An unusual case of hypoglycemia mediated by paraneoplastic production of insulin like growth factor-2(IGF-2) by gastrointestinal stromal tumour

P Przyłęcki-Bruce[1], MS Majeed[1], D Till[1]
Department of Diabetes and Endocrinology, East Sussex Healthcare NHS Trust(ESHT)

Background

- Non islet cell tumour hypoglycaemia (NICTH) is a very rare paraneoplastic phenomenon associated with tumours of mesenchymal origin
- There is an estimated incidence of approximately one per million person-years [1]

We present a rare case of hypoglycaemia secondary to paraneoplastic non-islet cell secreting tumour

Case history

A 79 year-old female, with a background history of hypertension and ischaemic heart disease was brought by ambulance to hospital following collapse, associated with low capillary blood glucose (CBG) - 2.1mmol/l. Her regular medications include ramipril, clopidogrel and atorvastatin. She did not have a history of diabetes. While an inpatient, the majority of low capillary blood glucose (CBG) readings were late at night or in the early mornings. She had normal hypothalamic pituitary adrenal (HPA) axis, with cortisol of 747nmol/L (N<430)

Investigations at time of hypoglycaemia

Venous glucose	**1.9mmol/l**
C peptide	**<94pmol/l**
Serum insulin	**<10pmol/l**

Fig. 1 Investigations at time of hypoglycaemia

Appropriate reduction in circulating insulin suggests non-islet cell hypoglycaemia.

Further investigations are shown below

IGF-2	**79.5nmol/l**
IGF-1	**3.6nmol/l** (4.4-21.8)
IGFBP3	**2.2mg/l** (2.0-5.5)
IGF-2:IGF-1 ratio	**22.1 (significantly high)**

Fig. 2 Levels of insulin like growth factor and respective ratio

This confirms a diagnosis of insulin like growth factor 2 (IGF-2) driven non islet cell hypoglycaemia.

Radiology

CT abdomen and pelvis with contrast showed an 18cm lobulated inhomogeneous pelvic mass with liver masses.

