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*Case report*

# Pancreatoblastoma with marked elevation of serum alpha-fetoprotein

## An autopsy case report with immunocytochemical study

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**Summary.** The autopsy findings in a pancreatoblastoma in a 7-year-old Japanese girl is reported. The tumour was in the head and body of the pancreas, and was associated with diffuse carcinomatous peritonitis and hepatic and pulmonary metastases. There was marked elevation (more than 10000 ng/ml) of serum alpha-fetoprotein (AFP). Histopathologically the tumour was composed of solid epithelial elements with fibrous stroma, showing acinar arrangement, squamoid clusters and tubular structures. The epithelial elements contained numerous fine PAS positive granules in the cytoplasm. Immunocytochemical results suggested epithelial differentiation with positivity to alpha-1-antitrypsin (AAT), keratin, CA19-9, and AFP. No endocrine elements were recognized. Characteristic feature of this tumour are discussed and compared with prevoius reports.

**Key words:** Pancreatic neoplasm – Glandular epithelial neoplasm – Child – Alpha – fetoprotein – Immunohistochemistry

## Introduction

Primary non-endocrine tumours of the pancreas are uncommon in childhood (Morohoshi et al. 1983), Pancreatoblastoma (Horie et al. 1977; Benjamin and Wright 1980) and solid-cystic tumour (SCT, Klöppel et al. 1981) which differ distinctly from the usual ductal carcinoma of the pancreas seen in adults may be found. We discuss here the histological and immunocytochemical examination of a rare case of pancreatoblastoma in a girl with marked elevation of serum AFP.

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## Case report

A 7-year-old Japanese girl was admitted on January 8, 1983 to the Department of pediatrics, SHOWA University Fujigaoka Hospital with complaints of persistant diarrhoea, abdominal expansion and vomiting for a month. Physical examination revealed abdominal hardness and marked swelling of neck and inguinal lymphonodes on both sides. A large tumour mass was revealed by abdominal ultrasonography and computer tomography in the upper abdomen associated with slight hepatosplenomegaly. Serum AFP was markedly elevated with level of over 10,000 ng/ml. Other tumour markers including CEA and other laboratory data were within normal limits.

The patient was transfered to the Department of pediatric Surgery on January 18, and exploratory laparotomy was performed. Neoplastic peritonitis with 700 ml of bloody ascites was found with a large solid tumour, adherention to the stomach, mesentrium, omentum and retroperitoneum. The pancreas was completely embedded in this mass. A piece of tumour was biopsied from an omental lesion. This was histopathologically suspected to be a yolk-sac tumour.

After the laparotomy, intensive anti-tumour chemotherapy was given. The tumour mass decreased slightly in size according to CT-scan and could not be palpated through the abdominal wall. The patient was discharged from the hospital in the middle of April. However, because the tumour grew again with abdominal expansion, anorexia and vomiting, she was admitted again on August first, when the serum AFP level was 9620 ng/ml. On November 13, she died due to disseminated tumour with cardiac failure and pneumonia.

## Materials and methods

All autopsy sypecimens were fixed in 10% buffered formalin and embedded in paraffin from which thin sections were prepared for examination. Sections for light microscopy were stained with H & E, PAS and Grimelius argyrophil reaction. Immunocytochemistry was carried out using the primary antisera listed in Table 1, according to either peroxidase-antiperoxidase (PAP) technique or the avidin-biotin complex (ABC) method.

**Table 1.** Primary antibodies used for immunocytochemical analysis

| Antigen to: | Antigen source | Antibody source | Dilution | Origin |
|---|---|---|---|---|
| CEA | Human | Rabbit | prediluted | DAKO-PATTS/ Denmark |
| CA19-9 | Human | Mouse | 1:400 | Centocor/ USA |
| AFP | Human | Rabbit | prediluted | BioGenex/ Ireland |
| NSE | Human | Rabbit | prediluted | BioGenex/ Ireland |
| Insulin | Human | Rabbit | prediluted | BioGenex/ Ireland |
| Glucagon | Human | Rabbit | prediluted | BioGenex/ Ireland |
| Somato statin | Human | Rabbit | prediluted | BioGenex/ Ireland |
| AAT | Human | Rabbit | prediluted | BioGenex/ Ireland |
| Alpha-Amylase | Human | Rabbit | 1:200 | own |
| Keratin | Human | Rabbit | 1:100 | BioScience/ Swiss |
| Vimentin | Calf | Rabbit | 1:100 | BioScience/ Swiss |
| Beta-HCG | Human | Mouse | prediluted | BioGenex/ Ireland |

