KAWASAKI MED. J. VOL. 16 : NO. 1, 51-56 (1990)

An Autopsy Case of Nonfunctioning Islet Cell Carcinoma

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Accepted for publication on May 18, 1990

ABSTRACT. A case of a 64-year-old man with a nonfunctioning islet cell tumor is reported. A slight increase in the serum levels of elastase I and CA19-9 were noted, while serum insulin and glucagon remained within normal limits. Abdominal US and CT-scanning showed diffuse swelling of the pancreas. ERCP showed interruption of the pancreatic duct at the tail of the pancreas. The patient died on the thirty-fourth hospital day and an autopsy disclosed a 7×5 cm tumor at the pancreas tail. Pathological studies revealed an islet cell tumor. A structure like that of neuroendocrine granules was noted electron microscopically. Immunohistological stains were negative for α_1-antitrypsin, pancreatic antigen, amylase, gastrin, insulin, glucagon and somatostatin. In addition, a clinical analysis was made of 117 cases of nonfunctioning islet cell tumors reported in Japan.

Key words : Nonfunctioning islet cell tumor — pathological and histological studies

Diagnosis of nonfunctioning islet cell carcinoma is known to be difficult because of the lack of excess endocrine activity even in the advanced stage. We experienced a case of nonfunctioning islet cell carcinoma with liver metastasis. A clinical analysis was also made of 117 cases of nonfunctioning islet cell tumors reported in Japan.

CASE REPORT

The patient was a 64-year-old man who was admitted to our hospital because of left hypochondriac pain. His past history was uneventful, while his family history revealed uterine cancer and rectal cancer in his mother and elder sister, respectively. The patient experienced a loss of appetite and general fatigue in April, 1985. Left hypochondriac pain appeared at the beginning of May. A tumor of the pancreas was detected by a CT-scan and he was admitted to our hospital on June 15, 1985.

On physical examination, his blood pressure was 120/78 mmHg and his pulse rate was 78/min. Heart and lung findings were normal. The liver was palpable 4 cm below the costal margin and its consistency was hard. Tenderness

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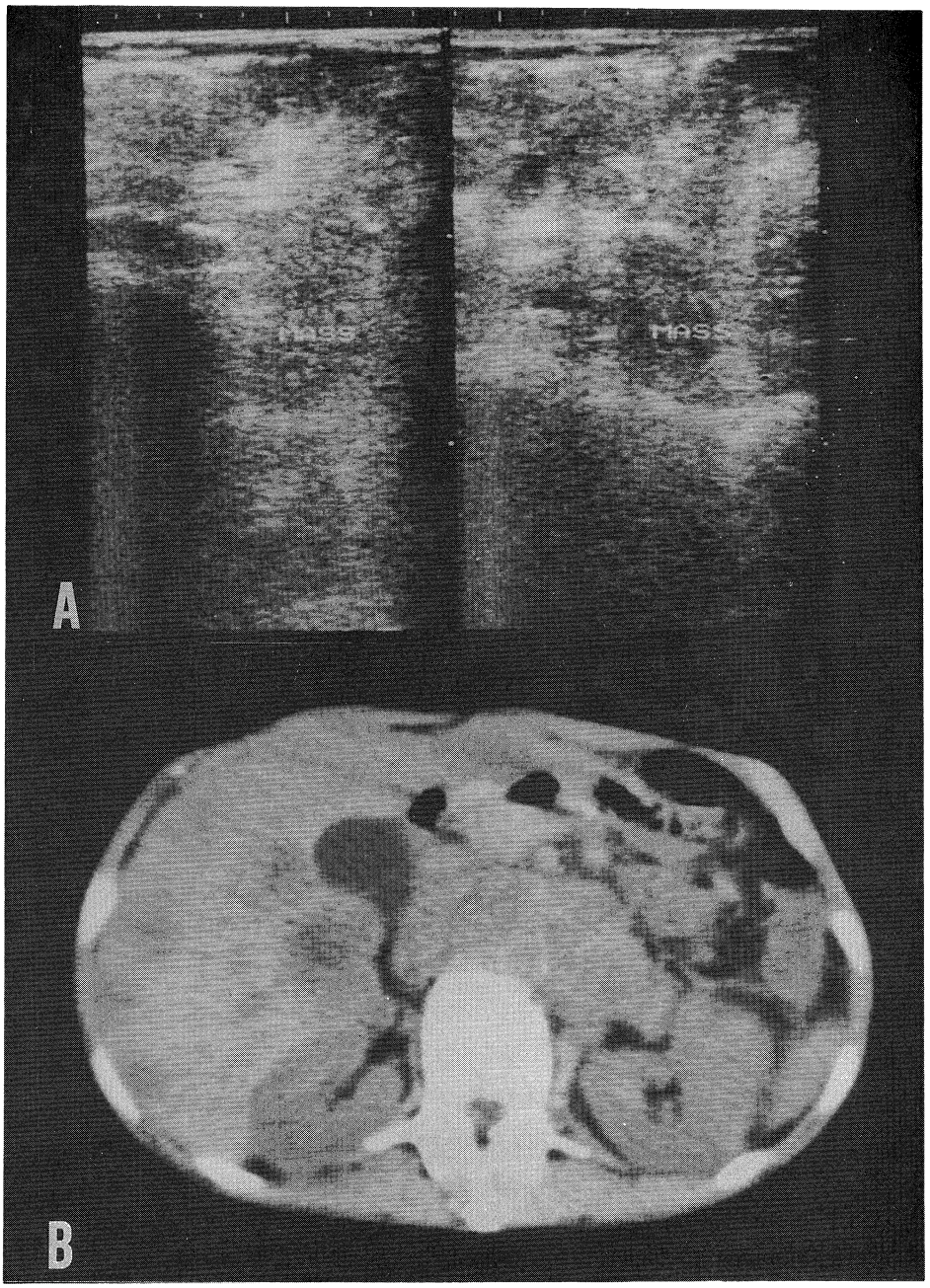

