed a midline hypodense area anterior to the posterior lobe, with deviation of the stalk to the right. CT scans of the adrenals appeared normal, prompting further investigation with an IPSS revealing a left sided pituitary source. Subsequent transsphenoidal surgery in 2000 successfully excised the adenoma, followed by a postoperative rise in cortisol levels necessitating treatment with metyrapone. In June 2003, she experienced severe headache and dysconjugate movements suggestive of pituitary apoplexy, leading to secondary adrenal failure persisting despite cessation of metyrapone. Hydrocortisone therapy was initiated at a dosage of 20/10/10 and then subsequently reduced to 15/5/5 mg. On further assessment low-dose dexamethasone suppression test results (353 to 45 nmol/l) and an ACTH level of 45.5 ng/l to 14.3 ng/l, off hydrocortisone. From 2014 to 2016, she received escalating doses of metyrapone, followed by a second transsphenoidal surgery in June 2017, excising a large pituitary adenoma with postoperative ACTH levels measuring 186 ng/l. Histology revealed positive staining for ACTH and GH, with a KI67 index exceeding 10%. Despite consideration of conventional radiotherapy, the patient's inability to tolerate the treatment led to the resumption of metyrapone. A new diagnosis of type 2 diabetes necessitated treatment with Metformin and Trulicity. Bilateral adrenalectomy was deliberated by the multidisciplinary team (MDT) but deemed high-risk due to concerns regarding hydrocortisone compliance. An application for Pasireotide to NHS England was rejected. In 2022, discontinuation of metyrapone due to taste intolerance led to an increase in ACTH levels to 228 ng/l. Subsequent clinical deterioration and non-compliance with oral metyrapone necessitated a renewed successful application for Pasireotide. Despite developing DKA while on Pasireotide, insulin was initiated, achieving moderate biochemical

control with Pasireotide, maintaining ACTH levels at 112 ng/l, hydrocortisone day curve of 600-700 nmol/l, serum testosterone reduced from 3.7 to 0.3 nmol/l. This case underscores the complex challenges physicians encounter when managing patients with learning difficulties. Pasireotide was chosen due to its subcutaneous administration, facilitating ease of delivery by healthcare providers. Additionally, her inability to tolerate radiotherapy further complicated the decision-making process. Pasireotide emerged as the more practical choice given the patient's circumstances.

DOI: 10.1530/endoabs.100.P43

P44

Ectopic cushing's syndrome: delayed recognition of a rare but sinister cause of hypokalaemic metabolic alkalosis

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Case history
A 53 year old lady was admitted with aggressive behaviour and confusion. Past medical history: Treated breast cancer 2017, no recurrence on mammogram 2021. Lifelong smoker. Initial investigations: persistent hypokalaemia with metabolic alkalosis, negative septic screen, unremarkable CT and MRI brain, failed lumbar puncture. Hypokalaemia only corrected with SandoK and spironolactone. She was empirically treated for encephalitis. CT TAP (septic screen): extensive mediastinal and hilar lymphadenopathy and bilateral bulky adrenals. Random cortisol, requested 15 days into admission, was 3059 nmol/l. O/E: Facial plethora, increased skin pigmentation, proximal myopathy and centripetal obesity.
Investigations
24hr UFC $>$5000 nmol, ACTH 529 ng/l, 1 mg ODST cortisol $>$3300 nmol/l, TSH 1.5 mIU/l, HbA1c 44 mmol/mol.
Results and treatment
The diagnosis was ectopic Cushing's syndrome. Metyrapone was started and uptitrated to 2 gm/day. She was moved to HDU for acute heart failure and severe agitation, where etomidate infusion was started. Rapid cortisol control was achieved with etomidate. A request for osilodrostat was made on compassionate grounds. Due to delay in procuring osilodrostat, she was initiated on mitotane, while etomidate was weaned. She was stepped down from HDU on metyrapone and mitotane. However, hypokalaemia and psychosis recurred with rising cortisol levels. Mitotane was stopped (potential neuropsychiatric toxicity) and metyrapone increased to 3 gm/day, while awaiting osilodrostat. Rapid deterioration ensued with desaturation and progressive CXR changes, without evidence of infection or heart failure. PCP prophylaxis was ongoing. She remained too unwell for bilateral adrenalectomy or invasive tissue diagnosis (EBUS or mediastinoscopy). Interval CT showed significant disease progression with new hepatic metastases. US-guided liver biopsy revealed metastatic small cell lung cancer, the likely source of ectopic ACTH secretion. Osilodrostat was only briefly given, as she deteriorated and passed away within a few days.
Conclusions and points for discussion
The clinical features of intense hypercortisolism include refractory hypokalaemia and metabolic alkalosis, as well as neuropsychiatric manifestations. Failure to recognise this constellation of features can lead to delay in diagnosing and managing both hypercortisolism and the underlying cause, often resulting in significant morbidity and even mortality. This case also illustrates the complexity in managing severe hypercortisolism with multiple agents which target the steroidogenesis pathway at different levels. 11 β-hydroxylase inhibitors include metyrapone and osilodrostat. Etomidate, an inhibitor of side chain cleavage and 11 β-hydroxylase, can achieve rapid cortisol control but requires administration in HDU. Mitotane, an adrenolytic agent, induces "chemical adrenalectomy".

