of the adenomas ($P < 0.0001$). There were also significantly more cancerous polyps with villous architecture (11%) than among the benign adenomas (3%) ($P < 0.001$) (χ^2 test).

Our results are in accordance with the assumption that certain features of adenomas are associated with a higher risk for development of the cancerous process. Although large size is one of the main features of cancerous polyps, tiny cancerous polyps may occur [5]. The finding of cancerous polyps certainly allocates the patient into a higher risk group, which means that a closer and more frequent colonoscopic surveillance is necessary.

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Adoptive Immunotherapy of Primary and Metastatic Liver Cancer via Hepatic Artery Catheter

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WE HAVE previously reported the results of adoptive immunotherapy with lymphokine-activated killer (LAK) cells and recombinant interleukin 2 (IL-2) [1, 2] in patients with hepatocellular carcinoma (HCC) [3] which suggested that administration of LAK cells directly into the hepatic artery was more effective and caused less side-effects than systemic administration [3, 4]. All four HCC cases in our study, given small numbers of LAK cells through the hepatic artery in a single dose, showed briefly decreasing serum alphafetoprotein (AFP) levels. This finding prompted us to treat patients with hepatic tumours by AIT via catheters placed into the hepatic artery. Since sustained low blood level of IL-2 has been reported to mediate better proliferation and higher antitumour activity of LAK cells than brief high levels of IL-2 [5], we infused IL-2 (10^6 U per day) through the catheters.

Table 1. Patients' characteristics, response and survival

Case (age/sex)	E	LAK cells ($\times 10^9$)	IL-2 ($\times 10^7$ U)	Size	Responses P.S.*	Survival (mo)
HCC						
1. (63/M)	4	119.0	38.0	PR	4/1	34
2. (21/F)	4	97.0	5.5	PR	4/1	9
3. (68/M)	4	7.5	2.3	NC	1/1	3
4. (34/M)	4	44.8	8.8	PD	2/4	4
5. (64/M)	3	9.6	2.7	NC	1/1	5
Colon						
6. (65/M)	4	14.6	5.2	PD	1/1	6
7. (65/M)	2	57.2	5.5	PD	2/3	7
8. (47/M)	3	54.0	2.4	PD	1/1	6

E = tumour extension in liver measured by area occupied by cancer: 4 = > 60%, 3 = 40–60%, 2 = 20–40% and 1 = < 20%.
PR = partial regression; NC = no change; PD = progressive disease.
*Performance status before/after immunotherapy: 4 = bedridden all day long, 3 = bedridden for more than half the day, 2 = bedridden for less than half the day and 1 = no limitations.

Two out of five patients with HCC had partial tumour regression (Table 1) and tumour sizes and serum AFP levels decreased. However, whilst the patients' general condition improved, tumour growth recommenced as therapy was given intravenously. In case 1 this second growth was suppressed by another course of intra-arterial AIT. Two patients responded to the therapy and lived for as long as 34 and 9 months, respectively, after initiation of adoptive immunotherapy, although they had advanced cancers. These patients had been treated with mitomycin C or 5-fluorouracil more than 1 month before adoptive immunotherapy, although chemotherapy failed to induce tumour regression and caused severe side-effects. Adoptive immunotherapy following chemotherapy is reported to be more effective than adoptive immunotherapy alone in animal models [6, 7] and such combined therapy may be of benefit. Metastatic liver tumours from colonic carcinomas were resistant to adoptive immunotherapy, confirming previous reports [1, 2, 8].

Fever and eosinophilia were less severe side-effects than with systemic adoptive immunotherapy [3]. However, bleeding gastroduodenal ulcers developed in three cases, which probably resulted from continuous administration of IL-2 into the hepatic artery. Thus, intra-arterial LAK cell infusion with continuous intravenous administration of IL-2 may be a better approach.

Many LAK cells are necessary to induce tumour regression [1, 2], but repeated leukaphereses impose great burdens on patients and medical staff. To overcome the problem, a long-term culture method of LAK cells was developed and used in three patients (cases 2, 7 and 8). In this method, half the cells were put aside at harvest, and were further cultured with IL-2. The procedure was repeated several times. This process enabled us to obtain a large number of cells with high LAK activity. Since only three cases have been treated with LAK cells generated by this method, further trials are needed to determine whether such cells can mediate antitumour effects *in vivo*, especially in patients with HCC.

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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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