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Jejunal Endocrine Tumour Composed of Somatostatin and Gastrin Cells and Associated with Duodenal Ulcer Disease

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Summary. A case of malignant endocrine tumour of the jejunum, associated with severe duodenal ulcer is described. The tumour and a local metastasis were examined by immunohistochemistry and found to contain abundant somatostatin-immunoreactive cells together with less numerous cells displaying gastrin immunoreactivity. This is to our knowledge the first case of intestinal somatostatinoma. The presence of gastrin cells in the tumour may explain the ulcer diathesis.

Key words: Mixed endocrine tumour – Somatostatinoma – Immunohistochemistry.

Introduction

Recently, three pancreatic somatostatinomas were described (Ganda et al., 1977; Kovacs et al., 1977; Larsson et al., 1977). Two of the patients had impaired glucose tolerance; one of them also had steatorrhoea. Immunohistochemical analysis of both these tumours failed to demonstrate peptide hormones other than somatostatin (Ganda et al., 1977; Larsson et al., 1977). The third patient displayed symptoms of ACTH overproduction, including hyperglycemia and increased serum levels of cortisol. Immunohistochemical analysis of this tumour revealed the presence of ACTH cells among somatostatin cells (Kovacs et al., 1977). It is well known that tumours arising within the gastro-entero-pancreatic (GEP) endocrine system may be composed of more than one peptide hormone-producing cell type (O'Neal et al., 1968; Pearse et al., 1974; Larsson et al., 1975; Arnold et al., 1976). Nevertheless the clinical picture is often dominated by the effects of the hormone produced by one of the cell types (Larsson et al., 1975).

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The present report concerns a case of malignant jejunal somatostatinoma associated with severe recurrent duodenal ulcer.

Case Report

The patient was a 55-year-old woman, with a recent onset of upper abdominal pain. Cholecystography showed gallstones. Barium meal revealed a deformed antrum but no signs of an active ulcer. At laparotomy, the gall bladder showed signs of chronic inflammation; in addition a pyloric ulcer, 2.5 cm in diameter, was found. Cholecystectomy and gastric resection (Billroth I) were performed. Two weeks later the patient was re-explored because of upper abdominal pain and haematemesis. An ulcer, 2×4 cm, was found to have penetrated from the posterior wall of the duodenum, distal to the anastomosis, into the pancreas. When mobilizing the first part of the jejunum, an umbilicated tumour was found in the wall, approximately 15 cm from Treitz' ligament. The tumour together with 15 cm of the jejunum was resected. Six months postoperatively the patient was in good condition.

Histological and Histochemical Methods

Specimens from the primary tumour and from a regional lymph node metastasis were fixed in 10% formalin, dehydrated and embedded in paraffin. Sections were stained with haematoxylin-erythrosin for routine histology. The method of Masson-Hamperl (Pearse, 1972) was used for the identification of argentaffin cells, and diazo-coupling and ninhydrin methods (Pearse, 1972) for the demonstration of 5-hydroxytryptamine. Sections processed for immunofluorescence were occasionally restained with silver according to Hellerström and Hellman (1960) or according to Grimelius (1968) for demonstration of argyrophil cells. The indirect immunofluorescence method (Goldman, 1968) or the PAP (peroxidase-antiperoxidase) technique of Sternberger (1974) were used for demonstration of somatostatin, gastrin and ACTH. The gastrin antiserum, which has been used in several previous immunohistochemical studies (Larsson et al., 1973, 1974, 1975) was applied in a dilution of 1:640 (immunofluorescence) or 1:2560 (PAP-staining). The antiserum was kindly supplied by Professor J.F. Rehfeld, Institute of Medical Biochemistry, Århus, Denmark. The ACTH antiserum, which has been characterized elsewhere (Håkanson et al., 1975), was used in dilution 1:80 (immunofluorescence). The somatostatin antiserum, kindly provided by Dr. M.P. Dubois, Inst. Nat. Rech. Agr., Nouzilly, France, has been characterized in detail elsewhere (Dubois, 1975). It was used in dilution 1:40 (immunofluorescence) or 1:320 (PAP-staining). The controls were sections incubated with antiserum inactivated by addition of excess of the respective antigen (100 µg of synthetic human gastrin I or 100 µg of synthetic somatostatin per ml of diluted antiserum). FITC-labelled sheep anti-rabbit IgG (Statens Bakteriologiska Laboratorium, Stockholm, Sweden) was used as second layer in the immunofluorescence procedure (dilution 1:20). PAP (peroxidase-antiperoxidase) complex was purchased from Cappel Laboratories, Downington, Pennsylvania, USA and used in dilution 1:320. Immunofluorescence was examined in a Leitz Orthoplan fluorescence microscope, equipped with an epi-illumination system. PAP-stained sections were examined in a standard light microscope.

