# *lesson of the month (2)*

## An unusual case of Cushing's syndrome: the importance of a stepwise approach to diagnosis

**This lesson describes a case of Cushing's syndrome secondary to ectopic adrenocorticotropin hormone (ACTH) secretion (EAS) by a thymic carcinoid tumour. This highlights the clinical features of EAS, its diagnosis and the importance of a methodical and logical approach to investigating this complicated condition. Literature relating to this unusual condition is also reviewed and a stepwise logical approach to its diagnosis is proposed.**

### Lesson

A 58-year-old woman presented with excessive weight gain, abdominal bloating and tiredness. Over the next few months she had excessive facial hair growth, easy bruising and increased pigmentation of skin. Examination showed excess facial hair, moon-shaped face, centripetal obesity, purple striae on abdominal wall, an obvious buffalo hump and some areas of pigmentation in her skin. Systems examination revealed proximal myopathy and a blood pressure of 152/82. Routine blood tests were all normal. 24-hour urinary cortisol was 3,082 nmol/d (0–260). Nine am cortisol was 855 nmol/l with midnight cortisol reaching 349 nmol/l. Thyroid function tests, 24 urinary catecholamines and serum testosterone were all normal. Chest X-ray was normal.

Clinical appearance and screening tests strongly suggested a diagnosis of Cushing's syndrome. Dexamethasone suppression test showed a lack of suppression of cortisol levels on low dose dexamethasone, confirming a diagnosis of Cushings Syndrome. The high dose dexamethasone suppression (HDDT) test demonstrated no suppression of serum cortisol with partial suppression of urinary cortisol. Magnetic resonance imaging showed normal pituitary and adrenal glands. Corticotrophin-releasing hormone (CRH) stimulation test demonstrated lack of adequate suppression of ACTH and cortisol, implying an ectopic source of ACTH production. Computed tomography chest scan revealed a 3 × 2 cm mass in the anterior mediastinum and an octreotide uptake scan demonstrated increased activity in this location (Fig 1). A diagnosis of ectopic ACTH secretion (EAS) secondary to a neuroendocrine mediastinal tumour was the most likely cause. The patient was initiated on metyrapone in order to reduce cortisol production and improve symptoms. Urinary cortisol levels responded well. The mediastinal mass was removed. Cytology showed benign thymic carcinoid. The tissue was positive for ACTH, chromogranin and synaptophysin, confirming a diagnosis of an ACTH-producing thymic carcinoid. The patient improved well after surgery with gradual disappearance of many symptoms, particularly proximal myopathy.

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### Discussion

EAS accounts for approximately 15% of all cases of Cushing's syndrome, with thymic carcinoid accounting for another 15%. Around 20 to 35% of thymic carcinoid tumours could present as EAS.[1] It is often difficult to diagnose EAS and a combination of endocrine tests and radiological imaging is required. First step is establishing a diagnosis of Cushing's syndrome. Initial screening is by means of overnight dexamethasone suppression test (9 am cortisol level <50 nmol/l) and a 24-hour urinary cortisol (>250 nmol/l). The low dose dexamethasone suppression test helps further confirm the diagnosis while the HDDT helps to differentiate pituitary dependent (PD) Cushing's (ie Cushing's disease) from non-PD Cushing's. As this case demonstrates there was a fall in urinary cortisol levels with the HDDT. In fact up to 50% of patients with EAS are believed to show some suppression of cortisol following HDDT while a recent series showed no suppression of cortisol with the HDDT.[2,3]

The recommended discriminating test is the CRH stimulation test. The response seen with this case is characteristic of EAS: after the injection of CRH the elevated levels of ACTH and cortisol remain unchanged. In the case of Cushing's disease, there should be a 50% rise in ACTH as pituitary tumours are responsive to CRH. However with cortisol producing adrenal tumours the high cortisol levels and low ACTH levels are unaffected.[4,5] Octreotide scanning is helpful in locating functionally active neuroendocrine or carcinoid tumours. On administration of octreotide, carcinoid tumours would be seen as an area of increased activity.[6] Octreotide scanning is a more valuable tool when the source of ACTH is unknown and for patient follow up in those who have already had surgery for thymic carcinoid tumours.

The diagnosis of EAS is often fraught with difficulties. These mainly arise from inconclusive endocrine tests and imaging. This case demonstrates how a stepwise diagnostic approach helps establish causes of Cushing's syndrome.

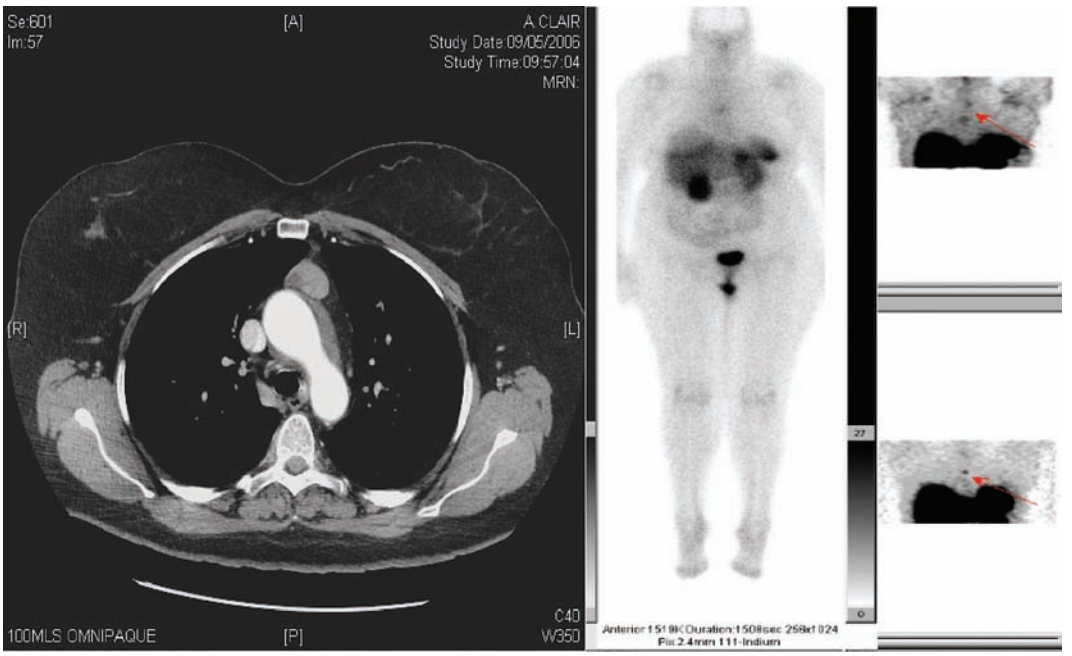


**Fig 1. High resolution computed tomography image and octreotide scan demonstrating anterior mediastinal mass.**

## References


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