was seen in our patient, but renal impairment in turn prevents oxalate excretion, establishing a self-perpetuating cycle. It is therefore imperative that oxalate absorption in the gut be maximally inhibited.

Final diagnosis

Enteric hyperoxaluria.

Keywords: renal calculi; short bowel syndrome; enteric hyperoxaluria; calcium

- 1 Chadwick VS, Modha K, Dowling RH. Mechanism for hyperoxaluria in patients with ileal dysfunction. *N Engl J Med* 1973;289:172–6.
- 2 Dobbins JW, Binder HJ. Effect of bile salts and fatty acids on the colonic absorption of oxalate. *Gastroenterology* 1976;70:1096–1100.
- 3 Smith LH, Fromm H, Hofmann AF. Acquired hyperoxaluria, nephrolithiasis and intestinal disease. Description of a syndrome. *N Engl J Med* 1972;286:1371–5.
- 4 Hylander E, Jarnum S, Nelsen K. Calcium treatment of enteric hyperoxaluria after JIB for morbid obesity. *Scand J Gastroenterol* 1980;15:349–52.
- 5 Barilla DE, Notz C, Kennedy D, Pak CYC. Oxalate absorption and excretion. *Am J Med* 1978;64:579–85.
- 6 Lindsjo M, Fellstrom B, Ljunghall S, Wikstrom B, Danielson BG. Treatment of enteric hyperoxaluria with calcium-containing organic marine hydrocolloid. *Lancet* 1989;ii:701–4.
- 7 Lyon ES, Borden TA, Ellis JE, Vermeulen CW. Calcium oxalate lithiasis produced by pyridoxine deficiency and inhibition by high magnesium diets. *Invest Urol* 1966;4:133–42.
- 8 Woolfson RG, Mansell MA. Hyperoxaluria and renal calculi. *Postgrad Med J* 1994;70:695–8.

Hypokalaemic alkalosis

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A 68-year-old woman was admitted with a 3-week history of swelling of the head and neck, breathlessness, anorexia, and weight loss. She had been previously well and, apart from long-standing systemic hypertension, her medical history had been unremarkable. A life-long smoker, she also enjoyed half a litre of spirits a day and had been taking enalapril for 3 years.

On examination, stigmata of chronic liver disease were noted and her face appeared swollen with fullness in the right supraclavicular fossa. Cardiovascular examination was unremarkable apart from a blood pressure of 165/85 mmHg. Abdominal examination revealed multiple striae and hepatosplenomegaly.

Investigations of note included a haemoglobin of 10.6 g/dl and a potassium of 1.8 mmol/l. Urea and creatinine were within normal limits. Arterial blood gases showed a pH of 7.58 and bicarbonate of 53.1 mmol/l. Alkaline phosphatase was 130 U/l and γ -glutamyl transferase 785 U/l. Chest X-ray showed widening of the superior mediastinum. Serum cortisol was >2000 nmol/l and urine cortisol was >9000 nmol/24 h (normal 60–250 nmol/24 h). Plasma adrenocorticotropin (ACTH) was 148 ng/l (0–50 ng/l) and ACTH precursors >1500 pmol/l (5–40 pmol/l). An 09.00 h serum cortisol after 2 mg dexamethasone administered orally at 23.00 h the previous night was >2000 nmol/l. Investigations with higher doses of dexamethasone failed because of inability to swallow the medication. Angiotensin-converting enzyme was not elevated.

Barium swallow showed diffuse mucosal irregularity affecting the oesophagus from the level of C7 down to the aortic arch. Ultrasound of the abdomen revealed liver metastases. Endoscopy showed frank nodular oesophageal carcinoma from 25 cm to 35 cm. Histologically this was an anaplastic small-cell carcinoma, which stained positive for Grimelius and chromogranin A but immunostaining for ACTH was negative. She was started on treatment but her condition deteriorated and she died four days later.

Questions

- 1 What is the diagnosis?
- 2 Suggest two other causes for the acid–base disturbance.
- 3 What treatment would you have started this patient on?

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Answers

QUESTION 1

Cushing's syndrome with ectopic ACTH production from an oesophageal small-cell carcinoma. Oesophageal small-cell carcinoma, mediastinal lymphadenopathy and the liver metastasis were confirmed on post-mortem. The lungs showed no evidence of tumour. Both adrenals were enlarged, with diffuse cortical hyperplasia consistent with ectopic ACTH production.

