Virchows Archiv A Pathol Anat (1991) 418:179–183

Virchows Archiv A
Pathological Anatomy and Histopathology

Case report

Solid-cystic (papillary-cystic) tumours within and outside the pancreas in men: report of two patients

G. Klöppel[1], R. Maurer[2], E. Hofmann[2], K. Lüthold[3], J. Oscarson[4], N. Forsby[4], I. Ihse[5], O. Ljungberg[6], and P.U. Heitz[7]

[1] Department of Pathology, Academic Hospital Jette, Free University of Brussels, Belgium
[2] Institute of Pathology, Stadtspital Triemli, Zürich Switzerland
[3] Department of Surgery, Kreisspital, Lachen, Switzerland
[4] Departments of Surgery and Pathology, Helsingborg Hospital, Helsingborg, Sweden
[5] Department of Surgery, University Hospital Lund, Sweden
[6] Department of Pathology, Malmö General Hospital, Malmö Sweden
[7] Institute of Pathology, University of Zürich, Zürich Switzerland

Received August 20, 1990 / Received after revision October 18, 1990 / Accepted October 19, 1990

Summary. Solid-cystic (papillary-cystic) tumours (SCT) of the pancreas are distinctive neoplasms with a predilection for young female patients. This is the first detailed report describing the occurrence of SCT in two young male patients. Except for the extrapancreatic occurrence of one of the tumours (in the retroperitoneal region behind the head of the pancreas), all other clinicopathological features were identical to those characterizing the SCT in women. Immunostaining was (at least focally) positive for Lu 5 (broad spectrum keratin marker), vimentin and alpha-1-antitrypsin. The tumours were negative for neuroendocrine markers (except for neuron-specific enolase), pancreatic hormones and enzymes, pancreatic stone protein, carcinoembryonic antigen, CA 19-9 and nuclear oestrogen and progesterone receptors. This report does not support the suggested female sex hormone dependence of SCT.

Key words: Solid-cystic tumour – Pancreas – Hormone dependence

Introduction

The solid-cystic tumour (SCT) (papillary-cystic or solid-papillary neoplasm) is an uncommon but increasingly recognized tumour of the pancreas (Frantz 1959; Klöppel et al. 1981; Oertel et al. 1982; Morohoshi et al. 1986; Lieber et al. 1987; Matsunou and Konishi 1990). At least 100 patients have been reported. The main features of SCT are a peculiar morphology, favourable prognosis, and predilection for women between 10 and 40 years of age. In men, the occurrence of SCT seems to be exceedingly rare. The largest series of SCT (74 patients), published by Oertel et al. (1982), includes a few male patients, but no details were given. The same is true for two male patients in the series of Friedman et al. (1985) and another patient in the series of Choi et al. (1988). We therefore give a detailed account on two SCT occurring in young men. While one of the SCT arose within the pancreas, the second was localized in the retroperitoneal tissue behind the head of the pancreas.

Offprint requests to: G. Klöppel, Dept of Pathology, Academic Hospital Jette, Free University of Brussels, Laarbeeklaan 101, B 1090 Brussels, Belgium

Case reports

Case 1

A 25-year-old male patient had been in good health until June 1987, when he was hit in his upper abdomen. This caused him considerable pain for several days. His general practitioner suspected a rupture or haematoma within his rectus abdominus muscle and prescribed a few days' rest. His pain subsided, but in the following year he experienced repeated episodes of minor pain in his upper abdomen. In August 1988, he again presented with severe upper abdominal pain after a minor blunt trauma to the upper abdomen, and was admitted to the Department of Surgery of Helsingborg Hospital. Clinical examination revealed a slight tenderness in the left epigastrium. Laboratory findings were all normal, except for an elevated serum amylase of 51.7 μkat/l. Ultrasonography and computed tomography (CT) revealed a mass, 10 cm in diameter, with varying echogenicity and irregular septa, probably arising from the tail of the pancreas. At angiography the tumour was found to be sparsely vascularized. A fine-needle biopsy revealed a well-differentiated tumour, with suspicion of adenocarcinoma.

