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Carcinoid Somatostatinoma of the Duodenum

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THE FIRST 3 cases of somatostatinoma were published in 1977 [1–3]. We report a rare case of carcinoid somatostatinoma of the duodenum.

On routine examination a 63-year-old man had abnormal upper gastrointestinal series and gastrofiberoptic findings, and was referred to the Department of Surgery at Niigata University Hospital. Routine laboratory examinations were normal, except for an elevated carcinoembryonic antigen (CEA) value of 25 ng/ml. Serotonin activity was also normal. Gastrofiberoscopy indicated a 2 × 3 cm granular-surfaced, reddish lesion in the descending portion of the duodenum, approximately 2 cm proximal to the papilla of Vater. Based on the biopsy diagnosis of carcinoid, the patient underwent a pancreaticoduodenectomy and local removal of 7 metastatic foci in the superficial regions of both lobes of the liver. The patient had an uneventful postoperative course and, after chemotherapy, had no signs of recurrence for over 5 years. A postoperative hormonal profile was normal except for serum somatostatin levels (17.0 and 56.0 pg/ml, normal 1.0–12.2). Tumour markers were all within normal limits.

The surgical specimen (2.8 × 3.5 cm) was composed of whitish-grey neoplastic tissue involving all layers of the duodenum and a small part of the head of the pancreas.

Histological examination revealed a trabecular pattern (B type [4]) with occasional areas of nodular (A type) and less differentiated (D type) structures showing a close similarity to the pancreatic islets. In small areas there were acinar structures (C type) with intraluminar periodic acid-Schiff reagent and alcian blue positive mucinous material (psammoma bodies). The cells had abundant eosinophilic finely granular cytoplasm and a small nucleus. Mitotic figures were negligible. An aldehyde fuchsin stain was positive in only a few cells within the neoplastic nodules. 9 of 44 regional lymph nodes and the 7 foci of the liver removed at surgery were histologically confirmed as metastatic.

Grimelius' silver staining was negative. Peroxidase staining showed a positive reaction for somatostatin in many neoplastic cells (antigen supplied by Dr S. Ito, Niigata University, Japan) and occasionally for calcitonin and S-100 protein in a few scattered cells (negative for serotonin and CEA).

Under electron microscopy the neoplastic cells showed round granules of the endocrine type surrounded by a fine membrane (120–1100, mean 610) nm (Fig. 1A) similar to somatostatin granules found in normal D cells in the human digestive organs. A few cells showed a narrow apical surface with irregularly developed microvilli surrounding the lumen (Fig. 1B) and some had a large pool of irregularly woven microfilamentous material with occasional migrating granules (Fig. 1A, B). Gold staining showed endocrine granules indicating somatostatin (Fig. 1C).

Of 84 cases of gastrointestinal-endocrinomas reported since 1977 as somatostatinomas or carcinoids, 44 (52%), including our case, had the primary site of neoplasm in the duodenum. Cases with carcinoid somatostatinoma of the duodenum may be summarised as follows: (1) the site of tumour growth is predominantly the second portion, the papilla of Vater (17 cases); (2) the histological pattern is principally B (trabecular) type complicated often by C (tubular or acinar) imitating an islet of the pancreas (carcinoid islet cell tumour [5]); (3) Grimelius' argyrophil reaction is positive for about one-third of cases (35%); (4) there is a high frequency of malignancy (72.7%) with metastases (46%) and intramural invasion; (5) round granules are likely to be or identical to those of D cells; (6) other hormones are simultaneously produced (18%); (7) calcifications or psammoma bodies may be present (39%); (8) either Von Recklinghausen's disease, neurofibromatosis and/or pheochromocytoma are found in 27% of cases; and (9) no increased preoperative serotonin activity even in the carcinoid syndrome case with flush and diarrhoea.

