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Pancreatoblastoma

—Histopathological and Ultrastructural Analysis of Two Cases—

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Pancreatoblastoma has been described in children and characterized by unique histologic features and excellent clinical course. Ultrastructural and immunohistochemical studies of pancreatoblastoma reveal either exocrine alone or both endocrine and exocrine differentiation.
We present two cases of pancreatoblastoma in children in which immunohistochemical and ultrastructural examination failed to demonstrate features of either enzyme or hormone production and which became worse in clinical course. We assume that pancreatoblastomas are tumors which differentiate more toward acinar or ductal elements than toward islet cell.

Key Words: *Pancreatoblastoma, Exocrine differentiation, Pancreas, Childhood*

INTRODUCTION

Pancreatic malignancies are rare in infants and children. Histologic variants of pancreatic malignancy in young patients include the ductal adenocarcinoma seen in adults, acinar cell carcinoma, islet cell tumors, pancreatoblastoma and papillary cystic-solid neoplasm of the pancreas.

Pancreatoblastoma has been described in children and consists of rosettes and tubules, as well as undifferentiated solid sheets of spindle cells and areas of squamous metaplasia (Horie et al., 1977). Foci of chondroid and osteoid tissue can also be seen (Cubilla et al., 1979).

Previous reports have documented evidence of exocrine and endocrine secretion in pancreatoblastoma (Frable et al., 1971), either of exocrine alone or of both together (Buchino et al., 1984). Electron microscopy of the pancreatoblastoma suggests that the tumors are differentiating more toward acinus than toward islet cell. The curability rate after resection in pancreatoblastoma is considerably better than in other malignant tumors of the pancreas (Buchino et al., 1984). We present two cases of pancreatoblastoma in which immunohistochemical and ultrastructural examination failed to demonstrate features of either enzyme or hormone production.

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CASE REPORT

Case 1

A 2-year-old girl presented with an abdominal mass which had been discovered accidentally by her parents 2 days before admission. She was transferred to Seoul National University Children's Hospital from a local clinic, where upper gastrointestinal series and an abdominal sonogram revealed an intraabdominal mass compressing the stomach. She was born normally and had been healthy until this time. On admission the vital signs were as follows; temperature 37.5°C, respiration rate 24 per min, pulse 110 per min, blood pressure 120/80mmHg, and body weight 12kg. Physical examination revealed an epigastric mass that was hard and movable. Laboratory findings were as follows: hematocrit 33.3%, hemoglobin 11.6g/100ml, alkaline phosphatase 653U/L, SGOT 29U/L, SGPT 9U/L, serum amylase 309 U/100ml, serum neuron specific enolase 19.5ng/ml (normal 12 ng/ml), α-fetoprotein 5ng/ml and urine vanillyl mandelic acid (VMA) 1.1mg/d. Computed tomography revealed an ill-defined 4cm mass in the pancreatic head and enlarged tracheobronchial lymph nodes. The child underwent laparotomy.

A large tumor was identified in the head of the pancreas. The liver and spleen appeared free of tumor. The tumor appeared well demarcated with extension

to the retrogastric space. There was tumor involvement of the portal vein and superior mesenteric artery.

The child had an uneventful postoperative course. Postoperative chemotherapy could not be done because her parents were against it.

Grossly the tumor was a relatively well demarcated firm mass, measuring 6×5×3.5 cm and weighing 42gm. The outer surface was dark red and irregular. The cut surface was bright yellow, solid and multilobulated by fibrous septa (Fig. 1). Scattered yellow spots of necrosis were also noted.

Light microscopic examination revealed an organoid structure divided by fibrous tissue. The organoid structure contained numerous tubular structures of cuboidal to tall columnar epithelial cells and squamoid cells with elongated nuclei arranged in a parallel fasciculating pattern (Fig. 2). The tumor cells of the acini had moderate-sized nuclei with coarse, clumped chromatin and a pale vacuolated cytoplasm with distinct cell borders in several areas and had small round to oval, hyperchromatic nuclei with fine chromatin, scant cytoplasm and indistinct cell borders in other areas (Fig. 3). The glandular lumina of some acinar structures contained a small amount of secretion. Numerous mitotic figures were noted in the tumor cells of acini. There was neither papillary growth nor islet-like structures. Multiple small scattered foci of necrosis and calcification were found. However, foci of foam cell collection were noted around the fibrous tissue.