Findings

The jejunal tumour measured approximately $1.5 \times 2 \times 0.5$ cm and showed pale, grey-white cut surfaces. The tumour had infiltrated into the tunica muscularis, and a lymph node metastasis, 1 cm in diameter, was found in the mesentery, close to the bowel wall. The tumour and the metastasis were histologically similar, being composed of nests and trabecules of cells with weakly stained cytoplasm (Fig. 1a). In some parts the nests of tumour cells were broken up

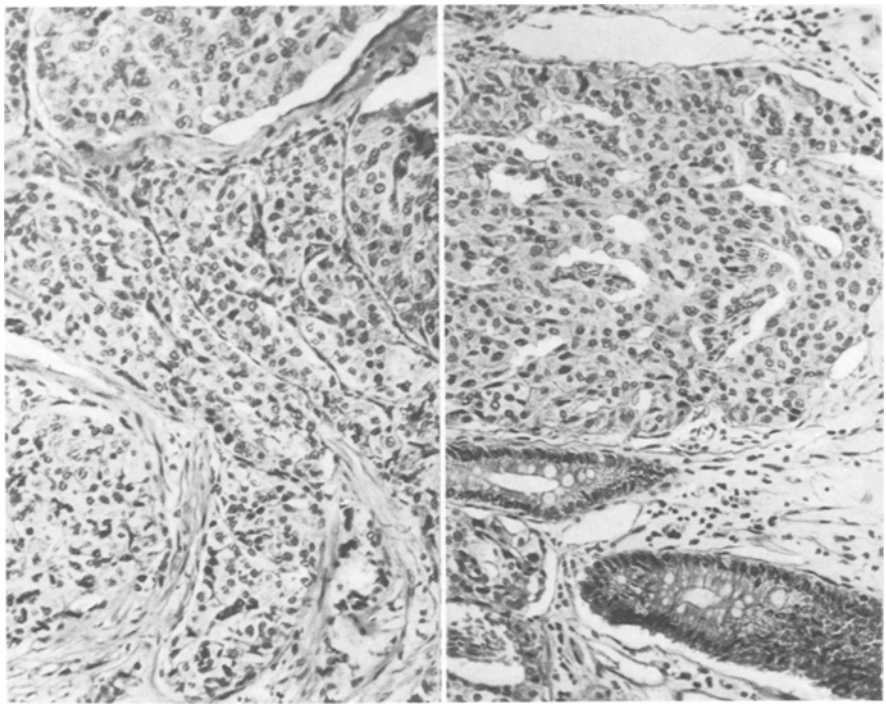

Fig. 1a and b. Growth pattern of jejunal endocrine tumour. Hematoxylin-erythrosin staining. **a** Nests and trabecules of weakly stained tumour cells (×300). **b** Looped ribbon growth pattern (×250)

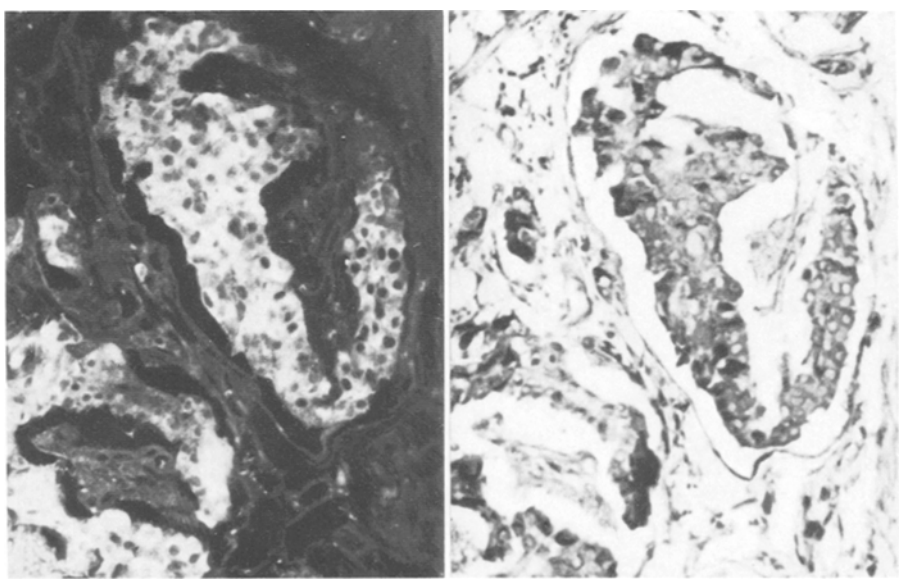

Fig. 2. a Somatostatin immunofluorescence in the majority of tumour cells. **b** Silver staining of the same section according to Hellerström and Hellman. Immunofluorescent cells are stained (×300)