DOI: 10.1530/endoabs.100.P44

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Just a routine thyroid check in pregnancy...

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A 24-year-old, Bengali female presented to her GP with fatigue. Blood tests demonstrated she was pregnant and had elevated thyroid hormones (Free T4 50.4 pmol/l, NR 10.5-24.5; Free T3 19.9 pmol/l, NR 3.1-6.8) with an inappropriately normal TSH (4.04 mU/l, NR 0.27-4.2), prompting referral to our endocrine unit. Her TFTs were repeated on a different platform which excluded assay interference. She reported a 5-year history of a goitre, associated with symptoms of hyperthyroidism (which had previously been investigated with a normal TSH). She was a primigravida and had no difficulties conceiving. Her past medical history was unremarkable, including no childhood symptoms suggestive of thyroid hormone resistance. She had a significant family history of consanguinity. On examination: BMI 18.39 kg/m^2; small, smooth goitre; mildly hyperthyroid (fine tremor, hyper-reflexia); visual fields: concentric reduction to confrontation with red pin. Genetic sequencing identified no abnormality in the thyroid hormone receptor beta. Non-contrast pituitary MRI demonstrated a 21 mm pituitary macroadenoma, in keeping with a TSH-oma. The remainder of her anterior pituitary function was normal. Somatostatin analogues are unlicensed in pregnancy and we sought advice from the UK Teratology Information Service. The patient was counselled carefully on the diagnosis and treatment options. She underwent an octreotide suppression test and commenced 4 weekly long-acting somatostatin analogue therapy at 13 + 4/40 gestation, resulting in normalisation of her TFTs within 3 days. She was monitored closely, including TFTs, CBG testing and serial fetal growth scans. Non-contrast pituitary MRI at 30/40 gestation demonstrated a significant reduction in the size of the macroadenoma and the patient was planned for a normal vaginal delivery. However, a fetal growth scan at 31 + 2/40 gestation demonstrated intrauterine growth restriction and oligohydramnios. She underwent an uncomplicated emergency caesarean section at 31 + 4/40. Her baby boy is well, following 5 weeks on SCBU. To preserve fertility, she will be considered for surgical management after she has completed her family. TSHomas make up less than 1% of all pituitary adenomas; with an incidence of 0.15 per million, although the incidence is increasing, possibly due to more sensitive TSH assays[1]. To our knowledge, this is the first case in the published literature of TSHoma diagnosed in pregnancy and managed throughout with somatostatin analogues. Somatostatin analogues have been used more routinely in pregnancy in acromegaly, with limited, but favourable safety data. The safety profile in those with TSHomas remains confounded by the initial hyperthyroid state in early pregnancy.