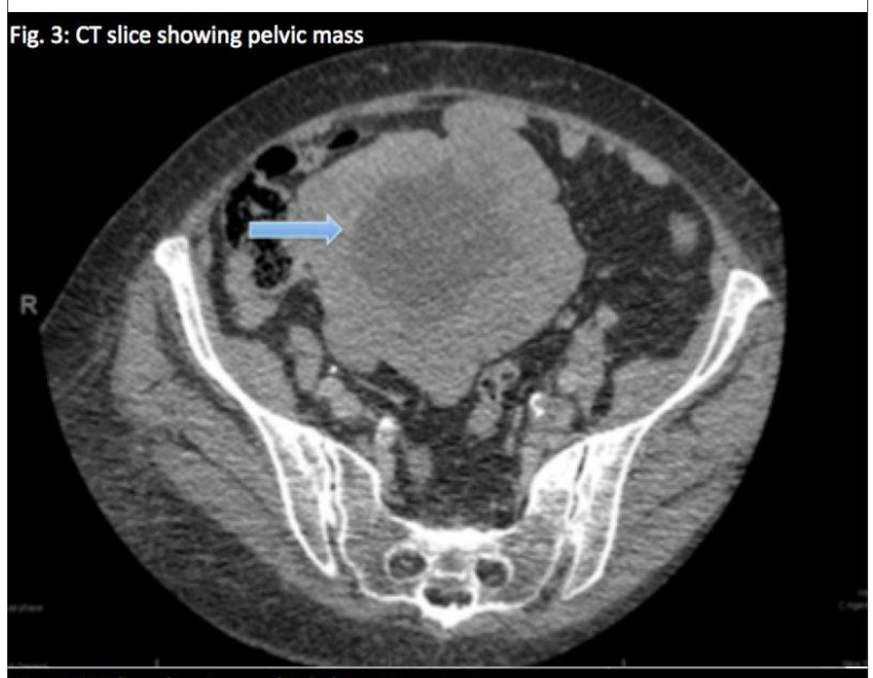


Fig. 3: CT slice showing pelvic mass

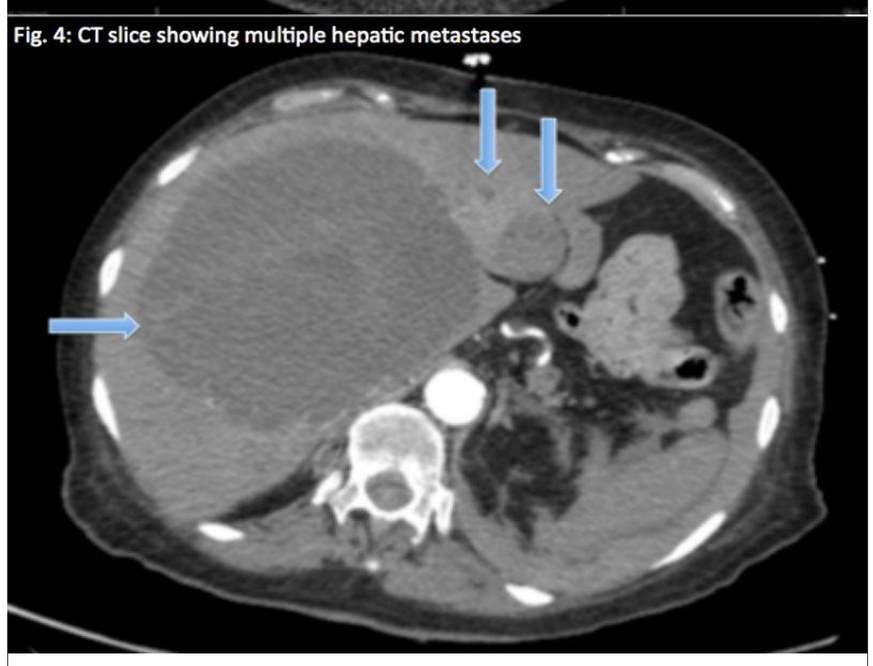


Fig. 4: CT slice showing multiple hepatic metastases

There was filling defect within the inferior vena cava extending into the left common iliac vein in keeping with venous thrombosis.

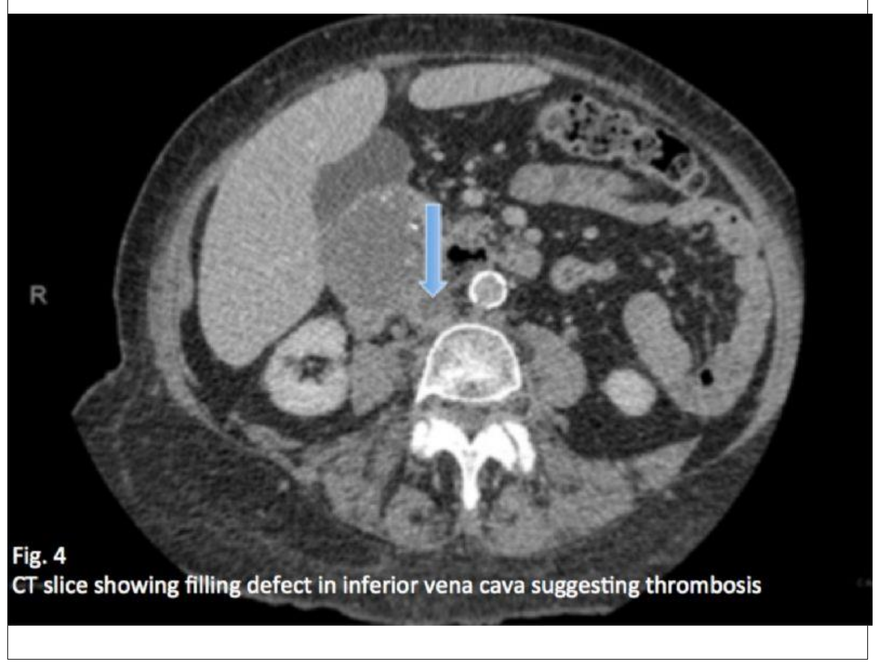


Fig. 4
CT slice showing filling defect in inferior vena cava suggesting thrombosis

Subsequent tissue biopsy confirmed a diagnosis of gastro-intestinal stromal tumour (GIST)

