Adrenocorticotropin-secreting carcinoid tumour identified and treated 12 years after presentation with Cushing's syndrome

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Summary

A case of Cushing's syndrome due to an adrenocorticotropin (ACTH) secreting bronchial carcinoid tumour is described. Endocrine assessment suggested ectopic ACTH syndrome, but imaging revealed no tumour. Bilateral adrenalectomy was performed, and computed tomographic scans of chest and abdomen were performed annually. A small nodule became apparent in the right lung 12 years after the presentation, which postoperatively was confirmed as the bronchial carcinoid tumour responsible for the ectopic ACTH syndrome.

Keywords: Cushing's syndrome, ectopic ACTH syndrome, adrenalectomy, bronchial carcinoid

The diagnosis of ectopic adrenocorticotropin (ACTH) syndrome due to a benign endocrine tumour is often a challenge. Its clinical presentation and hormonal evaluation can be indistinguishable from pituitary-dependent Cushing's disease. Furthermore, the causative tumour may be occult. We present a patient in whom the bronchial carcinoid tumour producing ectopic ACTH did not become apparent until 12 years after the presentation of the Cushing's syndrome.

Case report

A 60-year-old nonsmoking woman presented in March 1983 with a history of hirsutism, muscle weakness, polydipsia, polyuria and psychosis. She had classical Cushingoid features with central obesity, plethoric facies, hirsutism, acne, bruises, abdominal striae, proximal myopathy and hypertension.

Investigations (box 1) revealed hyperglycaemia, hypokalaemic alkalosis, elevated urinary free cortisol, and loss of diurnal variation of cortisol. There was no suppression of cortisol with high-dose dexamethasone suppression test (2 mg six hourly for eight doses). With metyrapone test (750 mg four hourly for six doses), cortisol was suppressed but there was no stimulation of ACTH or urinary 17-OH corticosteroids. Computed tomography (CT) scans revealed no tumour in pituitary, chest, adrenal glands, liver, pancreas or ovaries. A diagnosis was made of ectopic ACTH syndrome due to an occult tumour. Systemic

venous catheterisation for ACTH showed one possible hot spot in the azygous vein where the level of ACTH was 62 ng/l with concomitant peripheral level 13 ng/l. The results were felt not to be clear cut at that time, although in retrospect, it suggests a possibility of an ectopic ACTH source in lung or mediastinum.

She was initially treated with metyrapone but tolerated it poorly. She underwent bilateral adrenalectomy in August 1984 with remission in her Cushing's syndrome. Histology demonstrated normal adrenal tissue. She was maintained on hydrocortisone and fludrocortisone replacement. CT scans of chest and abdomen were performed annually in an attempt to detect the tumour.

In the latter part of 1984, she developed flushing, sweating and diarrhoea. Urinary 5-hydroxyindoleacetic acid was negative but plasma serotonin was elevated at 268 µg/l (normal 50–180). Gut polypeptides were normal. Barium follow-through, small bowel barium enema, meta-iodobenzylguanidine and Tc 99m-S colloid scans were normal.

Initial investigations

- plasma glucose (fasting): 10 mmol/l
- plasma potassium: 1.9 mmol/l
- plasma bicarbonate: 33.7 mmol/l
- basal urinary free cortisol: 3344 nmol/24 h (normal 35–255)
- basal urinary 17-OH corticosteroids: 168 µmol/24 h (normal 1.7–28)
- basal plasma cortisol:
09.00 h 1670 nmol/l normal 190–650
24.00 h 1200 nmol/l normal <200)
- basal plasma ACTH:
09.00 h 32 ng/l (normal ≤47)
24.00 h 26 ng/l
- after high-dose dexamethasone test:
plasma cortisol: 09.00 h 1425 nmol/l
- after metyrapone test:
plasma cortisol: 09.00 h 225 nmol/l
urinary free cortisol: 136 nmol/24 h
urinary 17-OH corticosteroids: 121 µmol/24 h
plasma ACTH: 09.00 h 36 ng/l
- urinary 5-hydroxyindoleacetic acid: negative
- urinary vanillyl mandelic acid: 28 µmol/24 h (normal <40)
- plasma calcitonin: undetectable
- chest X-ray: normal
- CT scan pituitary, chest, abdomen: normal

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In 1990, it was noted that she was once again becoming Cushingoid. Investigations off hydrocortisone confirmed recurrent active Cushing's syndrome with elevated urinary free cortisol of 413 and 442 nmol/24 h. ACTH profile ranged between 123–177 ng/l with a flat response to corticotropin-releasing hormone test. CT scan revealed a nodule in the 'bed' of the right adrenal. Cushing's syndrome improved after excision of the lesion. Histology demonstrated adrenal cell hyperplasia. Thereafter, she remained generally well although she was slightly pigmented and ACTH levels were elevated (150–300 ng/l).

In June 1995, at her annual scanning, a 1-cm nodule was noted in the middle lobe of the right lung (figure 1). Pentetreotide scan showed no abnormal uptake in the chest. In September 1995, she underwent right middle lobectomy. Histology was consistent with carcinoid tumour (figure 2). Immunoperoxidase staining was positive for ACTH, pro-opiomelanocortin, neurone-specific enolase, synaptophysin, and substance P, but negative for chromogranin. Her ACTH levels returned to normal and pigmentation disappeared after the surgery.