At laparotomy a well-demarcated $13 \times 11 \times 7$ cm large tumour was discovered in the tail and body of the pancreas. It did not infiltrate any adjacent organ, and there were no metastases. Splenectomy and an 80% distal pancreatectomy were performed.

The patient's postoperative course was uneventful. At follow-up 1 and 2 years postoperatively the patient was in excellent condition and at CT there was no sign of recurrence.

Table 1. Immunocytochemical findings in two SCT

Antigen	Species	Antibody Source	Dilution	Positivity
Cytokeratin Lu5	Mouse	Hoffmann-La Roche, Basel, Switzerland	1:20	1
KL1	Mouse	Immunotech, Marseille, France	1:2000	–
CAM 5.2	Mouse	Becton-Dickinson, Mountain View, Calif.	1:10	–
Vimentin	Mouse	Boehringer, Mannheim, FRG	1:20	2
Alpha-1-antitrypsin	Rabbit	Ortho, Neckargemünd, FRG	1:20	1
Neuron-specific enolase	Rabbit	Dako, Glostrup, Denmark	1:5000	1–2
Synaptophysin	Rabbit	Gift of Dr. Jahn, Munich, FRG	1:200	–
Leu7	Mouse	Becton-Dickinson, Mountain View, Calif.	1:3	–
Chromogranin A	Mouse	Enzo, New York, N.Y.	1:1000	–
Insulin	Mouse	Biogenex, Dublin, Calif.	1:5000	–
Glucagon	Rabbit	Milabn Malmö, Sweden	1:2500	–
Somatostatin	Rabbit	Immunonuclear, Stillwater, Michigan	1:2000	–
Pancreatic polypeptide	Rabbit	Gift of Dr. Chance, Indianapolis, Ind.	1:50000	–
Gastrin 17	Rabbit	Paesel, Frankfurt, FRG	1:3000	–
HCG-alpha	Rabbit	Own source	1:5000	–
Pancreatic stone protein	Mouse	Dianova, Hamburg, FRG	1:2000	–
Amylase	Rabbit	Own source	1:2000	–
Lipase	Rabbit	Own source	1:1000	–
Trypsin	Rabbit	Own source	1:2000	–
Chymotrypsin	Rabbit	Own source	1:2000	–
S100	Rabbit	Dako, Glostrup, Denmark	1:2000	–
CEA-BMA130c	Mouse	Behring, Marburg, FRG	1:10	–
CA 19-9	Mouse	Gift of Dr. Kalthoff, Hamburg, FRG	1:2	–
Oestrogen receptor	Rat	Abbott, Wiesbaden, FRG	Kit	–
Progesterone	Rat	Abbott, Wiesbaden, FRG	Kit	–

1, Focal staining; 2, diffuse staining

Case 2

A 25-year-old male patient was seen by his physician for an insurance check-up. Examination revealed a mass in his mid-abdomen. The patient indicated he had noted, but ignored, the presence of this slowly enlarging mass for approximately 2 years. All laboratory investigations were negative. Sonography revealed a retroperitoneal tumour in the upper abdomen. A CT scan confirmed this localization, and, in addition, showed a well demarcated, 7- to 8-cm mass in the vicinity of, but not clearly associated with, the head of the pancreas, the gall bladder, the liver and the upper pole of the right kidney. The diagnosis of a fine needle biopsy was "endocrine tumour". At laparotomy, a tumour was discovered in the retroperitoneum beneath the transverse mesocolon. The lesion was removed easily and showed no clear connection with, or infiltration of, the adjacent organs. There were no metastases. The patient's recovery was uneventful, with the exception of a short postoperative ileus, and he was well and clinically free of tumour 24 months later.

Materials and methods

The surgical specimens from both patients were fixed in 10% buffered formalin and processed for light microscopy. Two-micrometre-thick sections were stained with haematoxylin and eosin. Serial sections were immunostained by the ABC technique with the primary polyclonal antibodies or monoclonal antibodies listed in Table 1. Sections of normal pancreas served as positive controls for antisera to pancreatic hormones and enzymes, and pancreatic endocrine tumours as well as pancreatic ductal adenocarcinomas and breast carcinomas as positive controls for gastrin, human chorionic gonadotrophin-alpha, cytokeratins, carcinoembryonic antigen, and oestrogen/progesterone receptors, respectively.