Ultrastructurally the tumor cells were poorly differentiated, sometimes revealing acinar formation. The tumor cells had long spherical or ovoid nuclei with prominent nucleoli, flattened cisternae of rough endoplasmic reticulum, free ribosomes, lysosomes and lipid droplets. Some contained pools of glycogen particles. In areas of acinar formation electron dense granules resembling zymogen granules were seen around the luminal space which was provided with microvilli (Fig. 4). The acinar cells were joined together by junctional complexes and were surrounded by a continuous basal lamina. No evidence of islet cell differentiation was noted.

Immunohistochemical staining of representative sections of paraffin-embedded material revealed that the tumor cells of acinus and squamoid corpuscles were negative for somatostatin, insulin and glucagon.

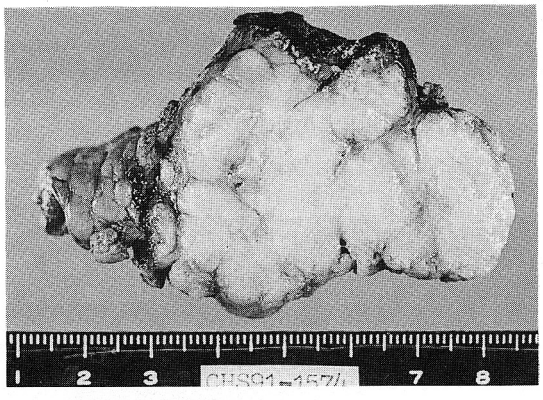

Fig. 1. Cut surface shows a relatively well demarcated firm mass which is multilobulated by fibrous septa.

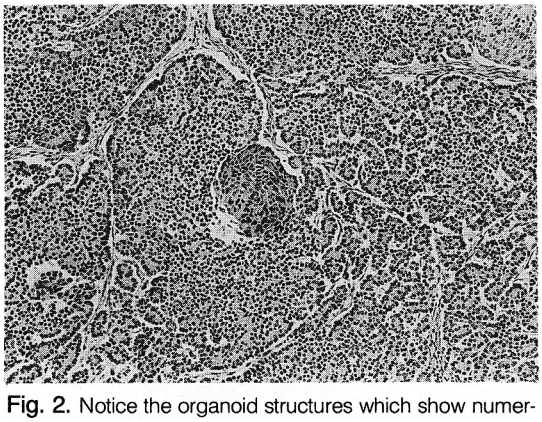

Fig. 2. Notice the organoid structures which show numerous tubular structures and squamoid cells with elongated nuclei arranged in a parallel fasciculating pattern. (H&E, ×40)

Case 2

A 3-year-old girl presented with an abdominal mass which was palpated by her parents in June, 1984 and had progressively increased in size. She was born normally and had beed previously healthy. On physical examinaton the mass was palpable above the umbili-

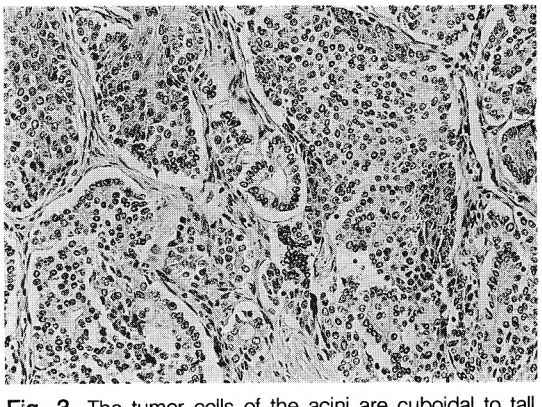

Fig. 3. The tumor cells of the acini are cuboidal to tall columnar epithelial cells (H&E, ×200)

