“Acromegaly in association with a bronchial carcinoid tumour” Andrzej Rys, Jamie Smith;

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ABSTRACT

Bronchial carcinoid tumours are uncommon pulmonary neoplasms. Manifestation of a bronchial carcinoid with acromegaly secondary to extra-pituitary growth hormone releasing hormone (GHRH) productionis rare, but bronchial carcinoid tumours are the most common cause of ectopic GHRH secretion.

We report the case of 60 year old female, ex-smoker with hypertension presenting with cough,dyspnoea and right lower lobe opacity on the chest X-ray.

Patient was noted to have features of acromegaly and IGF-1 was requested. Subsequent CT TAP showed a right lower lobe collapse, 4.5 cm mass obstructing the lower lobe bronchus which was visualised but could not be biopsied during bronchoscopy. 18-FDG PETCTscan showed only mildly avid right lower lobe mass, likely to be a slow growing carcinoid tumour, with chronic collapse of the right lower lobe. Pre-operative IGF-1 level came back elevated at 67 nmol/l. Patient underwent right mid and lower lobectomies and the histology showed morphological appearance of grade 1 neuroendocrine carcinoma (classic carcinoid tumour) with no lymph node involvement. Patient underwent the oral glucose tolerance test (OGTT) with growth hormone (GH) levels reaching a nadir value of 0.82 µ/L.

Patient's pituitary hormone profile and the MRI of the pituitary gland were both normal.

The GHRH assay was not available.The most recent postoperative random GH level was 0.6 µ/L and IGF-1 was 20 nmol/L.

Bronchial carcinoid tumours are one of the commonest causes of ectopic GHRH production, with similar cases reported in the literature. In the view of possible insufficient normalisation of the GH levels post OGTT our patient will require further close follow up. Our case represents the classic carcinoid tumour which is reported to have very good prognosis following surgical resection. The results of staining for GHRH on tissue samples are still awaited as the samples are being processed abroad.

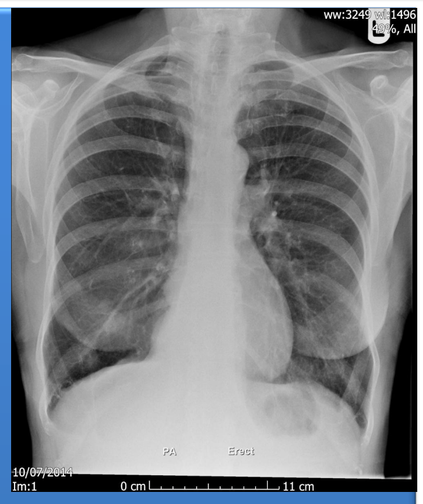
SITUATION

-60 year old female,

-cough, dyspnoea since October 2013

- chest X-ray showing lobular opacity in the right lower lobe and possible lobar collapse

In July 2014 referred urgently to respiratory clinic



BACKGROUND

-Ex-smoker, 25 pack-year history, stopped 7 years ago

-hypertension treated with Losartan 50mg daily;

-FH: CVE, ischaemic heart disease

ASESSMENT

- inspiratory wheeze, some breathlessness on walking uphill, no haemoptysis, weight loss, chest pain

On examination:

- coarsening of features, enlargement of jaw, hands, feet, no clubbing, no lymphadenopathy
- mild stridor, right tracheal deviation, reduced expansion over right lower lobe
- BP 160/100, normal heart sounds

PLAN

- CT thorax and abdomen with contrast
- fibre optic bronchoscopy, spirometry and flow volume loop,
- blood tests for: UEs, LFTs, calcium, FSH, LH, prolactin, IGF-1

RESULTS

Pre-operative IGF-1 level 67 nmol/l, FSH 53 IU/L, LH 29 IU/L, TSH 2.47 mIU/L, Prolactin 211 mU/L, Ca 2.43 mmol/L

HISTOLOGY:

- tumour with the morphological appearance of grade 1 neuroendocrine carcinoma (classic carcinoid tumour).
- tumour clear of the bronchial resection margin.
- lymph nodes - no evidence of malignancy

ENDOCRINOLOGY CLINIC (after the operation):

Acromegalic features, macroglossia, increase in shoe and ring size, excessive sweating, no visual symptoms

Plan:

- repeat IGF-1 23 nmol/L (4 – 23) , random GH at 10:00 am 0.88 µg/L (0.33 - 3.33) followed by oral glucose tolerance test with growth hormone levels
- visual field testing - no defect seen
- MRI of the pituitary gland
- GHRH assay - not available in the UK

MRI Pituitary with contrast :

Thickened skull vault noted as a result of acromegaly. The pituitary gland and pituitary stalk appear normal with, no evidence of focal tumour.