Discussion

'Occult' ectopic ACTH syndrome is most often due to a carcinoid tumour, the commonest site being bronchus. Other less frequent sites are thymus, stomach, appendix, pancreas, ileum and ovaries. Bronchial carcinoid tumours are responsible for 1% of endogenous Cushing's syndrome.¹ They are small, classically ranging from 0.4–2 cm² and as such may be inconspicuous not only on chest X-ray but also on CT scan or magnetic resonance imaging. In our patient, biochemical and endocrine tests were suggestive of ectopic ACTH syndrome but no tumour was visualized radiologically. She was intolerant to metyrapone and had to undergo bilateral adrenalectomy following which she had a reasonable quality of life. Bilateral adrenalectomy in patients with an unknown tumour secreting ACTH is beneficial in symptom relief, and has low morbidity and mortality.³

An interesting feature of this case is the recurrence of Cushing's syndrome after bilateral adrenalectomy due to recurrent adrenal tissue. It is presumably due to continued high levels of ACTH stimulating an adrenal 'rest' or a postoperative remnant. It is a rare occurrence and can cause diagnostic difficulties.⁴

Recently, pentetreotide scan has been shown to be helpful in localising these tumours.⁵ However, no abnormal uptake with pentetreotide scan was found in the chest in this case. It was only with the annual CT scanning that the bronchial carcinoid tumour was detected after 12 years. This case illustrates that even after such a long time, these lesions may still be small and treatable. This emphasizes that it is

Figure 1 CT scan showing a pulmonary nodule (arrow)

Figure 2 Histology showing typical carcinoid tumour (H&E stain)

Learning points

- ectopic ACTH syndrome due to a benign endocrine tumour may be identical in clinical features and hormonal assessment with pituitary-dependent Cushing's disease
- the causative tumour may be occult, and remain occult for a very long period
- even when ectopic ACTH syndrome has been present for many years, these lesions may be small and entirely treatable
- it is important to undertake repeated scanning at regular intervals to localize these tumours
- bilateral adrenalectomy is beneficial in symptom control in patients with an unknown tumour secreting ACTH and intolerant to medical therapy
- relapse of Cushing's syndrome in a patient with bilateral adrenalectomy can occur due to recurrence of adrenal 'rest' or postoperative remnant and cause diagnostic difficulties

Box 2

worthwhile to keep attempting to localise these lesions with repeated scanning at regular intervals.

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Perforated diverticulitis following extra-abdominal surgery

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Summary

The peritonitis of perforated diverticular disease is a life-threatening condition. We report three cases where it occurred following unrelated extra-abdominal surgery and where surgical intervention proved to be the correct course of management. All cases were treated with a Hartmann's procedure; this is probably the safest option for purulent peritonitis in patients who are a high operative risk and have recently undergone major surgery.

Keywords: perforation; diverticulitis

Diverticular disease has an increasing incidence in Western countries which can be explained by an increasing elderly population and also the relatively low-fibre diet of western culture. Fifty per cent of the population over 50 years of age have diverticulosis, and it is estimated that acute diverticulitis will develop in 15-20% of these cases.¹ Spontaneous perforated sigmoid diverticulitis is an unusual complication following unrelated extra-abdominal surgery. Three cases are reported here, and the pathogenesis is discussed.

Case reports

Case 1

A 76-year-old man was admitted through Accident and Emergency with a 24-hour history of worsening abdominal pain two weeks after triple coronary artery bypass grafting. He was pyrexial, tachycardic and hypotensive. Abdominal examination revealed generalised peritonitis. After resuscitation, a laparotomy revealed a purulent peritonitis secondary to a perforated sigmoid diverticular abscess. A Hartmann's procedure was performed with end colostomy and closure of rectal stump. Postoperatively he spent a period in intensive care and required a blood transfusion for acute gastric erosions. He was discharged home after four weeks. He has since had a successful reversal of his Hartmann's procedure, and is well.

Case 2

A 61-year-old man presented to Accident and Emergency with severe abdominal pain three weeks after the excision of a malignant glioblastoma from his right temporoparietal region. His medication included nonsteroidal anti-inflammatory drugs, dexamethasone and atenolol. On examination he was pale, with a pulse rate of 80 beats/min. His abdomen was distended and generally tender with guarding. Bowel sounds were absent. An abdominal X-ray showed dilated loops of small bowel. He underwent an emergency laparotomy which revealed a perforated sigmoid diverticulum. A Hartmann's procedure was performed. Postoperatively he made a good recovery.

Case 3

A 73-year-old asthmatic woman was admitted for an elective left total hip replacement. Seven days postoperatively she started vomiting, and experienced pain over the lower abdomen. Her symptoms worsened over the following 48 hours. Her abdomen became distended and bowel sounds were absent. A chest X-ray revealed gas under both diaphragms. At laparotomy a perforated sigmoid diverticulum was found. A Hartmann's procedure was performed. Postoperatively her asthma worsened, she developed a right pneumothorax, a right basal pneumonia and became septicaemic. She was ventilated and later underwent tracheostomy. She remained in intensive care for 38 days, after which her clinical condition continued to improve. She was recently discharged from hospital.

Discussion

Acute postoperative perforated diverticulitis has been associated with cardiac surgery or renal transplant surgery.² General surgical complications following cardiac surgery include gastroduodenal ulcer, acute cholecystitis, small bowel ischaemia or pancreatitis; colonic complications are relatively rare.³⁻⁵ Patients with extensive diverticular disease are recommended for colon resection before renal transplantation, as the occurrence of colonic

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