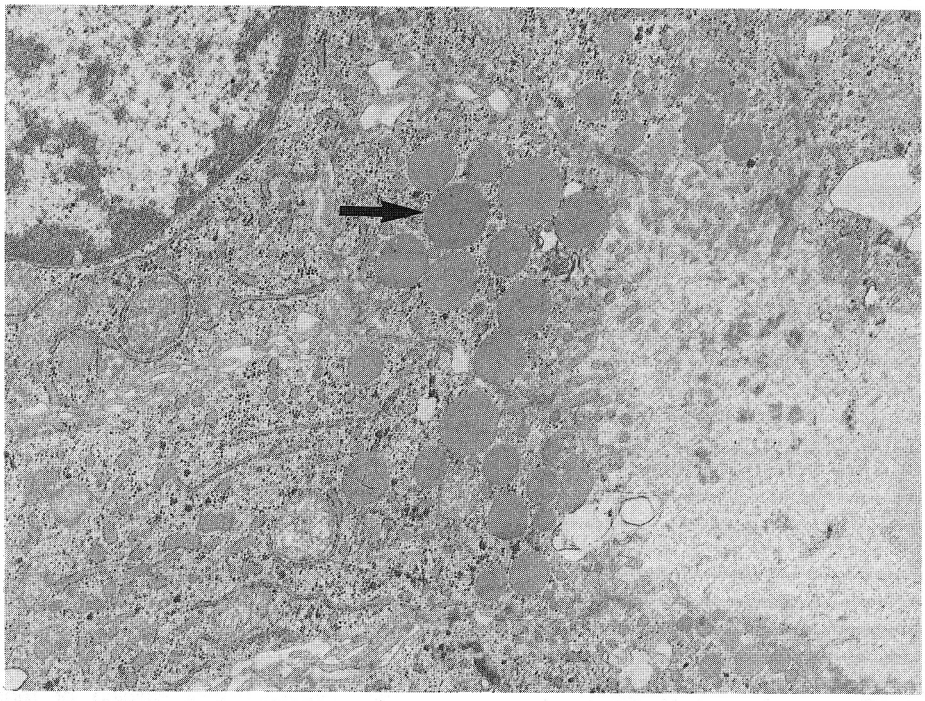

Fig. 4. Electron dense structures resembling zymogen granules (arrow) are noted around the luminal space lined with microvilli. (×13,800)

cus, freely movable, hard and non-tender. An ultrasonogram revealed a well demarcated mass with cystic change in the body of the pancreas. Laboratory examinations were as follows: hemoglobin 12.6 g/100ml, hematocrit 36.2%, SGOT 10 U/L, SGPT 8 U/L, alkaline phosphatase 190 U/L, serum amylase 100 U/100ml, serum α-fetoprotein 24ng/ml, serum carcinoembyonic antigen 2.2 ng/ml, cortisol 60 μg/dl, ACTH 410 pg/ml, 17-ketosteroid 5.9 mg/d, 17-hydroxycorticosteroid 22.10 mg/d. She underwent laparatomy with the impression of pancreatic carcinoma on June 28, 1984. A tumor was noted in the body of the pancreas, measuring 7 cm in diameter. It was relatively well demarcated. The mass showed a small cystic portion containing bloody fluid. The liver and spleen appeared free of tumor. The child had an uneventful postoperative course. However, she was admitted again because of abdominal distension and pain on October 19, 1984. Physical examination revealed a distended abdomen and 2 finger breadth palpable liver with a firm nodular mass. An ultrasonogram revealed a metastatic nodule in the liver. Bone scan and chest X-ray were normal. She received chemotherapy of regimen for pancreatic adenocarcinoma but the size of the metastatic nodule in the liver remained same.

Grossly the tumor was pinkish gray, and well encapsulated. It measured 6×5×5 cm and weighed 70gm. The outer surface was smooth and glistening. The cut surface was mainly pinkish white, solid and partly cystic. Scattered hemorrhage and foci of yellow spots representing necrosis were found.

Light microscopic examination showed lobular structures circumscribed by loose fibrous stroma. The fun-

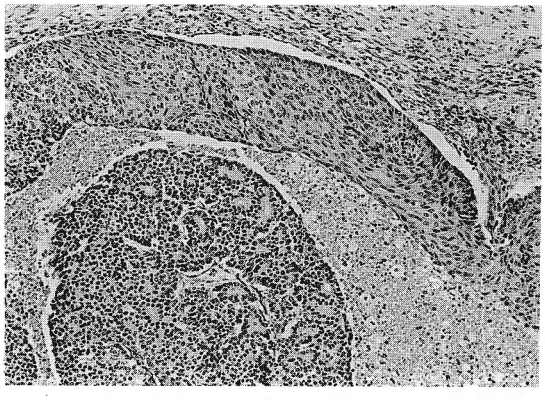

Fig. 5. Tumor necrosis is prominent within the organoid structure.

