

## Short reports

### Oat cell carcinoma of bronchus presenting with somatostatinoma syndrome

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Somatostatinoma syndrome describes the clinical, biochemical, and morphological features of endocrine-producing pancreatic tumours.<sup>1</sup> The clinical presentation is variable and includes maturity-onset diabetes mellitus, steatorrhoea, and cholelithiasis. In addition to somatostatin, the tumour may secrete adrenocorticotrophic hormone (ACTH) and calcitonin. Several cases have come to light during the course of abdominal operations such as cholecystectomy, and diagnosis has been achieved by pathological examination of pancreatic tumour with immunocytochemical techniques and electron microscopy. A preoperative diagnosis of somatostatinoma syndrome has been made on the basis of characteristic clinical features, and a high plasma concentration of immunoreactive somatostatin.<sup>1,2</sup> We have observed a patient with elevated plasma somatostatin who presented with a wasting illness, diabetes mellitus and steatorrhoea, who was found to have an oat cell carcinoma of bronchus.

#### Case report

A 56-year-old woman complained of fatigue and loss of two kilograms in weight over a six-month period. She noted thirst and polyuria. She had smoked 20 to 30 cigarettes daily for many years and had a history of mild angina pectoris. Apart from evidence of slight wasting physical examination was normal. Initial investigations included haemoglobin 11.7 g/dl, MCH 34.1, erythrocyte sedimentation rate 20 mm fall in one hour, plasma viscosity 1.45%, serum sodium 141 mmol/l, osmolality 296 mOsm/kg, potassium 2.6 mmol/l, chloride 96 mmol/l, total bicarbonate 33.5 mmol/l, urea 10.3 mmol/l, creatinine 99 µmol/l, calcium 2.21 mmol/l, magnesium 0.87 mmol/l, albumin 37 g/l, inorganic phosphate 0.7 mmol/l; glucose ranged from 9.0 to 15.2 mmol/l, over several days' random sampling, bilirubin 8.0 µmol/l, alkaline phosphatase 10.7 KA units, aspartate transaminase 6.1 IU/ml, pH 7.55, Pco<sub>2</sub> 6.2 kPa standard bicarbonate 38.4 mmol/l. Further investigation of hypokalaemic alkalosis showed that when serum potassium concentration was 2.6 mmol/l urinary potassium excretion was

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79 mmol/l/24 hours. Total exchangeable potassium was 28.75 mmol/kg (normal for age and sex, 34.91 mmol/kg). Plasma aldosterone was 310 pmol/l (normal range 100 to 550 pmol/l), cortisol 2913 nmol/l (normal 165 to 715), ACTH 3400 pg/ml (normal 10 to 80 pg/ml). Further investigation of hyperglycaemia on day 3 showed that after a 50 g glucose load, plasma glucose was 14.1 mmol/l at 0 min, 18.9 mmol/l at 30 min, 21.3 mmol/l at 60 min, 20.9 mmol/l at 180 min, and 23.8 mmol/l at 240 min. Simultaneous plasma insulin levels were 3.1 u/l at 0 min, 3.0 u/l at 30 min, 2.3 u/l at 60 min, 3.3 u/l at 180 min, and 3.0 u/l at 240 min. On the basis of this result the patient was given glipizide 2.5 mg daily but became violently nauseated and ill, with persistent hypoglycaemia so the drug was discontinued after a few days.

From the time of admission diarrhoea had been noted, with the passage of three or four loose, pale stools a day. While the patient was taking a normal diet, a five day faecal collection showed a mean fat excretion of 15.7 g/24 hours (55.7% dry weight). Chest radiograph and barium enema and meal examinations were normal. On day 5 there was rapid enlargement of the liver which became hard and nodular. Serum bilirubin rose to 35 µmol/l, aspartate transaminase to 155 IU, and alkaline phosphatase to 64.6 KA units. Liver scan suggested metastatic deposits, and this was confirmed by biopsy. Repeat chest radiograph showed no abnormality.

The patient's clinical condition deteriorated progressively. Plasma gut hormone profile became available on day 21 and is shown in the table. Plasma growth hormone was 1.0 u/ml (normal 0 to 10), thyroid stimu-

Table Plasma gut hormone profile

	Day			Normal range
	3	7	21	
Somatostatin	425	190	>1000	<50 pmol/l
Gastrin	18	20	120	<30 pmol/l
Pancreatic polypeptide	6	23	175	<100 pmol/l
Glucagon	<5	<5	<5	<30 pmol/l
Vasoactive intestinal polypeptide	<5	<5	<5	<30 pmol/l

lating hormone 5.0 u/ml (normal), thyroxine 35 nmol/l (normal 68 to 175), free thyroxine 6.0 pmol/l (normal 18.5 to 38.5).