DOI: 10.1530/endoabs.100.P45

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Cranial DI underlying diagnosis unmasked by exacerbating secondary Nephrogenic DI

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I present a case of a 32 year old woman who presented in September 2023 with abdominal pain and vomiting. Her blood tests showed; Hb 151 g/l, WCC 18.3, Na 130 mmol/l, K 1.8 mmol/l, Ur 4.7 mmol/l, Creatinine 91 umol/l, Corrected Calcium 2.93 mmol/l, Phosphate 0.54 mmol/l, Lipase 191 unilts/l. Venous Blood Gases showed pH 7.25, Bicarbonate 15.6, Lactate 1.9, pCO2 4.5, Glucose 7.0 mmol/l. She had a background of treated TB aged 25, recent diagnosis of H. Pylori gastritis, and gave birth in September 2022. Her son was born with congenital complete heart block and she had positive Anti-Ro and Anti-La antibodies. She was managed in the ITU and received concentrated potassium infusions and Hartmann's. Her urine output after admission to ITU was up to 8L per day with doses of 0.5 -1 mg parenteral DDAVP intermittently. The DDAVP was not effective at reducing her urine output initially. Her Sodium climbed to 161 mmol/l after 48 hours. She was also noted to have a mildly low Cortisol and therefore underwent a Pituitary MRI to rule out Sheehans Syndrome. The MRI showed a potentially thickened pituitary stalk and a loss of posterior pituitary bright-up. She returned for an Insulin Tolerance Test on 24th October. The Nadir glucose was 1.4 mmol/l. The peak Cortisol was 476 nmol/l, and GH was 4.03 mg/l. Hydrocortisone was stopped. She then had a Water Deprivation Test 5th December. At the start of the test the Serum Osmolality 291 mmol/kg, with a Urine Osmolality of 140 mmol/kg. At 8 hours the Serum Osmolality was 298 mmol/kg with a Urine Osmolality of 228 mmol/kg. Her Insulin Tolerance test ruled out Cortisol insufficiency and the Water Deprivation test is suggestive of Vasopressin Deficiency / Resistance. Given the good response to low dose oral DDAVP, alongside the loss of posterior pituitary bright up, she is being managed as Cranial Diabetes Insipidus secondary to presumed Lymphocytic Hypophysitis. The fascinating point within this case is we suspect that her lack of improvement initially, despite Desmopressin, is due to nephrogenic DI secondary to hypokalaemia and gradient washout secondary to a history of polyuria. Both are under-recognised causes of polyuria. Therefore, this is a woman with Cranial DI which was diagnosed due to an exacerbating secondary Nephrogenic DI.

DOI: 10.1530/endoabs.100.P46

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Relapsed thyrotoxicosis presenting as thyroid storm with likely thyrotoxic cardiomyopathy and acting as a trigger for diabetic ketoacidosis

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Case history
41-year-old lady with background of T1DM (1993), previous DKA (2017), and treated thyrotoxicosis (2017-2019) presented with 3 day history of vomiting, diarrhoea, poor oral intake, and shortness of breath. She was anxious, though not agitated. She denied palpitation though remained tachycardic. She denies abdominal pain, jaundice, or oedema legs. Her only medication was basal-bolus regimen to which she was compliant. She does not smoke, drink or use illicit drugs. O/E: PR 140/min, BP 121/55 mmHg, Temperature 38.2^0C, RR 24/min, Saturation 96% (air). She was severely dehydrated with hand tremors and a nontender diffuse goitre without bruit, thyroid eye disease or heart failure signs. Systemic examination was otherwise unremarkable.
Investigations
VBG: pH 7.176, $HCO3^-$ 8.9, base excess -17.8, glucose 23.2, lactate 5.8. Ketones 6.4. Bloods showed Na^+ 135, K^+ 2.9, Urea 8.4, Creatinine 53, eGFR >90, Mg^{2+} 0.54, Ca^{2+} 2.45, CRP 3.7, FBC mild neutrophilic leucocytosis, β-hCG negative. ECG showed sinus tachycardia, Chest X-ray was normal, and urine dip ruled out infection. TSH <0.01, Free T4 >100, Free T3 47.7, TRab positive, NT-pro-BNP 4390, and bedside ECHO mild LVSD.
Results and treatment
DKA protocol initiated on arrival. As sinus tachycardia persisted despite adequate hydration, and no other specific trigger for DKA found, in view of previous thyrotoxicosis, a relapse was considered. Bloods confirmed thyrotoxicosis and Burch-Wartofsky Point Scale (BWPS) score of 55 was highly suggestive of thyroid storm. Urgent endocrine review was sought and patient put on PTU [500 mg stat, 200 mg Q4H], hydrocortisone [200 mg stat, 100 mg TDS], propranolol [40 mg TDS], and cholestyramine [4 gram TDS]. Patient was managed in ITU for 48 hours with endocrinology and cardiology inputs. Electrolyte imbalance were corrected.
Conclusion and points for discussion
When common triggers for DKA including infection, infarction, 'infant-on-board', indiscretion, and insulin deficiency are excluded, we should look for rare triggers like drugs, thyrotoxicosis, Cushing's or acromegaly. Vomiting and shortness of breath are so common with DKA that, we may fail to consider possibility of thyroid storm. Renal loss of Mg^{2+} from DKA and GI loss from thyrotoxicosis could explain the hypomagnesemia and resultant hypokalaemia. Fever, acute confusion, and deranged LFTs could all be misleading, as they may point towards sepsis, whereas they might have originated from thyroid storm. Both DKA and thyroid storm are procoagulant states. Diagnosis of thyroid storm is clinical, and is not proportionate to the severity of thyroid dysfunction. Early diagnosis which requires a high index of suspicion would improve the outcome.