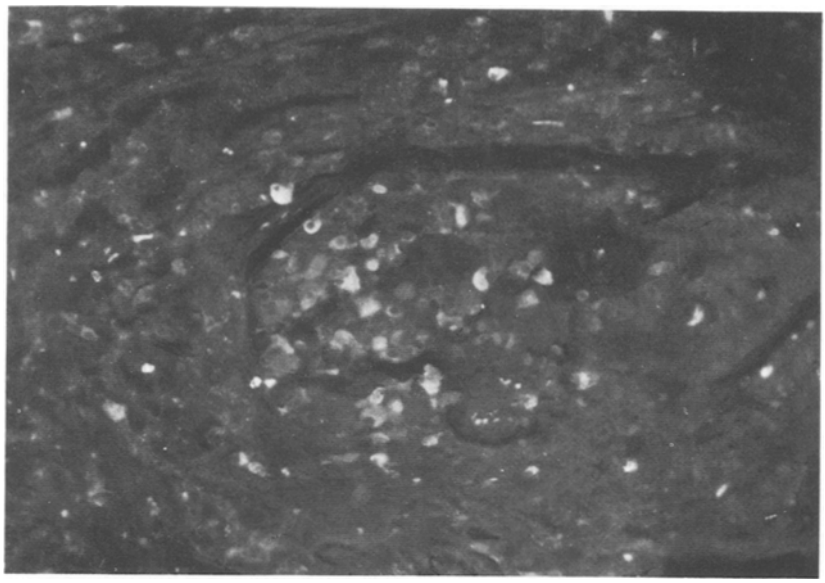

Fig. 3. Gastrin immunofluorescence in scattered tumour cells (×250)

into anastomosing cords, one or a few cells in thickness forming trabecular or looped ribbon patterns (Fig. 1b). Immunohistochemical analysis revealed numerous somatostatin–immunoreactive cells forming large clusters both in the primary tumour and in the metastasis (Fig. 2a). Controls were negative. The somatostatin cells stained with silver using the Hellerström-Hellman technique (Fig. 2b) but not with that of Grimelius. In addition single or clustered tumour cells displayed weak to moderate gastrin immunoreactivity (Fig. 3). Gastrin immunoreactive cells were more numerous in the metastasis than in the primary tumour. On the whole they were much fewer than the somatostatin cells. The gastrin cells were argyrophil with the method of Grimelius but not with that of Hellerström-Hellman (not shown in figure).

ACTH immunoreactivity could not be demonstrated in the tumour. The tumour did not contain 5-hydroxytryptamine, nor did it display argentaffinity.

Discussion

Gastrointestinal endocrine tumours are sometimes collectively referred to as "carcinoids". According to current pathological practice the diagnosis is often made on morphological grounds alone. Endocrine tumours appear to be rare in jejunum–less than 10 per cent of the "carcinoids" of the small intestine have this location (Godwin, 1975; Berge and Linell, 1976). All gastrointestinal endocrine tumours seem to produce, store and secrete peptide hormones; some of them in addition contain 5-hydroxytryptamine. A proportion of these "true" carcinoids produce and store both substance P-immunoreactive material and 5-hydroxytryptamine (Alumets et al., 1977; Håkanson et al., 1977).

This is the first report of an intestinal somatostatinoma. The symptoms do not seem to reflect overproduction of somatostatin, which is known to inhibit different release processes, including gastric acid secretion and gastrin mobilization (Bloom et al., 1974). The tumour contained gastrin cells as a minority constituent, which may explain the ulcer diathesis. However, the lack of information on somatostatin and gastrin levels in serum as well as of gastric acid secretion makes such an interpretation purely speculative. It may be noted that scattered somatostatin cells have previously been observed within C cell tumours of the thyroid (Sundler et al., 1977) and within glucagonomas of the pancreas (Orci et al., 1976; Arnold et al., 1977). Conceivably, somatostatin cells may turn out to be fairly common constituents in endocrine tumours.

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