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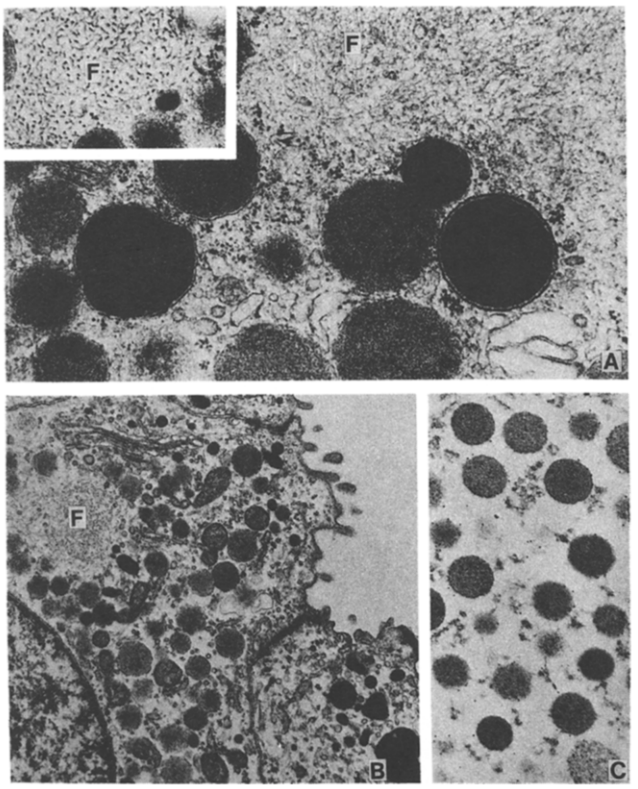

Fig. 1. Electron micrographs: A = large round endocrine granules with fine wavy limiting membrane, × 20 000; inset shows cross-cut profile of microfilaments (F) (up to 15 nm in diameter, × 22 000). B = neoplastic cell showing irregularly developed microvilli on the luminar surface, numerous endocrine granules and a pool of microfilamentous structures, × 7800. C = endocrine granules showing somatostatin (gold staining), × 13 350.

The tumour of our case is undoubtedly a member of the carcinoid family [7], and one of primitive-gut endocrinomas [8]. Demonstration by peroxidase staining of somatostatin in many neoplastic cells, and calcitonin only in a few cells, led us to the diagnosis of carcinoid somatostatinoma.

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Phase II Study of Carboplatin in Untreated Inoperable Advanced Stomach Cancer

Peter Preusser, Hansjochen Wilke, Wolf Achterrath, Luigi Lenaz, Michael Stahl, Jochen Casper, Hans-Joachim Meyer, Jürgen Meyer, Michael Blum and Hans Joachim Schmoll

CISPLATIN, one of the most active agents in stomach cancer, has limited application because of toxicity [1]. Carboplatin has shown some activity in stomach cancer [2, 3] and causes less nephrotoxicity, vomiting and ototoxicity than cisplatin [4]. We did a non-randomised phase II study of carboplatin, given on days 1, 3 and 5 every 4 weeks, as the antineoplastic activity of carboplatin is schedule-dependent in animals [5, 6].

Patients with inoperable, metastatic, histologically confirmed stomach cancer with measurable lesions were enrolled. Eligibility requirements included: age less than or equal to 70 years, life expectancy greater than or equal to 3 months, WHO status less than or equal to 2, no brain metastases, no previous chemotherapy or radiotherapy, adequate bone marrow, renal and liver functions, and normal serum electrolytes and audiogram. All patients gave informed consent. Neoplastic lesions were measured before each cycle and 4 weeks after the last cycle. Complete haemogram, serum creatinine and creatinine clearance, electrolytes and liver function were similarly monitored. During chemotherapy, complete blood counts were done twice weekly.

Chemotherapy consisted of 130 mg/m^2 carboplatin on days 1, 3 and 5 by intravenous infusion over 30 minutes without hydration. After the first course, dose modifications were planned to adjust drug doses to individual patients. If the nadirs of leucocytes and platelets were between 1500–2500/μl and 75 000–100 000/μl, respectively, full treatment was administered. If the lowest leucocyte and platelet count was greater than 2500/ l and 100 000/ l, respectively, the dose of carboplatin was increased to 160 mg/m^2. If the nadirs of leucocytes and platelets were less than 1500/μl and 75 000/μl, respectively, carboplatin was given at a dose of 100 mg/m^2. Cycles were to be repeated every 4 weeks if white blood cells and platelets were greater than 4000/μl and 100 000/μl, respectively, or delayed until these values were achieved. Low-dose anti-emetics were prophylactically administered. Patients with progressive disease after the

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