Results

In case 1, gross examination revealed a circumscribed tumour with a fibrous capsule, separating it sharply from the normal pancreatic tissue. The cut surface showed large cystic areas filled with haemorrhagic and necrotic material, and with brownish edges. Histology of preserved tissue from the tumour periphery revealed an epithelial neoplasm with a solid and focally pseudopapillary architecture. The tumour cells were monomorphous and slightly eosinophilic, occasionally with a clear cytoplasm (Fig. 1). Mitoses were lacking. Adjacent to the preserved tissue there were large areas with haemorrhage, hyalinization and cholesterol granulomas (Fig. 2). The tumour was separated from the adjacent pancreatic tissue by a fibrous capsule that was occasionally infiltrated by tumour cells. The surrounding normal tissue showed no infiltration. The results of the immunocytochemical analysis are listed in Table 1 (Fig. 3).

In case 2, the resected specimen revealed a round encapsulated tumour. The cut surface showed a variegated appearance due to a combination of solid brownish tissue, haemorrhage and pseudocystic degeneration. Histologically and immunocytochemically (see Table 1),

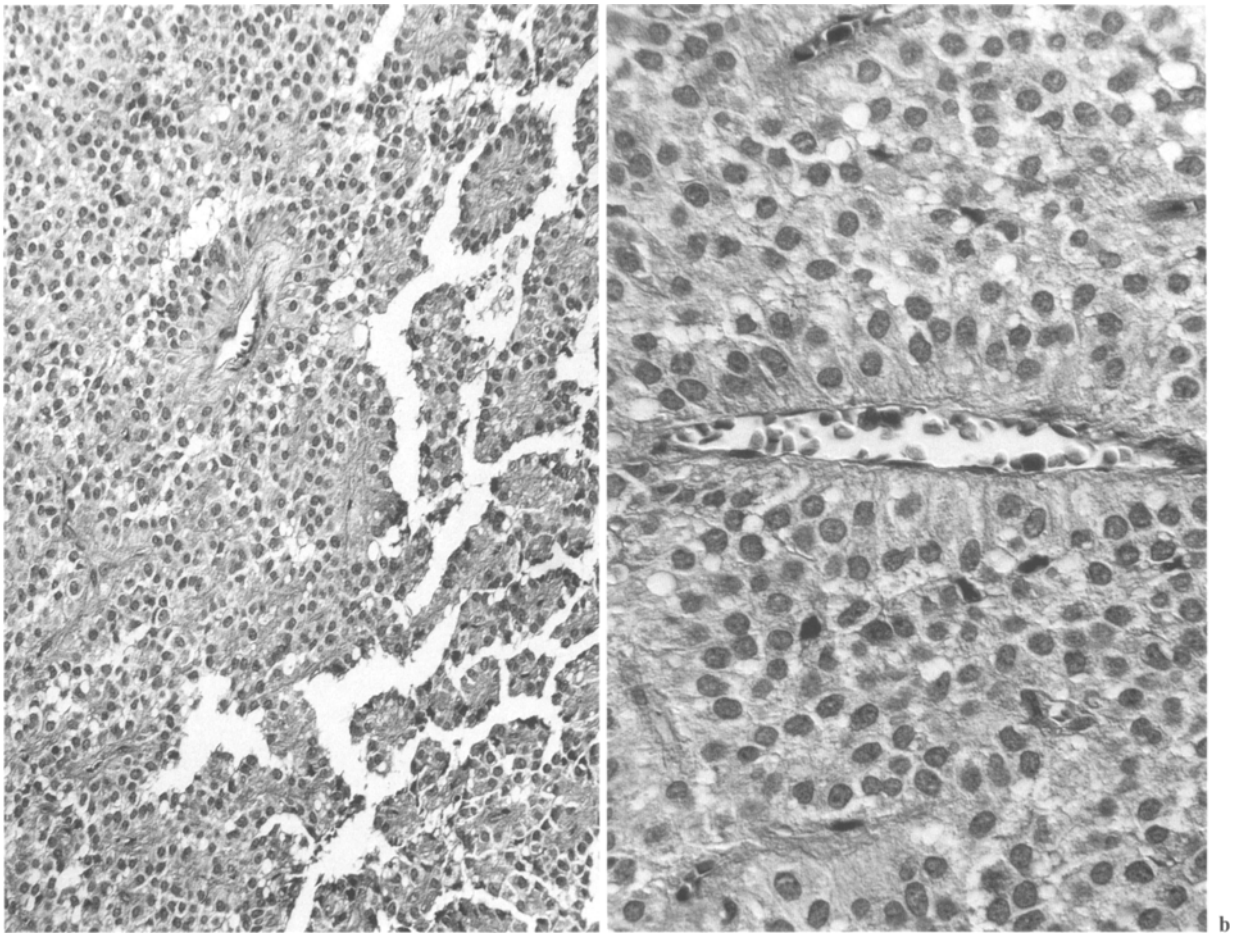


Fig. 1a, b. Solid-cystic tumour of the pancreas. **a** Area with solid and pseudopapillary pattern. H & E, ×125. **b** Rosette-like arrangement of tumour cells around a vessel. Some cells are vacuolated. H & E, ×250

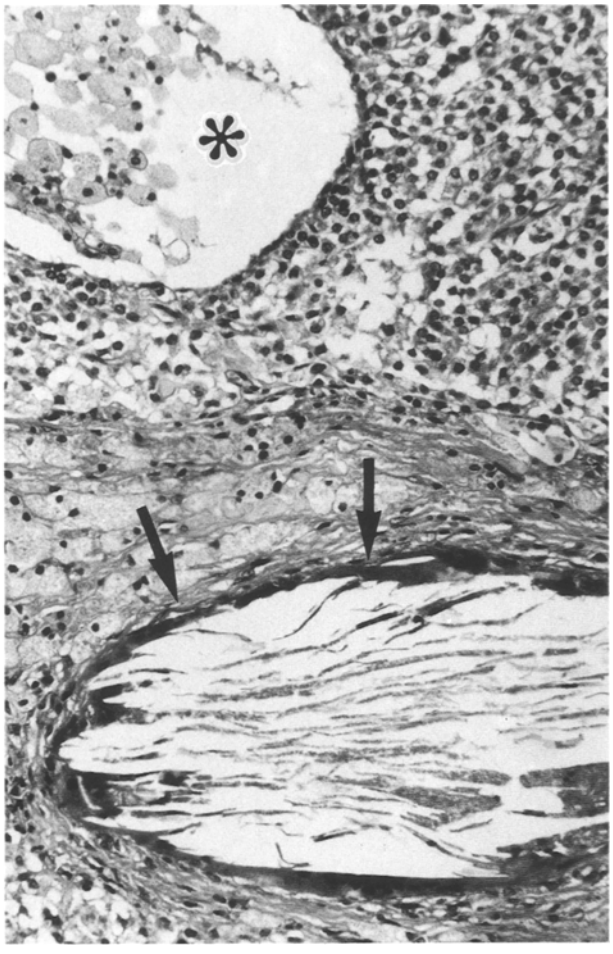
the lesion was similar to that in case 1. The fibrous capsule contained ductular structures, resembling pancreatic ducts.

Discussion

The so-called SCT has so far been described almost exclusively in young women. The two pancreatic tumours reported here exhibited the well-known clinicopathological features of SCT (Klöppel et al. 1981; Oertel et al. 1982; Morohoshi et al. 1987; Lieber et al. 1987), with the exception that they occurred in young men. Another peculiarity was the localization of one of the tumours outside the pancreas.