CEA: Carcinoembryonic antigen; AFP: alpha-fetoprotein; NSE: neuron-specific enolase; AAT: alpha-1-antitrypsin; Beta-HCG: beta-human chorionic gonadotropin

**Table 2.** Immunocytochemical results

| Primary antibody | Epithelial elements | | | Stroma |
|---|---|---|---|---|
| | Acinar arrangement | Squamoid corpuscle | Tubular structure | |
| AAT | +++ | ++ | +++ | – |
| Amylase | – | – | – | – |
| CEA | – | – | – | – |
| CA19-9 | – | – | + | – |
| AFP | + | – | ++ | – |
| NSE | – | – | – | – |
| Hormones* | – | – | – | – |
| Keratin | + | ++ | + | – |
| Vimentin | – | – | – | ++ |
| β-HCG | – | – | – | – |

* Insulin, glucagon and somatostatin

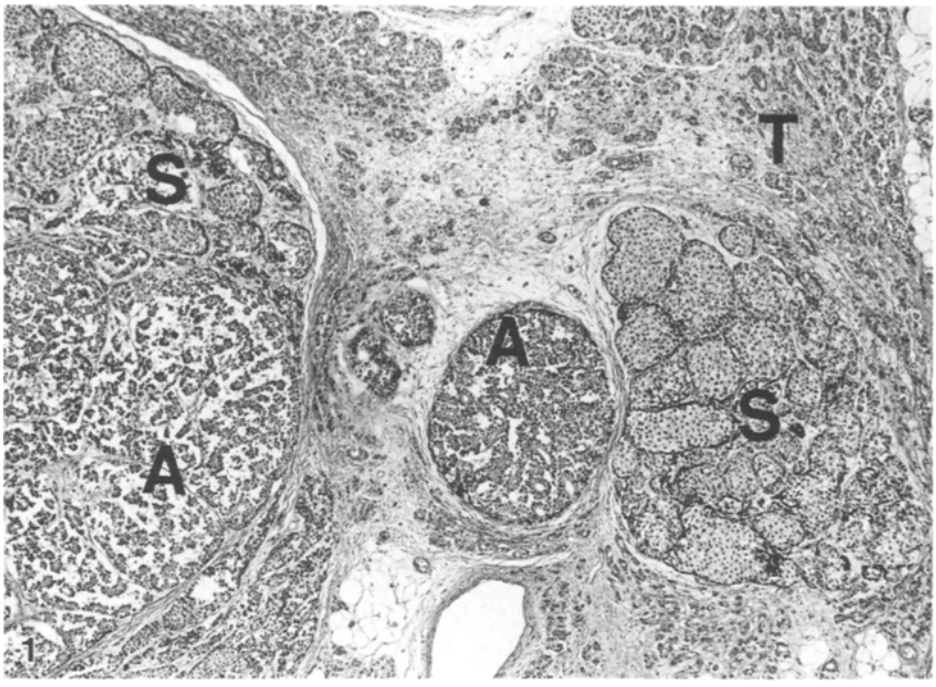
## Results

Autopsy was performed about 5 h postmortem. A large tumour mass with irregular adhesion to omentum, stomach, spleen and pancreas occupied the upper abdominal lumen with marked disseminated carcinomatous peritonitis. The head and body of the pancreas were embedded in a tumour mass measuring 6 × 5 ms and completely replaced by it. Cut section showed a lobular pattern with massive necrosis and a grayish-yellow color. Intra-abdominal lymph nodes including parapancreatic, paragastric, hepatic hilar, splenic hilar and paraaortic lymph nodes were diffusely swollen by metastasis. Multiple small metastatic nodules were noted (up to 1.5 cm in diameter in the liver and up to 1 cm in diameter in both lungs). Pulmonary interstitial fibrosis and marked carcinomatous pleuritis were also evident. Other pathological signs were: moderate myocardial hypertrophy of the right ventricle of the heart, bilateral renal infarction and benign duodenal ulcer.

Histologically the tumour consisted of epithelial nests, lobulated by fibrous stroma. The polygonal epithelial cells had round or oval nuclei and eosinophilic or clear cytoplasm. There was little evidence of mitosis. These atypical epithelial cells formed various solid epithelial nests, characterized by acinar arrangement, squamoid corpuscles and tubular structures. (Fig. 1). Squamoid corpuscles and acinar arrangements were commonly and diffusely recognized in the main tumour in the pancreas. Tubular structures were more dominant in metastic tumour.