Fig. 5 – Histology slide

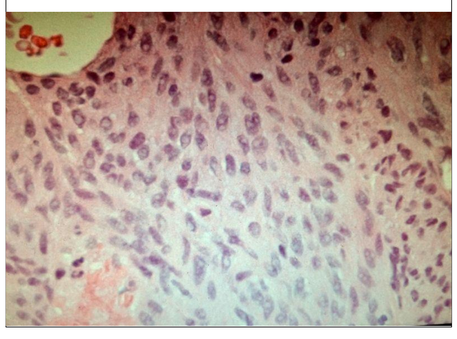
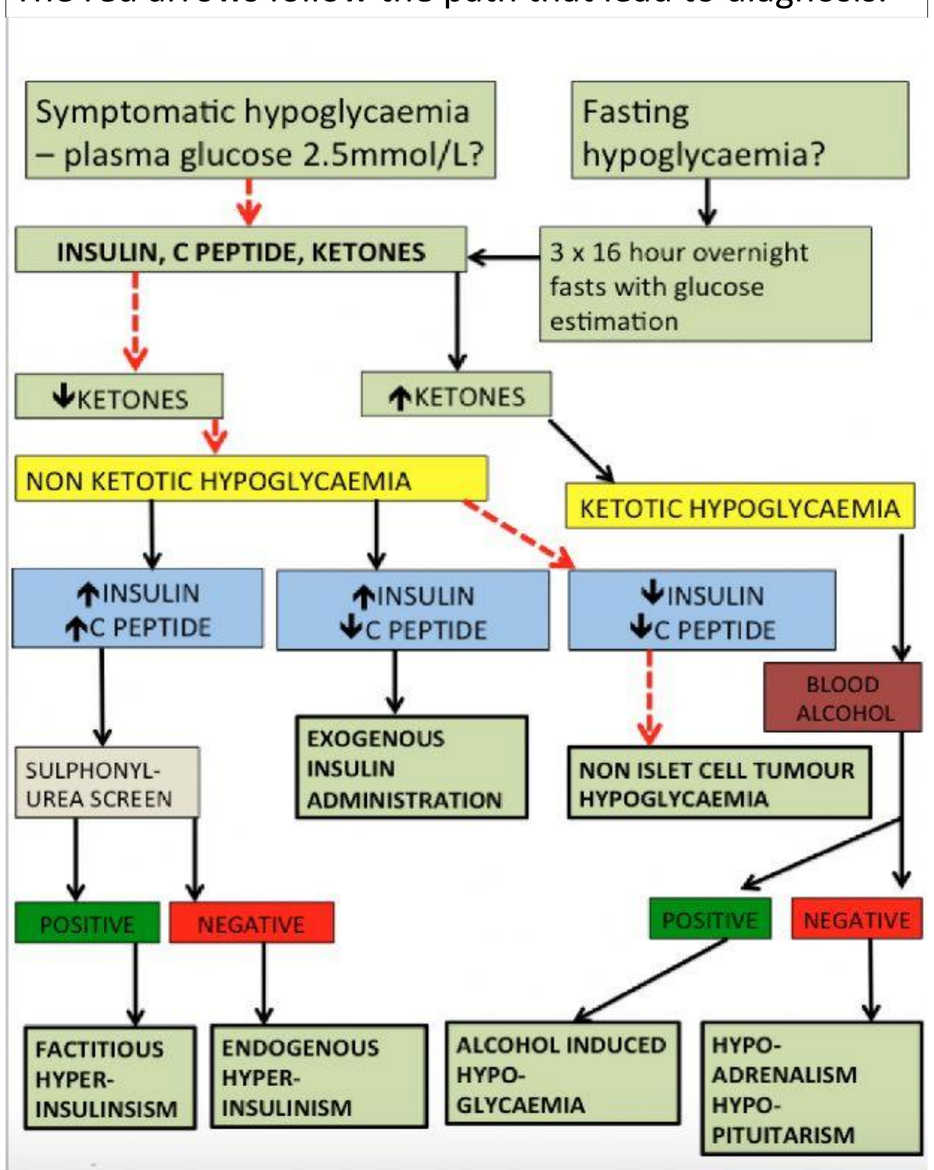


Fig. 6
Schematic flow chart showing stratification and investigation of hypoglycaemia
The red arrows follow the path that lead to diagnosis.



Further management

- Multidisciplinary Team discussion decided that the tumour was surgically inoperable.
- Further management was conservative.
- Hypoglycaemia was treated initially with prednisolone but showed little improvement.
- A switch to dexamethasone produced a good response.
- Treatment dose enoxaparin was initiated to treat inferior vena cava and left common iliac thrombus

Unfortunately patient developed retroperitoneal bleed secondary to treatment dose enoxaparin for inferior vena cava thrombosis.
She died within 8 weeks of her diagnosis.

Discussion/Conclusions

- NICTH should be considered when non-ketotic hypoglycaemia occurs in the setting of low serum insulin levels. (2)
- The number of reported cases of GIST remains low, however, it is suggested that the occurrence of hypoglycaemia prior to tumour diagnosis tends to be less common. (4-5)
- Glucorticoids remain the first line treatment to avoid NICTH. Their use is advocated even when tumours are inoperable(2).
- However one study has showed proven effectiveness of Imatininb, even when patients have metastatic or unresectable GISTs and as such it is suggested as a first line treatment. (6)
- Due to the rarity of this condition, evidence is limited to only a few cases. Further case reports and studies are required.

References
1. Marks V, Teale JD. Tumours producing hypoglycaemia. Diabetes Metab Rev. 1991;7(2):79–91
2. Saeed Z, Taleb S, Evans-Molina C. A case of extragastrointestinal stromal tumor complicated by severe hypoglycemia: A unique presentation of a rare tumor. BMC Cancer. 2016;16(1):930.
3. Hirai H, Ogata E, Ohki S, et al. Hypoglycemia associated with a gastrointestinal stromal tumor producing high-molecular-weight insulin growth factor II: A case report and literature review. Intern Med. 2016;55(10):1309–14.
4. Beckers MM, Slee PH, van Doorn J. Hypoglycaemia in a patient with gastrointestinal stromal tumour. Clin. Endocriniol (Oxf) 59: 402-404. 2003
5. Pink D, Schoeler D, Lindner T et al. Severe hypoglycaemia caused by paraneoplastic production of IGF-II in patients with advanced gastrointestinal stromal tumours: a report of two cases. J Clin Oncol 23 6809-6811. 2005
6. Demetri GD, von Mehren, Blanke CD et al. Efficacy and safety of imatinib mesylate in advanced GIST. N Eng J Med 347:472-480. 2002

BES2018 69--EP
Neoplasia, cancer and late effects
Muhammad shakeel Majeed
Poster presented at: SfE BES 2018 19-21 November GLASGOW
PosterSessionOnline.com