Fig. 1. (A) Abdominal US showed enlargement of the pancreas tail.
(B) Abdominal CT showed swelling of the pancreas and paraaortic lymphnode. Multiple low density areas were noted in the liver.

on the left hypochondriac region was noted. Neurological examinations were negative.

Laboratory data revealed slight anemia and liver dysfunction was noted. His serum amylase was 359 IU/l and urine amylase was elevated to 2949 IU/l.

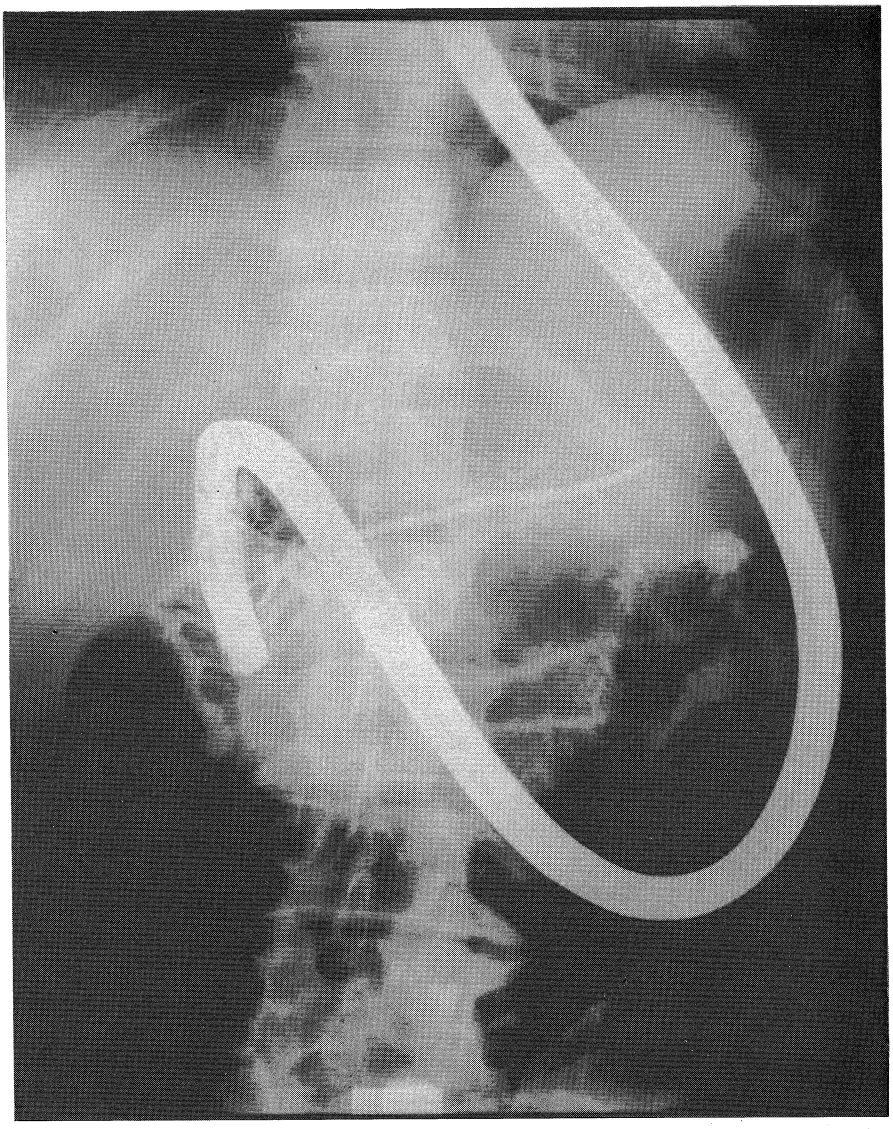

Fig. 2. Endoscopic retrograde pancreatography revealed cessation of the pancreatic duct at the tail of the pancreas.