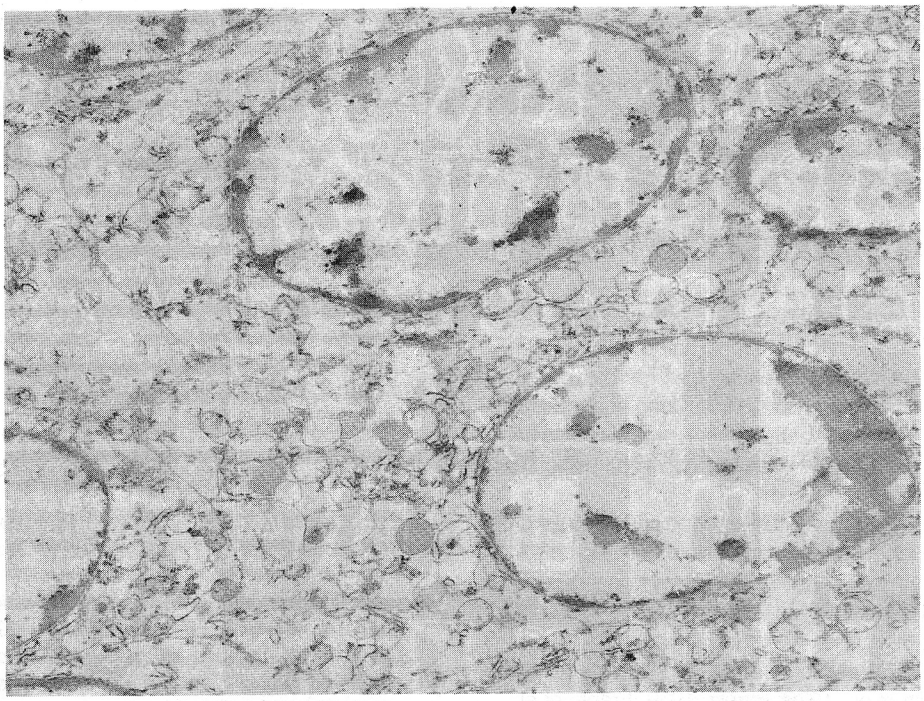

Fig. 6. The nuclei of the tumor cells are round to oval and the cytoplasm contains fair amounts of rough endoplasmic reticulum, mitochondria and lysosomes. There is neither acinar formation nor cytoplasmic zymogen granules (×6300)

damental histologic features were basically identical to those of case 1. However, tumor necrosis was more extensive than in case 1 (Fig. 5). Some tumor cells of acinar formation showed PAS-positive granules in the cytoplasm. The glandular lumina of some of the acinar structures showed a small amount of secretion which was positive in PAS staining.

Ultrastructural examination revealed that the tumor cells were poorly differentiated. The nuclei were round to oval and the cytoplasm contained fair amounts of rough endoplasmic reticulum, mitochondria and lysosomes. There were no acinar formation of tumor cells and cytoplasmic zymogen granules (Fig. 6).

DISCUSSION

Pancreatic carcinoma in children can present in one of two basic clinical forms which are less common variants of functioning islet cell carcinoma or nesidioblastoma presenting with symptoms of hypoglycemia and the more common variant of nonfunctioning carcinoma of which the most common type is that of ductal cell origin. As a group, pancreatic carcinomas excluding islet cell tumors have a three year survival rate of approximately 2%, with average survival, following diagnosis, of 4 to 6 months (Beszley et al., 1981). A notable exception to these poor prognoses is a tumor of uncertain histogenesis which has been reported under various names such as pancreatoblastoma, pancreatic carcinoma of infantile type, or nonfunctioning islet cell tumor. The literature relating to pancreatoblastoma presents a confusing picture, partly because a variety of names has been applied to the same tumor, and partly because several authors have used the term for apparently different neoplasms.