DOI: 10.1530/endoabs.100.P47

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Adrenal leiomyosarcoma and primary hyperparathyroidism- a rare co-presentation

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A 76-year-old lady was admitted to a Spanish Hospital with vertigo and dizziness. Investigations revealed hypercalcaemia and a right adrenal mass on an MRI abdomen. On returning to the UK, she was referred to endocrinology. Additional symptoms included fatigue, memory loss and some leg weakness over the preceding months. She was noted to be hypertensive, controlled on Amlodipine 5 mg od. Investigations revealed an elevated serum corrected calcium of 2.85 mmol/l and serum PTH raised at 13.4 pmol/l. Mild hypercalcaemia had been present for five years. The Non-contrast CT adrenals showed a heterogeneous mass arising between the right kidney and the right adrenal (4.6 × 4 × 4.3 cm) with an average peak density of 35 Hounsfield Units. This mass was not present on a previous CT seven years earlier. Adrenal hormone investigations including urinary metanephrines and plasma Aldosterone: Renin ratio were unremarkable A sestamibi SPECT CT scan revealed a 12 mm parathyroid adenoma in the right inferior to the lower right thyroid lobe which was confirmed on ultrasound. Following adrenal MDT discussion she underwent CT scan- Chest Abdomen and Pelvis followed by a robotic right adrenalectomy. The histological examination of the adrenal mass revealed that the tumour is diffusely positive for smooth muscle myosin and caldesmon, and there is patchy positivity for smooth muscle actin and desmin. The proliferation fraction on ki67 stainings is around 5-10%. Features and immunoprofile were compatible with an adrenal leiomyosarcoma with incomplete local excision. Surgical parathyroidectomy has been delayed until a period of time has elapsed and reassured that all is stable from the sarcoma perspective.
Conclusion
Primary adrenal leiomyosarcoma (PAL) is extremely rare, with less than 50 cases reported worldwide. PAL is a mesenchymal tumour that originates from the smooth muscle wall of the adrenal vein. They are usually large and grow rapidly. The incidence increases with age. Most PAL tumours do not secret adrenal hormones. There are no specific tumour markers or imaging characteristics that easily enable a preoperative diagnosis. Surgery is the mainstay of treatment. Adjuvant chemotherapy or radiotherapy is often used for PAL patients with poor prognosis. postoperative adjuvant radiation therapy is recommended for the treatment of locally advanced malignancy. Hyperparathyroidism is an uncommon endocrine disorder. There is no known association between adrenal leiomyosarcoma and hyperparathyroidism. This case represents the first known case of these conditions existing simultaneously.

DOI: 10.1530/endoabs.100.P49

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A case of undetected amiodarone induced thyrotoxicosis type 1 without a goitre