The patient died on day 22. Necropsy (Dr OG Williams) revealed a carcinoma in the left main bronchus involving hilar glands. Pleural nodules were present in both lungs. The liver contained innumerable metastatic deposits. Cervical and mediastinal lymph nodes were involved by carcinoma and the pancreas contained a 1 cm carcinomatous nodule. The adrenal glands were enlarged, with a combined weight of 30 g. Histology revealed oat cell carcinoma of the bronchus with widespread metastases to lymph nodes, liver, and pancreas (figs 1 and 2).

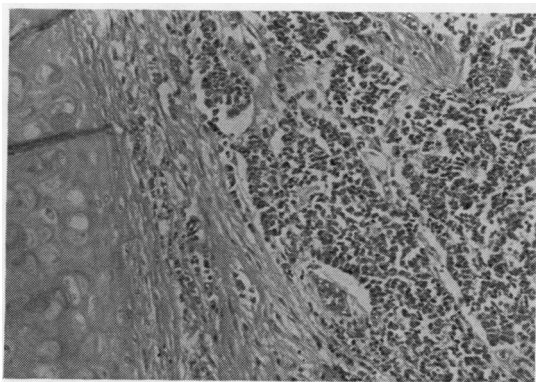


Fig 1 Photomicrograph of bronchial lesion showing oat cell carcinoma to the right of bronchial cartilage. Original magnification  $H$  and  $E \times 60$ .

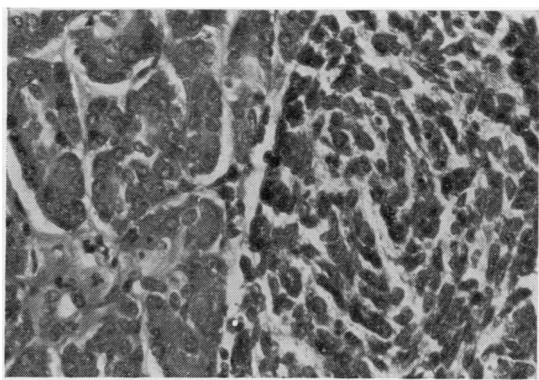


Fig 2 Photomicrograph of pancreas showing metastasis from oat cell carcinoma to the right. Original magnification  $H$  and  $E \times 250$ .

## Discussion

Multiple hormone secretion of the amine, precursor, uptake and decarboxylation (APUD) series is well recognised with oat cell bronchial carcinoma,<sup>3,4</sup> but hypersomatostatinaemia has not been described before. In our patient the clinical picture was dominated by ectopic ACTH secretion, manifested by hypokalaemia, and hypersomatostatinaemia, presenting with diabetes and steatorrhoea. Somatostatin, a peptide hormone widely distributed throughout the central nervous system and gastrointestinal tract, exerts a neurocrine or paracrine action, but ectopic tumour secretion in this case indicated an endocrine effect. Diabetes mellitus presumably resulted from suppressed insulin and glucagon secretion, with an additional contribution from excessive ACTH. Somatostatin exerts widespread inhibiting effects on pituitary, pancreatic, and thyroid function. Steatorrhoea probably resulted from inhibition of pancreatic enzymes, with failure of intraluminal digestion. Pancreatic polypeptide and gastrin are normally suppressed by somatostatin and the terminal rise in plasma concentration suggested tumour secretion.

Hypersomatostatinaemia supports a diagnosis of somatostatinoma, but provocation tests such as glucose loading or tolbutamide administration may be necessary to demonstrate a pancreatic source of somatostatin.<sup>3</sup> If suggestive, then further investigation with pancreatic angiography or computerised tomography may be needed before proceeding to abdominal laparotomy. The present case shows the need to consider all sources of somatostatin, and oat cell carcinoma of bronchus must be included in the differential diagnosis of hypersomatostatinaemia. Medullary cell carcinoma of thyroid has been shown to secrete somatostatin, and serial levels of hypersomatostatinaemia provided a useful index of therapeutic success.<sup>5</sup>

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## References

- Krejs GJ, Orci L, Coulonoo, *et al*. Somatostatinoma syndrome. Biochemical, morphological and clinical features. *N Engl J Med* 1979;301:286-92.
- Pipeleers D, Somers G, Gepts W, De Nutte N, De Vroede M. Plasma pancreatic hormone levels in a case of somatostatinoma: diagnostic and therapeutic implications. *J Clin Endocrinol Metab* 1979;49:572-9.
- Rees LH, Bloomfield GA, Rees GM, Corrin B, Franks LM, Ratcliffe JG. Multiple hormones in a bronchial tumour. *J Clin Endocrinol Metab* 1974;38:1090-7.
- Hattori M, Imura H, Matsukura S, *et al*. Multiple-hormone producing lung carcinoma. *Cancer* 1979;43:2429-37.
- Saito H, Saito S. Clinical significance of plasma somatostatin determinations in medullary carcinoma of thyroid. *Lancet* 1980;1:1191.