PAS-positive fine granules were recognized in most tumour cells (Fig. 2). Many of these granules were in the apical region of the eosinophilic cytoplasm, which tended to form acinar arrangements and tubular structures. A few PAS-positive granules were present in the clear cytoplasm of the tumour cells in the squamoid corpuscles. All tumour-cell Grimelius' argyrophil reactions were negative.

Immunocytochemical results are listed in Table 2. The AAT positive reaction was diffuse and marked in all epithelial tumour elements. (Fig. 3). AFP was diffusely recognized in tumour cells showing tubular structures and acinar arrangements (Fig. 4). CA19-9-positivity was noticed in only a few tumour cells in tubular structures (Fig. 5). Keratin-positive cells predominated in squamoid corpuscles. No epithelial elements showed positive reaction to vimentin. Alpha-amylase, CEA or beta-HCG were completely negative. Pancreatic hormones including insulin, glucagon, somatostatin, and NSE were also negative.



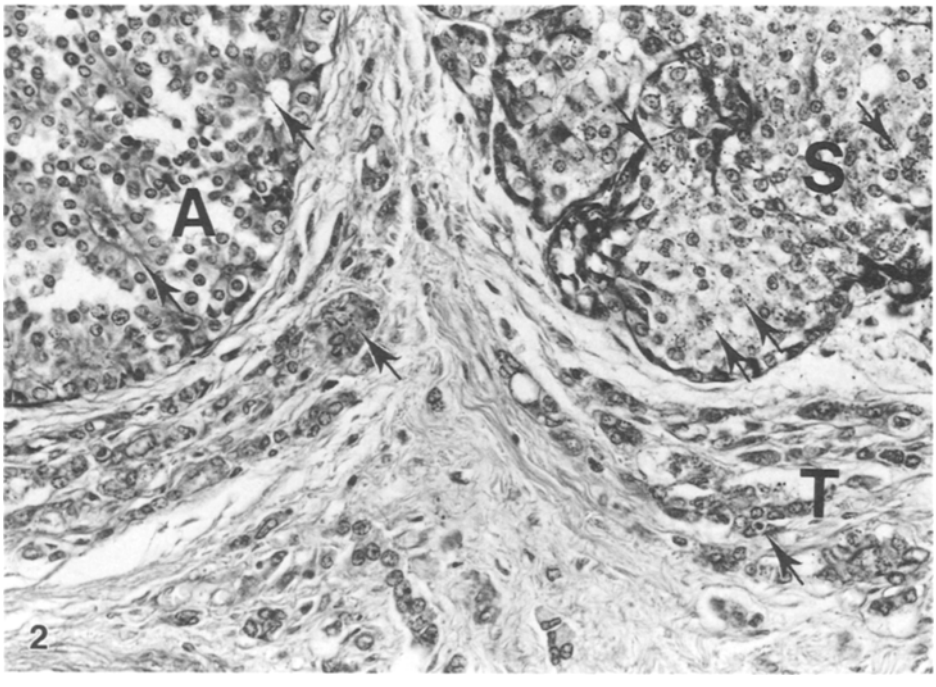



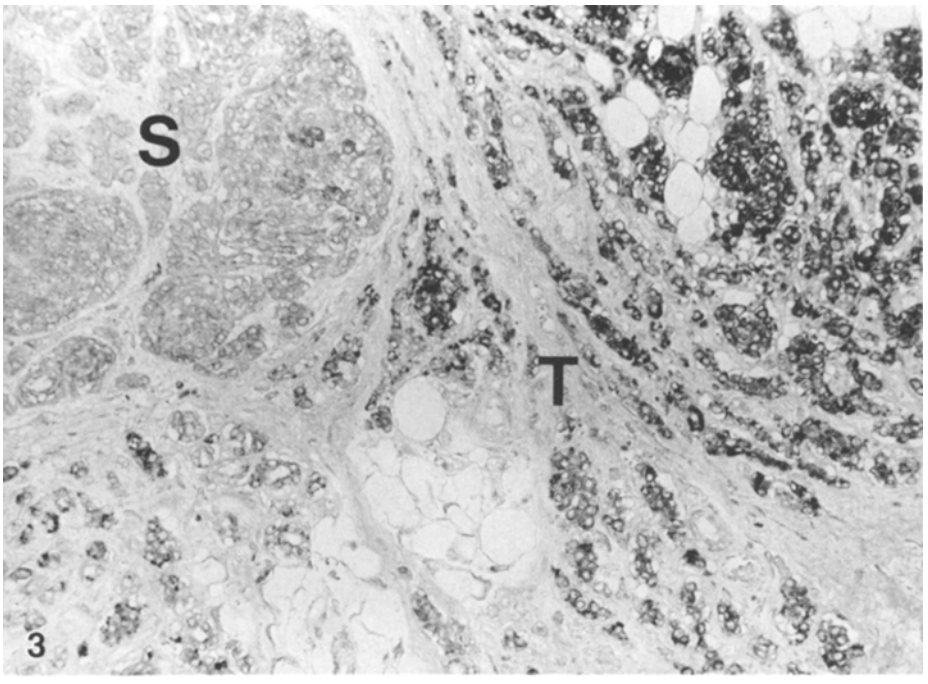

**Fig. 1.** Epithelial tumour nests showing squarmoid corpuscle (S), acinar arrangement (A) and poorly to moderately differentiated tubular structure (T). H & E stain, ×100

**Fig. 2.** PAS-stain positive fine granules (*arrows*) in the tumour cells composing squamoid corpuscle (S), acinar arrangement (A) and tubular structure (T). PAS-stain, ×200

## Discussion

Pancreatic non-endocrine tumours are rare in childhood. However, they are known to include various types of tumours, including the usual ductal carcinoma