Pancreatoblastoma was first described by Frantz in 1959 (Frantz, 1959). The histologic and ultrastructural findings were defined by Frable et al in 1971 under the name of carcinoma of the pancreas, infantile type (Frable et al., 1971). They emphasized the biphasic pattern of acinar and squamoid cells, and confirmed acinar differentiation ultrastructurally by demonstrating apical microvilli projection into luminal spaces and identifying intracellular zymogen granules. Cooper et al. also demonstrated the biphasic pattern in differentiation by enzyme histochemical techniques to localize the activity of glucose-6-phosphatase, acid phospha-

tase, esterase and esteroprotease (Cooper et al., 1989). Horie et al described morphologic criteria of pancreatoblastoma as infantile carcinoma of the pancreas. They stated it should show "an encapsulated mass, distinct organoid pattern containing globular structures with elongated cells (squamous corpuscles) and acinar cells with zymogen granules" (Horie et al., 1977). Cihak et al. stated histogenesis of the squamoid corpuscle which might originate in totipotential epithelial cells from pancreatic primordia which are precursors of duct cells showing squamous metaplasia (Cihak et al., 1972). Two cases of pancreatoblastoma in children which showed typical histologic features have been reported in Korea (Cho et al., 1980; Jung et al., 1982). The present cases showed the typical histological features described above, the only exception being the encapsulation of the tumor.

As is known from previous reported cases, the short term prognosis for pancreatoblastoma is favorable in resectable tumors but, the long-term prognosis for pancreatoblastoma is as yet not well understood because so few cases have adequate follow-up data (Becher, 1957; Beszley et al., 1981; Buchino et al., 1984; Cubilla et al., 1979; Frantz, 1959; Frable et al., 1971; Horie et al., 1977; Palosaari et al., 1986). We presume that the long term prognosis of our cases would be poor because both of them had either extensive tumor invasion or distant metastasis. In case 1 the tumor extended into the retrogastric spaces and involved the portal vein and superior mesenteric artery. In case 2 tumoral metastatsis to the liver and extensive local tumor invasion were identified during the postoperative follow-up.

The endocrine and exocrine differentiation in the tumor cells of pancreatoblastoma has been decribed by some authors. Benjamin & Wright demonstrated focal positivity with anti-α1-antitrypsin antibodies in two cases of pancreatoblastoma, in both of which zymogen granules were seen by electron microscopy (Benjamin et al., 1980). In 1984, Buchino et al. found positive immunoreactivity of tumor cells with anti-somatostatin antibodies and identified membrane-bound granules such as somatostatin and insulin granules which can be found in ß and α islet cells (Buchino et al., 1984). We could find only acinar differentiation with zymogen granules by ultrastructural examination in case 1. The immunohistochemical staining of tumor cells with anti-insulin, somatostatin and glucagon antibodies exhibited negative immunoreactivity in case 1.

REFERENCES

Becher WF: *Pancreatoduodenectomy for carcinoma of the pancreas in an infant. Ann Surg 145:864-872, 1957.*

Benjamin E, Wright DH: *Adenocarcinoma of the pancreas of childhood: a report of two cases. Histopathology 4:87-104, 1980.*

Beszley RM, Cohn I: *Pancreatic cancer. CA 31:346-358, 1981.*

Buchino JJ, Castello FM, Nagaraj HS: *Pancreatoblastoma. A histochemical and ultrastractural analysis. Cancer 53:963-969, 1984.*

Cho HJ, Joo JE, Lee HS, Ko IH, Baik NH: *Infantile carcinoma of pancreas. Korean J Pathol 14:23-36, 1980.*

Cihak RW, Kawashima T, Steer A: *Adenoacanthoma (adenosquamous carcinoma) of the pancreas. Cancer 29:1133-1140, 1972.*

Cooper JE, Lake BD: *Use of enzyme histochemistry in the diagnosis of pancreatoblastoma. Histopathology 15:407-414, 1989.*

Cubilla AC, Fitzgerald PJ: *Classification of pancreatic cancer (non endocrine). Mayo Clin Proc 54:449-458, 1979.*

Frantz VK: *Tumor the pancreas: In atlas of tumor pathology, section 3, fascicle 27. Wahington DC: Armed Forces institute of pathology, 1959.*

Frable WJ, Still WJS, Kayt S: *Carcinoma of the pancreas, infantile type Cancer 27:667-673, 1971.*

Horie A, Yano Y, Kotoo Y, Miwa A: *Morphogenesis of pancreatoblastoma, infantile carcinoma of the pancreas. Report of two cases. Cancer 39:247-254, 1977.*

Palosaari D, Clayton F, Seaman J: *Pancreatoblastoma in adult. Arch Pathol Lab Med 110:650-652, 1986.*

Jung WH, Park CI, Choi IJ: *Pancreatoblastoma. Korean J Pathol 16:856-859, 1982.*

Taxy JB: *Adenocarcinoma of the pancreas in childhood. Cancer 37:1508-1518, 1976.*