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A 73-year-old gentleman due to undergo prostatectomy for adenocarcinoma was found to have biochemical secondary hyperthyroidism at a preoperative assessment. His thyroid stimulating hormone (TSH) was 5.08 μIU/ml and free T4 (fT4) was 22.7 pmol/l. He was clinically euthyroid and did not have a goitre. His past medical history was of subclinical hypothyroidism, atrial fibrillation, and hypertension. Subclinical hypothyroidism was diagnosed in 2020 based on findings of TSH 11.9 μIU/ml and fT4 16.8 pmol/l. Anti-TSH receptor and TPO antibodies were negative. He was started on levothyroxine 50 mg daily. Two weeks later, he was prescribed amiodarone 300 mg daily for management of atrial fibrillation. In 2021, he underwent catheter ablation which successfully restored sinus rhythm, yet amiodarone was continued. He has since had six measurements of elevated TSH and fT4, while remaining asymptomatic. His levothyroxine dose was reduced to 25 mg by the general practitioner. In 2023, he was diagnosed with adenocarcinoma of the prostate and he was scheduled for robotic-assisted radical prostatectomy. An endocrinologist was consulted preoperatively regarding the abnormal thyroid function tests. A diagnosis of amiodarone induced type 1 thyrotoxicosis was confirmed, three years after secondary hyperthyroidism was first noted on routine monitoring blood tests. The patient underwent successful prostatectomy. This case of three-year delay in the diagnosis of amiodarone induced type 1 thyrotoxicosis highlights the need for improved awareness of thyroid function test interpretation among clinicians, as well as integrated communication between primary and secondary care specialists.

DOI: 10.1530/endoabs.100.P50

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The expanding phenotypic spectrum of silver-russell syndrome may confound decisions to investigate for (epi)genetic causes

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Case History
A 5-year-old South Asian female patient was born at term with very low birth weight (-3.8 SDS). She exhibited short stature (height -3.9 SDS), feeding difficulties (BMI -3.0 SDS) and microcephaly (HC -4.9 SDS). Maternal height was reduced (-3.5 SDS), paternal height was normal (-0.2 SDS). The girl had characteristic syndromic features including triangular face, high-pitched voice, and high-arched palate. She displayed developmental delay manifesting as inattention and poor motor, writing, and reading skills. Silver-Russell syndrome (SRS) was suspected but she did not fulfil Netchine-Harbison Clinical Scoring System (NH-CSS) criteria (score 3/6).

Investigations
Investigations established normal female karyotype (46,XX) and short stature screen with elevated serum IGF-1 levels (+4.4 SDS). Testing for common molecular causes of SRS did not detect hypomethylation of chromosome 11p15 (11p15LOM) or maternal uniparental disomy of chromosome 7 (UPD(7)mat). Whole exome sequencing identified a maternally inherited, heterozygous predicated damaging missense *HMGA2* gene variant (c.166A>G; p.K56E). We report the first missense mutation in a highly conserved region (2nd AT-hook adjacent), impacting DNA binding.
Management
SRS is a multisystem disorder requiring early, multidisciplinary clinical management. The identification of a genetic cause for this patient's phenotype allowed an end to diagnostic testing and the initiation of tailored clinical management including active surveillance for co-morbidities, growth monitoring, nutritional support and referral for genetic counselling.
Conclusions and discussion points
SRS is rare (epi)genetic disorder characterised by pre- and post-natal growth restriction and distinct features. SRS has a varied phenotype and clinical features diminish with age, making diagnosis challenging. ~60% of cases are attributed to 11p15LOM or UPD(7)mat and frequently identified by NH-CSS criteria. Recently, rare (<5%) monogenic defects (*CDKN1C*, *IGF2*, *PLAG1*, *HMGA2*) have been implicated. Clinical SRS diagnosis (≥4/6 NH-CSS criteria) must include relative macrocephaly and prominent forehead at birth. However, the NH-CSS utility in diagnosing rare monogenic causes of SRS is uncertain. (Epi)genetic testing is recommended for patients scoring ≥3/6 NH-CSS criteria. Rarer monogenic cases should not be overlooked. We analysed the 17 *HMGA2* cases reported to date: 35% failed to fulfil NH-CSS criteria, 71% lacked relative macrocephaly and 6% had no body asymmetry. Our patient also had atypical features (developmental delay and microcephaly). Our case highlights that NH-CSS <4/6 and atypical features, such as microcephaly, should not preclude clinicians from investigating SRS. Molecular diagnosis is crucial for stratification of cases and clinical management, enhancing outcomes and reducing the diagnostic odyssey for patients and families.