observed in adults and some tumours with unique clinicopathological features including pancreatoblastoma (Horie et al. 1977) and solid-cystic tumour (SCT: Klöppel et al. 1981) which is also known as papillary-cystic tumour (Cubilla and Fizgerald 1984). The age distribution of pancreatic neoplasms in childhood is bimodal: one peak before five years with males dominant, and the other among teens with females dominant (Benjamina and Wright 1980; Morohoshi et al. 1982).

Histopathologically, pancreatoblastoma is characterized by epithelial proliferation with or-



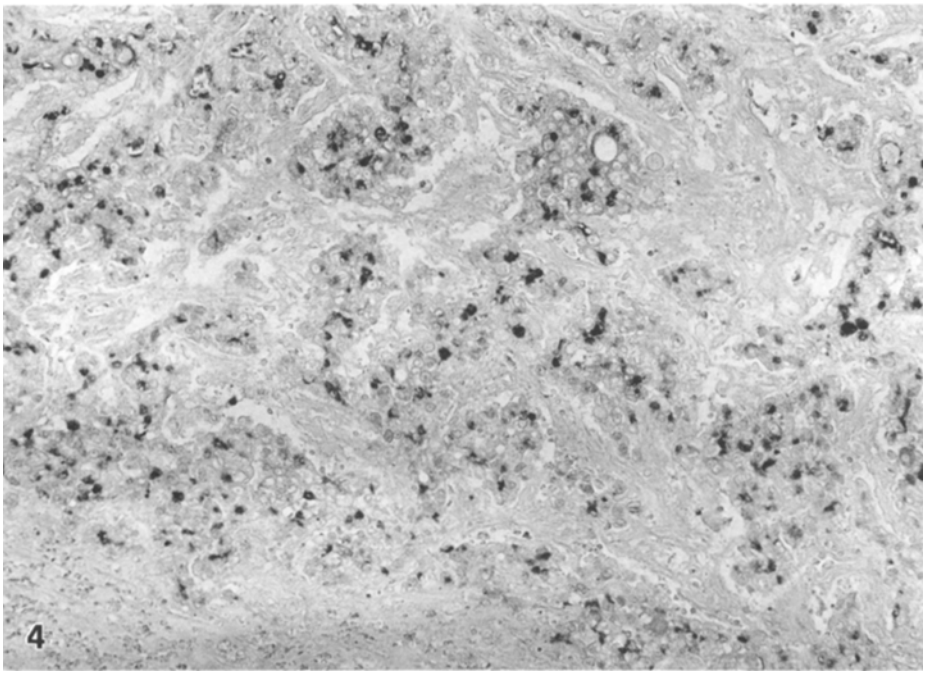




**Fig. 3.** Immunocytochemical positivity to alpha-1-antitrypsin (AAT) in most tumour cells showing acinar arrangements as well as tubular structures (T) and squamoid corpuscle (S). PAP-method, ×200

**Fig. 4.** Immunocytochemical positivity to alpha-fetoprotein (AFP) in most of tumour cells. PAP-method, ×100

ganoid structure showing squamoid corpuscles surrounded by acinar arrangements and tubular structures, which is lobulated by dense fibrous connective tissue. Because these organoid structures are similar to pancreatic primordium, pancreatoblastoma is believed to originate from multipotential primordial cells in the pancreas (Horie et al. 1977; 1987). In addition to epithelial organoid structures, Benjamin and Wright (1980) found myxoid and cartilaginous tissues in the fibrous tumour stoma. This suggests that pancreatoblastoma is composed of multipotent neoplastic elements including some which are non-epithelial. No mesenchymal neoplastic elements were evident in the present tumour.