His serum elastase I was 929 ng/dl and CA19-9 was 79 U/ml. The serum levels of insulin, glucagon and gastrin, however, were within normal limits.

On abdominal US (Fig. 1A) the tail of the pancreas was found to be swollen and a hypoechoic lesion was noted. A CT scan (Fig. 1B) disclosed diffuse swelling of the pancreas and of the paraaortic lymphnodes. Multiple low density areas were also noted within the liver. Endoscopic retrograde pancreatography (Fig. 2) showed the main pancreatic duct to be interrupted at the tail of the pancreas. Ascites, abdominal pain and loss of appetite were aggravated and the patient died on the thirty-fourth hospital day.

An autopsy revealed a 7×5 cm mass in the tail of the pancreas.

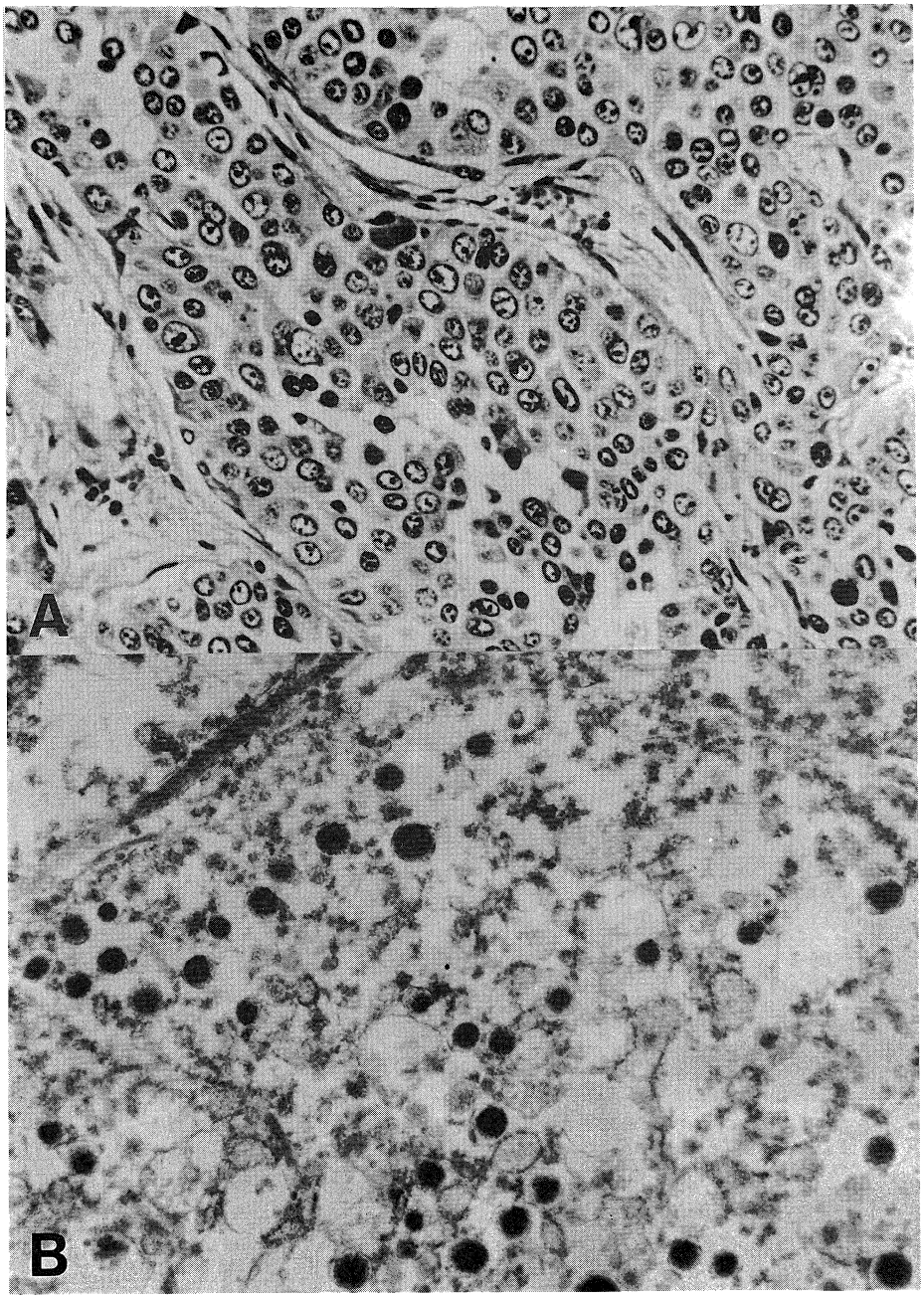

Fig. 3. (A) Microscopic examination of the tumor showed cylindrical cells in a funicular arrangement (HE×66).
(B) Electron microscopic findings of the tumor. Electron dense granules were noted (<×1000).