DOI: 10.1530/endoabs.100.P51

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Normalisation of parathyroid hormone in a patient with pseudohypoparathyroidism type 1b following a diagnosis of lymphoma

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Clinical case
A 23-year-old woman with genetically confirmed pseudohypoparathyroidism type 1b (PHP1b) reported a one-month history of progressive bilateral cervical lymphadenopathy at her most recent outpatient visit. This was associated with night sweats and a dry cough, but no weight loss, haemoptysis or recent foreign travel. Clinical examination revealed widespread non-tender cervical and inguinal lymphadenopathy with no hepatosplenomegaly. An expedited ultrasound guided lymph node biopsy was arranged following discussion with haematology.
Investigations
Lymphocytosis 5.2 × 10^9/l (1-3) with reactive forms were seen on blood film with normal total white cell, haemoglobin and platelet counts. For her PHP1b, the patient was stable for eighteen months on 1 microgram twice daily alphacalcidol and 2000 units daily vitamin D3, maintaining an adjusted serum calcium just below the lower reference range, with elevated but down trending parathyroid hormone (PTH) and ALP levels; six months prior, adjusted calcium 2.19 (2.20-2.60 mmol/l), phosphate 0.94 (0.8-1.5 mmol/l) with PTH 44.7 (1.6-6.9 pmol/l) and ALP 163 (30-130 u/l), down from 143 pmol/l and 717 u/l respectively, alongside severe symptomatic hypocalcaemia (1.56 mmol/l) at diagnosis two years previously. Normal PTH (5 pmol/l) and ALP (100 units/l) alongside adjusted calcium 2.43 mmol/l, normophosphataemia and preserved renal function were seen at the current visit. Histopathology confirmed t-cell lymphoblastic lymphoma with a high proliferation index; Ki67 90-95%. Diffuse sclerotic bony lesions were seen on staging CT.
Results and treatment
Following an acute presentation with nausea and vomiting, an LDH serum >1800 (0-249 u/l) and an acute severe transaminitis with no other identifiable cause, urgent admission was required to initiate treatment for acute lymphoblastic lymphoma. Day four post first cycle of chemotherapy, adjusted serum calcium was 2.21 mmol/l. Her alphacalcidol and vitamin D3 are being continued at the same doses. The results of serum 1,25-dihydroxy vitamin D3 (1,25(OH)2 D3) and parathyroid hormone related peptide (PTHrP) are awaited.
Discussion
In our patient, normalisation of PTH with mild elevations in serum calcium concurrent with her diagnosis of lymphoma, suggest an ectopic contributor affecting calcium homeostasis. Tumour induced overproduction of 1,25(OH)2 D3 by extrarenal 1a hydroxylation from lymphoma cells or surrounding macrophages is the proposed mechanism. Whilst her end organ resistance to PTH signalling is likely protective against the development of hypercalcaemia and its associated risks, in those with pseudohypoparathyroidism, targeting serum calcium towards the lower end of reference to avoid renal complications is paramount. Elevation of PTH with reduction in serum calcium is expected as remission of malignancy is achieved.

DOI: 10.1530/endoabs.100.P52

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Refractory arrhythmias secondary to severe amiodarone-induced-thyrotoxicosis: the MDT approach

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Case history
A 64 year old male attended the Emergency Department with palpitations on 02/11/2023. He had previous extensive cardiovascular disease: Ventricular Tachycardia (VT) - ICD (2021) and 2 ablations (2022, 2023); Myocardial Infarctions (2005, 2021); and moderate Left Ventricular Systolic Dysfunction (LVSD). He was treated with amiodarone from July 2021 which was stopped after his second ablation in August 2023. Interrogation of his pacemaker showed new atrial fibrillation with rapid ventricular response (fAF); 2 shocks had fired due to VT. He was admitted for rate control with monitoring. Thyroid Function Tests (TFTs) showed a new severe thyrotoxicosis (TRAB negative). Amiodarone-Induced-Thyrotoxicosis was the suspected aetiology. He was commenced on carbimazole and prednisolone, with digoxin and bisoprolol for rate control. He continued to have runs of VT with refractory fAF, and developed signs of cardiac decompensation. Ten days after admission, he was transferred to the tertiary hospital cardiac unit.
Results and treatment
He had input from multiple specialties: endocrinology, cardiology, general surgery, haematology and anesthetists. Emergency total thyroidectomy would take weeks to schedule. He was on an ATD cocktail of Propylthiouracil, IV hydrocortisone, lithium, cholestyramine, and propanolol MR, but now also required Plasma Exchange therapy (PLEX). This did cause thyroid improvement, but with temporary effect, and also caused hypocalcaemia. To achieve cardiac stability, his treatment was escalated to IV lidocaine. The prolonged course raised toxicity concerns, but cessation caused VT. He had to be weaned onto oral mexiletine as an alternative until surgery. Still mildly thyrotoxic, he had a total thyroidectomy on 30/11/23 with minimal complications. Post-surgery, all ATDs were stopped and was in sinus rhythm on 4 medications – including amiodarone. He required multiple specialty outpatient follow-up, which included thyroid and calcium replacement.
Conclusions and points for discussion
Patients with AIT and LVSD are at a higher risk of morbidity and mortality. This case demonstrates the complexity of multi-specialty input required to manage intricate life-threatening conditions. In particular it shows the value of thyroidectomy as a rapid euthyroid strategy, but highlights the reality in co-ordinating logistical aspects, especially with considering therapeutic toxicities and responses to therapy.

