CLINICAL REPORTS

Pancreatic polypeptide and calcitonin secretion from a pancreatic tumour-clinical improvement after hepatic artery embolization

A. MANCHE
L.R.C.P., M.R.C.S.

T. E. ADRIAN
Ph.D.

S. M. WOOD
B.Sc., M.B., B.S.

R. B. WELBOURN
M.D., F.R.C.S.

S. R. BLOOM
M.A., D.Sc., M.D., F.R.C.P.

Departments of Medicine and Surgery, Royal Postgraduate Medical School, London W12 0HS

Summary

We present a case in which plasma pancreatic polypeptide and calcitonin were found to be raised in association with an islet cell tumour of the pancreas and its hepatic metastases. In this patient, no specific endocrine syndrome was found. Therapeutic hepatic artery embolization improved the general health of the patient with no change in plasma pancreatic polypeptide, but a fall in calcitonin.

KEY WORDS: pancreatic polypeptide, calcitonin, hepatic artery embolization, islet cell tumour.

Introduction

Pancreatic polypeptide (PP), a 36 amino acid peptide, is found principally in small granules in the islets of Langerhans and, to a lesser extent, in the exocrine parenchyma. Its release by food is under both vagal and hormonal control and it is likely to play an important part in the physiological control of pancreatic and gallbladder function (Greenberg *et al.*, 1978). Over 50% of pancreatic endocrine tumours secrete pancreatic polypeptide in addition to another hormone. In this situation, PP does not seem to contribute to the clinical features of these tumours (Polak *et al.*, 1976).

Calcitonin, a 32 amino acid peptide, found mainly in the C cells of the thyroid gland, has no clearly defined physiological role in man. It is thought to be important in regulating bone resorption during times of physiological calcium stress such as growth, pregnancy and lactation (Stevenson, 1980). This

action may explain its elevation in patients with a variety of tumours.

Case report

A 58-year-old man presented with a 6 week history of constant dull epigastric pain unrelated to meals. He was constipated, anorexic and had lost 14 kg in weight. Past history included mild Type II diabetes and angina for 7 years. On examination, he was cachectic and the liver enlarged 5cm below the right costal margin. Fibreoptic endoscopy revealed a normal oesophagus, stomach and pylorus. The duodenal cap was scarred, but no active ulcer was present. The duodenum was narrowed by an extrinsic mass, and ultrasound demonstrated a large solid lesion in the region of the head and body of the pancreas, with liver metastases. The histology of a liver biopsy taken at laparoscopy was compatible with a tumour of APUD-cell origin. Plasma pancreatic polypeptide was found to be elevated at 40000-60000 pmol/litre (normal, under 200), but there was no elevation of other pancreatic peptides. To characterise the molecular form of pancreatic polypeptide, gel chromatography was carried out using a Sephadex G50 superfine column. All the tumour-secreted PP coeluted in a single peak in the position of human PP (Kav 0.55). Plasma calcitonin was 0.74 µg/litre (normal <0.08). Serum calcium and phosphate were normal. Selective coeliac axis arteriography and indirect splenoportography confirmed the presence of extensive hepatic metastases,

the majority in the right lobe, the portal vein was patent.

In this situation where there are multiple metastases secreting peptides into the circulation, experience has shown that selective embolization of the arteries supplying the metastases is the optimum line of treatment. This procedure reduces the viability and hormone production of the metastases, resulting in considerable symptomatic improvement (Wood and Bloom, 1982). The right hepatic artery was therefore embolized using lyophilised human dura mater. This procedure was carried out under local anaesthesia, and the patient given prophylactic antibiotics to prevent the rare complication of hepatic abscess formation.

One month later, the patient was asymptomatic and had gained 5 kg in weight. The plasma PP remained elevated at 40000-50000 pmol/litre, but the plasma calcitonin had fallen to 0.14 µg/litre.

Discussion

It has been shown that infusions of PP resulting in plasma levels comparable with the postprandial plasma concentration of PP inhibit pancreatic enzyme secretion and bile output (Greenberg *et al.*, 1978). Its elevation in plasma many hours after food has led to the suggestion that PP may play a part in conserving pancreatic enzymes and promoting the storage of bile between meals. There was however no evidence of steatorrhoea or other features of malabsorption in this patient that might have been expected from the effect of PP on pancreatic and bile secretion.

Calcitonin release has been reported from a wide variety of tumours (Coombes *et al.*, 1974) and the diarrhoea of medullary carcinoma of the thyroid has been attributed to it. Our patient, however, had constipation, despite a grossly elevated plasma calcitonin concentration. This may be explained by PP masking the effect of calcitonin on the gut, since PP has recently been shown to produce a net fluid absorption in the rat small intestine (Mitchener *et al.*, 1981). The patient's other symptoms were those commonly associated with neoplasia, namely malaise, anorexia, and cachexia. These improved considerably after embolization, at a time when his plasma calcitonin had fallen to almost normal, perhaps suggesting an association between the two.

References

- COOMBS, R.C., HILLYARD, C., GREENBERG, P.B. & MACINTYRE, I. (1974) Plasma immunoreactive calcitonin in patients with non-thyroid tumours. *Lancet*, **i**, 1080.
- GREENBERG, G.R., MCCLOY, R.F., ADRIAN, T.E., CHADWICK, V.S., BARON, J.H. & BLOOM, S.R. (1978) Inhibition of pancreatic and gallbladder function by pancreatic polypeptide in man. *Lancet*, **ii**, 1280.
- MITCHENER, P., ADRIAN, T.E., KIRK, R.N. & BLOOM, S.R. (1981) Effect of gut regulatory peptides on intestinal luminal fluid in the rat. *Life Sciences*, **29**, 1563.
- POLAK, J.M., BLOOM, S.R., ADRIAN, T.E., HEITZ, P.H., BRYANT, M.G. & PEARSE, A.G.E. (1976) Pancreatic polypeptide in insulinomas, gastrinomas, vipomas and glucagonomas. *Lancet*, **i**, 328.
- STEVENSON, J.C. (1980) The structure and function of calcitonin. *Investigative and Cell Pathology*, **3**, 187.
- WOOD, S.M. & BLOOM, S.R. (1982) Glucagon and gastrin secretion by a pancreatic tumour and its metastases. *Journal of the Royal Society of Medicine*, **75**, 42.

(Accepted 20 October 1982)