Histologically atypical round and eosinophilic cells had proliferated in a funicular arrangement (Fig. 3A) and an electron microscopic examination (Fig. 3B) disclosed electron dense granules of 200 nm in diameter. Special stains for

Grimelius, Chromogranin A and Leu7 were positive, but immunohistological stains for α_1-antitrypsin, pancreatic antigen, amylase, gastrin, insulin, glucagon and somatostatin were negative. These findings confirmed the diagnosis of nonfunctioning islet cell carcinoma. In addition, metastasis to the liver, spleen, vertebrae and paraaortic lymphnodes were also found.

ANALYSIS OF 117 REPORTED CASES

A Clinical analysis was made of 117 cases of nonfunctioning islet cell tumors reported in the Japanese literature. There were 40 men (34.2%) and 77 women (65.8%) in this series and their mean age was 40.7 years old. Concerning symptoms and signs, an abdominal mass (42%) and abdominal pain (20.6%) were fairly common, but jaundice was noted only in 4.5%. Localization of the tumor was noted most frequently in the head of the pancreas and less frequently in the body and tail. Histologically, there were three times more malignant tumors than benign ones. Of 25 cases with an angiographic diagnosis, abundant tumor vessels were noted in 8 cases, vascular displacement in 6 cases, and complete venous obstruction in 4 cases. The median survival time of the 117 cases was one year and two months.

DISCUSSION

Islet cell tumors are classified into two groups; functioning and nonfunctioning. Kent *et al.*[1] reviewed islet tumors of the pancreas encountered at the Mayo Clinic between 1960 and 1978 and reported that among 168 cases, insulinoma was the most common form of tumor (60%), followed by gastrinoma (18%), islet cell tumors (7%), and 25 cases (15%) with clinically nonfunctioning tumors. Miyoshi *et al.*[2] reported 21 cases of islet cell adenoma (67.7%) and 10 cases of islet cell carcinoma (32.3%) among 31 cases collected in the Japanese literature. Kent *et al.*[1] reported that 23 (92%) out of 25 cases of nonfunctioning islet cell tumors were malignant. Tomioka *et al.*[3] reported 92 cases in the Japanese literature, of which 46.7% were malignant. Our analysis of 117 collected cases showed that the rate of malignancy was 53.8%. The occurrence of these tumors was about two times greater in women. Histological studies of islet cell tumors have classified them into three groups based on the arrangement of tumor cells; 1) an islet cell pattern, which shows a structure like Langerhans' islets, 2) a rossete pattern, in which a rossete forms centered around a capillary blood vessel, and 3) a ribbon pattern, in which the cylindrical cells of one or two layers show a funicular arrangement. Our case was thought to be of the third type. In our case Grimelius, Chromogranin A and Leu7[4,5] were positive.

CONCLUSION

A case of nonfunctioning islet cell carcinoma in a 64-year-old man was reported. Metastasis to the liver was noted.

REFERENCES

1) Raleigh, B., Jonathan A.K., van Heerden, J.A. and Weilland, L.H.: Nonfunctioning islet cell tumors. Ann. Surg. **193** : 185–190, 1981
2) Miyoshi, A., Naito, T., Ueki, T., Tomokiyo, A., Uchiyama, H., Mano, M., Kobayashi, S., Nakayama, Y., Yoshida, K., Nakayama, T., Koga, M. and Yamaguchi, T.: Two cases of treatment of nonfunctioning islet cell carcinoma. Surgery **41** : 1401–1405, 1979
3) Tomioka, T., Miyagi, N., Nakata, T., Miyata, A., Amano, M., Mori, H., Hayashida, M., Saeki, S. and Matsuo, T.: A case report of nonfunctioning islet cell tumor—a review of Japanese literature—. Jpn. J. Gastroenterol. Surg. **16** : 1389–1394, 1983
4) Ricardo, V., Lloyd, M.C., Rosa, P., Hille, A. and Huttner, W.B.: Distribution of chromogranin A and secretogranin I (Chromogranin B) in neuroendocrine cells and tumors. Am.J. Pathol. **130** : 296–304, 1988
5) Tsutsumi, Y.: Leu7 immunoreactivity as a histochemical marker for paraffin-embedded neuroendocrine tumors. Acta Histochem. Cytochem. **17** : 15–21, 1984