Pseudo-Cushing's syndrome with chronic alcohol abuse could give a similar clinical picture with impaired hepatic cortisol clearance. A severe metabolic alkalosis in the absence of a history of vomiting and the elevated ACTH precursors seen in this patient make alcoholic pseudo-Cushing's unlikely.

QUESTION 2

This patient has a hypokalaemic alkalosis, the most common causes of which are persistent vomiting, diuretic therapy or hyperaldosteronism. Less commonly it is seen with excess liquorice ingestion, carbenoxolone sodium therapy, the milk-alkali syndrome or with excess ingestion (orally or intravenously) of sodium bicarbonate.

QUESTION 3

Treatment included oral potassium, spironolactone and metyrapone. She also started chemotherapy with etoposide.

Discussion

Small-cell carcinoma of the oesophagus, first reported by McKeown in 1952,¹ is a rare condition with less than 200 cases reported in the literature. It forms a small percentage (between 0.8 and 2.4%) of the total number of cases of primary oesophageal cancer. The male to female ratio is 2:1 and the mean age of the patients described is 64 years.² The most common presenting symptoms include dysphagia, chest pain, anorexia and weight loss. Ectopic

hormone production is also a recognised, although rare, complication of this tumour.²⁻⁴

Review of the literature shows ectopic hormone production in a small number of reports with 11 cases of ACTH production, four of calcitonin (three of which were also producing ACTH), and one each of vasoactive intestinal polypeptide, gastrin, somatostatin and antidiuretic hormone production.²⁻⁴ Of the 11 ACTH-producing cases only one, in the Japanese literature, had the clinical features of Cushing's syndrome.² Biochemically, in this case the pre-operative plasma 11-hydroxycorticosteroids and the urinary 17-hydroxycorticosteroids and 17-ketosteroids were all within the normal range, although there was a loss of diurnal variation in plasma 11-hydroxycorticosteroids.²

The clinical features and biochemical changes in the case described here are unequivocal. Cases of ectopic ACTH production can differ from the classical clinical presentation of Cushing's syndrome and hypokalaemic alkalosis may be a major feature, as in our case.⁶ Ectopic sources of ACTH may cleave the hormone from its precursor molecule inefficiently so that the ratio of the circulating concentrations of precursor to those of ACTH is high, as found in this case.⁷ Therapy is directed towards correction of the hypokalaemia, reducing cortisol production and treatment of the underlying tumour.

Primary oesophageal small-cell cancer is a rapidly progressive tumour with a 6-month survival rate of 37%.³ Treatment includes chemotherapy, radiation therapy, surgery and palliative oesophageal dilatation.

Final diagnosis

Cushing's syndrome caused by ectopic ACTH production by an oesophageal small-cell carcinoma.

Keywords: Cushing's syndrome; ectopic ACTH production; small-cell carcinoma; alkalosis

1 McKeown F. Oat-cell carcinoma of the oesophagus. *J Pathol Bacteriol* 1952;64:889-91.

2 Taniguchi K, Iwanaga T, Kosaki G, *et al*. Oat-cell carcinoma of the esophagus producing ACTH. Report of two cases. *Saishinigaku* 1973;29:1834-7.

3 Beyer KL, Marshall JB, Diaz-Arias AA, Loy TS. Primary small-cell carcinoma of the esophagus. Report of 11 cases and review of the literature. *J Clin Gastroenterol* 1991;13:135-41.

4 Nishimaki T, Suzuki T, Fukuda T, Aizawa K, Tanaka O, Muto T. Primary small cell carcinoma of the esophagus with ectopic gastrin production. *Dig Dis Sci* 1993;38:767-71.

5 Muto I, Nishimaki T, Aizawa K, Suzuki T, Tanaka O, Hatakeyama K. Primary small cell carcinoma of the esophagus: report of a case. *Jpn J Surg* 1995;25:830-3.

6 Howlett TA, Drury PL, Perry L, *et al*. Diagnosis and management of ACTH-dependent Cushing's syndrome: comparison of the features in ectopic and pituitary ACTH production. *Clin Endocrinol* 1986;24:699-713.

7 Stewart PM, Gibson S, Crosby SR, *et al*. ACTH precursors characterise the ectopic ACTH syndrome. *Clin Endocrinol* 1989;60:20-4.