Neurotensin-secreting carcinoma of the bronchus

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Summary

Neurotensin, a neuroendocrine peptide present in gut and brain has previously been found in pancreatic tumours secreting several other peptides. We report here the first case of a patient with a neurotensin-secreting adenocarcinoma of the bronchus.

KEY WORDS: neurotensin, bronchus, adenocarcinoma.

Introduction

In recent years a number of new regulatory peptides have been isolated from the gastrointestinal tract and central nervous system. Neurotensin, originally found in bovine hypothalamus and subsequently isolated from the human gastrointestinal tract, is a new member of this peptide group which has a wide range of potent biological actions. In man these include inhibition of gastric acid secretion, relaxation of the lower oesophageal sphincter and vasoconstriction in adipose tissue (Hamer and Lee-man, 1981). Neurotensin-like material has recently been isolated from pancreatic tumours secreting vasoactive intestinal polypeptide and other regulatory peptides (Gutniak *et al.*, 1980; Feurle *et al.*, 1980; Blackburn *et al.*, 1981). We report here the presence of neurotensin-like immunoreactivity in tumour and plasma of a patient with an adenocarcinoma of the bronchus.

Case report

A 68-year-old retired engineer presented with a six week history of pain in both knees, unrelated to movement and relieved by analgesics. He had a dry cough without other respiratory symptoms and had recently lost half a stone in weight. Past medical history included a partial gastrectomy for duodenal ulcer and a right axillary basal cell carcinoma. There was no history of diabetes mellitus. He smoked 15

cigarettes a day and had had occupational exposure to asbestos between 1971 and 1976.

Examination was normal except for finger clubbing and tenderness over the lower third of his left tibia. Routine haematology, urea, electrolytes and liver function tests were normal. A fasting blood glucose was 13.4 mmol/litre. Chest X-ray showed an irregular opacity in the posterior and lateral segments of the right lower lobe and an enlarged hilum. A chest X-ray 6 years previously had been normal. Changes of hypertrophic pulmonary osteoarthropathy were seen on radiographs of the left tibia. A technetium bone scan showed no evidence of metastases. A diagnosis of bronchial carcinoma was made on percutaneous needle biopsy and a right pneumonectomy performed. Histological examination of the resected lung revealed two discrete areas of mucin-secreting adenocarcinoma in the right upper and lower lobes with involvement of hilar and oesophageal lymph nodes.

Results

Extracts from the patient's tumour contained 8 pmol/g wet weight of neurotensin-like immunoreactivity measured by radioimmunoassay using a specific rabbit antiserum and I¹²⁵ labelled synthetic neurotensin (Blackburn and Bloom, 1979). Gel permeation chromatography showed the presence of two molecular forms of neurotensin-like immunoreactivity one of which coeluted with the synthetic tri-decapeptide (Fig. 1). Neurotensin was undetectable in macroscopically normal lung tissue taken distant from the tumour site. Somatostatin, bombesin, vasoactive intestinal polypeptide (VIP), gastrin, substance P and cholecystokinin were all undetectable in tumour extracts.

Fasting plasma contained 200 pmol/litre of neurotensin-like immunoreactivity (normal < 10 pmol/litre) which fell to 37 pmol/litre postoperatively.

FIG. 1. Gel permeation chromatography profile of the extract of the patient's tumour run on a Sephadex G50-superfine gel column calibrated with dextran blue (V_o), cytochrome C, ^{125}I -labelled neurotensin and Na^{125}I (V_t) as molecular size markers.

Somatostatin, bombesin, gastrin, cholecystokinin, substance P, VIP, calcitonin, thyroid stimulating hormone, adrenocorticotrophic hormone, follicle stimulating hormone and luteinising hormone were all undetectable in plasma.

Discussion

This is the first description of neurotensin-like material in a lung tumour. Neurotensin-like immunoreactivity has recently been found in pancreatic tumours in association with abnormal production of other peptides. Six out of twenty-one tumours producing VIP also contained neurotensin-like immunoreactivity (Blackburn *et al.*, 1981), two of which were associated with high plasma neurotensin concentra-

tions. Neurotensin-like immunoreactivity has also been found in two other mixed endocrine tumours, one patient presenting with the Zollinger-Ellison syndrome (Feurle *et al.*, 1980), the other with watery diarrhoea (Gutniak *et al.*, 1980).

In contrast to pancreatic tumours only neurotensin (within the limitation of the peptides measured) was detected in the present tumour. This case therefore provided an opportunity to assess the clinical effects of neurotensin hypersecretion. The contribution of an elevated plasma neurotensin to the clinical course of the present patient, however, remains speculative. Fasting hyperglycaemia in a cachectic, anorexic man is unusual and may be relevant as neurotensin induces hyperglycaemia in animals. The patient reported by Gutniak and colleagues was also diabetic but this may have related to the elevated VIP concentration. Neurotensin has vascular effects in animals and might therefore have contributed to the clubbing and hypertrophic pulmonary osteoarthropathy.

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