Histology specimen send for staining for GHRH to France – results awaited 2015/02/15:

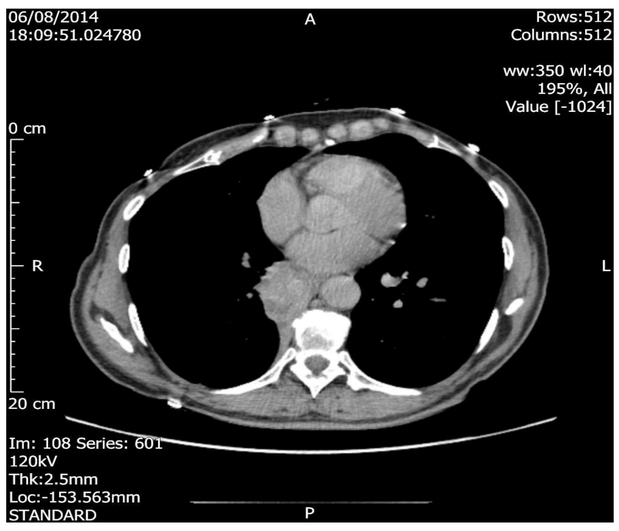
IGF-1 20 nmol/L (4 – 23) , random GH 0.6 µg/L (0.33 - 3.33)

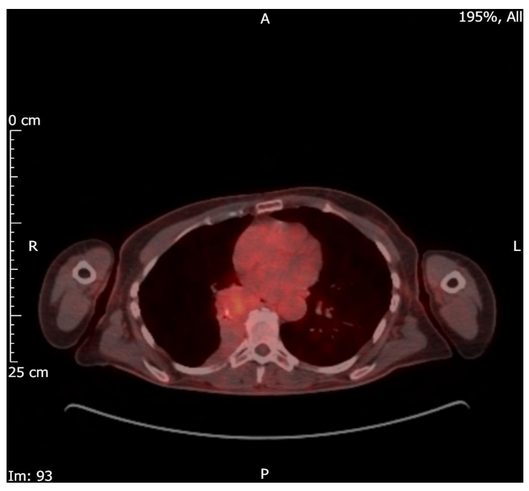
GTT with GH - 2014/10/10

Time	Interval (min)	Glucose [mmol/L]	GH [µg/L]	IGF-1 [nmol/L]
09:00	0	5.5	9.37	30
09:30	+30	8.0	3.45	
10:00	+60	7.9	1.88	
10:30	+90	5.9	1.00	
11:00	+120	4.5	0.82	

CT TAP – 2014/08/06:

- right lower lobe (RLL) collapse, proximal 4.5 cm mass obstructing the lower lobe bronchus.
- prominent subcarinal and pre-tracheal nodes of 12 mm in the short axis.
- clear left lung and upper, middle lobes of right lung, no effusion.





NM Whole body PET FDG 2014/08/21:

- 4.5cm right lower lobe mass obstructing the RLL bronchus containing a small amount of calcification.
- No significantly FDG avid nodes seen.
- The liver and adrenals clear. No aggressive bone lesions.
- Uptake elsewhere - physiological

Fibre optic bronchoscopy

- vascular tumour
- unable to biopsy
- bronchial brushings and washings RLL - no malignant cells

Patient was referred to lung cancer MDT and to Cardiothoracic Surgical Team

2014/09/10

Right thoracotomy , right mid and lower lobectomies for a tumour occluding bronchus intermedius.

DISCUSSION

Bronchial carcinoid tumours are an uncommon group of pulmonary neoplasms, comprising 1-2% of all lung malignancies in adults and 20-30% of all carcinoid tumors[1-4].

Less then 1% of patients with acromegaly have a GHRH releasing tumour – pancreatic or bronchial carcinoid[6]. There were 74 cases reported in the literature until 2012[5].

In cases of ectopic GHRH secretion - bronchial origin varying between 33-79%[8,9]

Ectopic cases of acromegaly are more common in women (60%), with median age at presentation - 39 years and median diameter - 55 mm[7]. Bronchial carcinoids causing ectopic acromegaly are usually of the typical type and located centrally[8,10].

In cases of ectopic secretion of GHRH, pituitary MRI was reported as normal in 19% of cases, showing hyperplasia in 60% or adenoma in 21%[5]

Criteria for cure of acromegaly

1. Epidemiological evidence suggest that post operative GH levels < 1 µg/L are associated with normal life expectancy[6]
2. Post operative cure - GHDC (GH Day Curve) with mean GH < 2.5 µg/L, or GTT GH with nadir GH < 1 µg/L + normal IGF-1[11]
3. Assessment of biochemical activity at 3 to 6 months after surgery is considered more valid in determining surgical efficacy[12.] Surgical remission defined as achievement of a normal level of IGF-I and a nadir GH < 1.0 µg/L during an OGTT by 3 to 6 months, although use of a lower nadir GH of < 0.4 µg/L is suggested[12]
4. Test IGF-1 and random GH > 12 weeks after operation[13:]

- serum GH < 0.4 µg/L -”surgical remission”
- serum GH < 1 µg/L – “control” + normalisation of mortalilty risk

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