DOI: 10.1530/endoabs.100.P53

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Nephrogenic DI - How to improve our management

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Abstract P53
Investigations

	range	units	27/07	Admit4/11	Transf 14/11	1st PLEX 15/11	3rd PLEX 17/11	18/11	Surg 30/11	clinic 5/12	clinic 04/01
TSH	0.23 - 5.6	mU/l	1.9	<0.001	<0.001	<0.001	0.27	<0.001	0.01	0.23	22.4
Free T4	9-28	pmol/l	24	>100	>100	64	33	49	43	20	14

Case History

We present a very interesting and challenging case of a 71-year-old male, with a significant medical history including Bipolar affective disorder, drug-induced parkinsonism, benign prostatic hyperplasia (BPH), and hypothyroidism. The admission was prompted by a catheter-associated urinary tract infection and subsequent hypernatremia secondary to lithium induced Diabetes Incipidus. Despite initial therapeutic interventions, such as amiloride therapy, the patient continued to manifest symptoms of polyuria and polydipsia. Sepsis and altered consciousness necessitated his transfer to a level 1 care facility. The management of fluid balance proved arduous given the intricate interplay of his comorbidities and the inherent challenges posed by lithium-induced nephrogenic DI.

Investigations

Upon admission, comprehensive investigations revealed a serum osmolality of 332 mmol and a urine osmolality of 180 mmol, indicative of nephrogenic DI. Concurrently, the patient experienced recurrent infections, further complicating the clinical scenario.

Results and Treatment

Despite the implementation of therapeutic modalities such as amiloride and thiazides aimed at managing nephrogenic DI, the patient's polyuria persisted, necessitating a trial of Desmopressin therapy. Desmopressin demonstrated efficacy in reducing urine output. Given the persistent challenges with fluid homeostasis compounded by recurrent infections and hypernatremia, the decision was made to initiate hydration via a radiologically inserted gastrostomy (RIG) tube. This approach facilitated consistent fluid intake and yielded improvements in renal function.

Conclusions and Points for Discussion

In conclusion, the management of nephrogenic DI in this patient presented formidable challenges exacerbated by the presence of complex comorbidities, notably bipolar affective disorder. Despite diligent efforts to optimize fluid balance through interventions such as desmopressin and oral hydration, the patient's clinical course was marked by protracted hospitalization and eventual discharge to a nursing home with comprehensive instructions for ongoing community-based management. This case underscores the critical importance of a multidisciplinary approach in navigating the intricate terrain of fluid and electrolyte imbalances, particularly in individuals grappling with psychiatric and renal comorbidities. Furthermore, it's worth noting that individuals receiving lithium carbonate commonly develop nephrogenic DI, for which there exists no universally effective and practical treatment. However, emerging evidence suggests that large doses of desmopressin (DDAVP) may offer effective therapy with minimal adverse effects. Understanding the partial resistance to antidiuretic hormone (ADH) in most patients with nonhereditary AVP-R sheds light on the potential efficacy of supraphysiologic hormone levels in augmenting kidney response to ADH.

DOI: 10.1530/endoabs.100.P54

Author Index for Clinical Update

Author Index for National Clinical Cases