In addition to squamoid corpuscles, previous reports have emphasized acinar arrangement (Horie et al. 1977; Benjamin and Wright 1980; Bu-

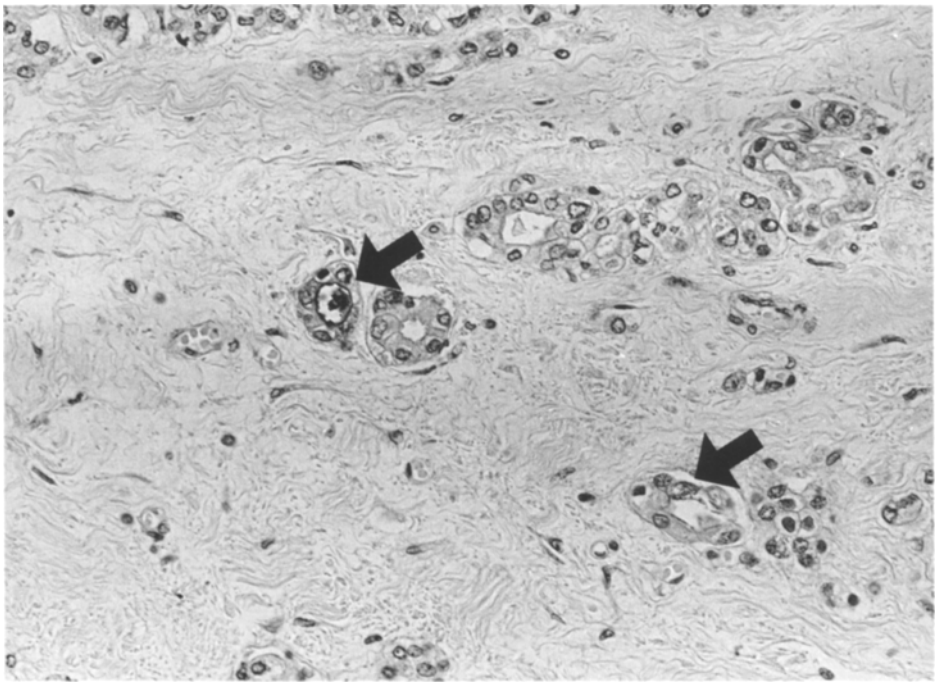


**Fig. 5.** Immunocytochemical positivity to CA19-9 in a few tumor cells (*arrows*) showing well differentiated tubular structure. PAP-method, ×200

chino et al. 1984; Ichijima et al. 1985; Ohaki et al. 1985; Iseki et al. 1986), and suggested acinar differentiation.

CEA and CA19-9 are useful serum tumour markers in patients with pancreatic carcinoma. Immunocytochemically both markers are evident in tumours showing ductal differentiation, and are negative in epithelium showing acinar differentiation (Morohoshi et al. 1987). Though tubular structures were evident microscopically in the present tumour, CEA was not revealed. However, CA19-9 was seen in a few tumour cells that showed tubular structure. Compared with previous pancreatoblastomas, the present tumour showed mostly ductal differentiation from the point of positivity to CA19-9.

AFP is also a useful marker of primary liver tumours and some embryonal tumours including those of the yolk-sac (Narita et al. 1988). The latter are usually associated with marked elevation of serum AFP. For pancreatic tumours other than pancreatoblastoma, AFP is not a useful marker because elevation of serum AFP is evident in only 5% of patients (Moosa and Levin 1981) mostly suffering from liver metastases (Hamazoe et al. 1987).

Pancreatoblastomas are frequently associated with the elevation of serum AFP levels. Horie et al. (1987) reported the elevation of serum AFP levels in three out of 12 patients (25%) with pancreatoblastoma. Immunocytochemically AFP also appeared in epithelial tumour in previous reports (Buchino et al. 1984; Ohaki et al. 1985; Iseki et al. 1986) as well as in the present tumour. From the findings of Ohaki et al. and our own; serum AFP levels decreased after successful excision or chemotherapy. When the tumor recurred, they increased and examination of serum AFP levels may thus be useful for diagnosis and prognosis in pancreatoblastoma.

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