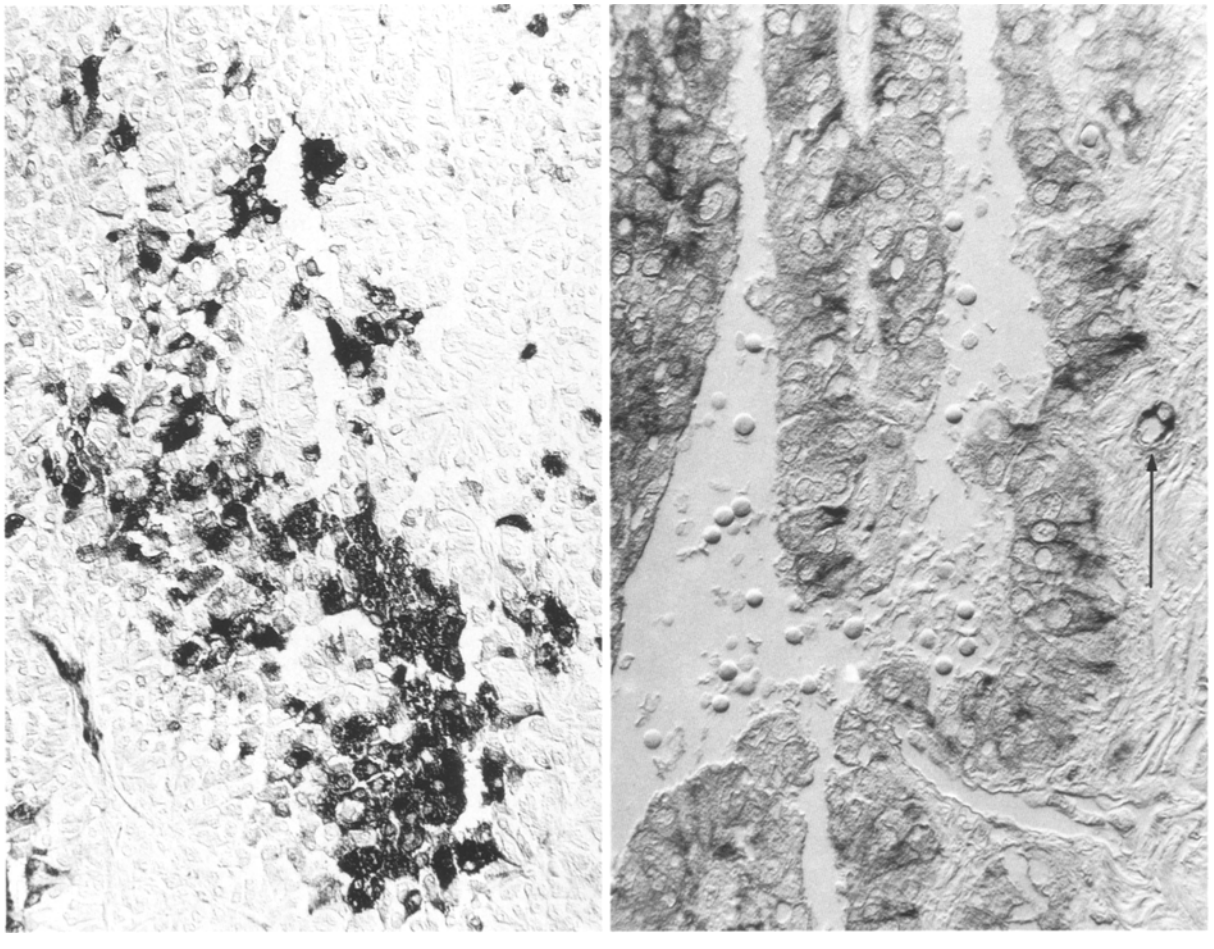
The unique age and sex distribution of SCT suggests that hormonal factors, expecially oestrogen and progesterone, may play a role in the pathogenesis of this neoplasm (Klöppel et al. 1981; Cubilla and Fitzgerald 1984). However, there is no conclusive evidence for this assumption. First, SCT does not exclusively occur in young women but may also arise in young men. The clinical and morphological features of the SCT in male patients, as evidenced by our two cases, are identical to those observed in women. Second, no endocrine diseases and, in particular, no disorders with overproduction of oestrogen or progesterone have yet been reported in women with SCT, nor were they present in our male patients. Moreover, only very few women were found to have an SCT after long-term use of contraceptives or during pregnancy (Sanfey et al. 1983; Cubilla and Fitzgerald 1984; Duff and Greene 1985). Third, oestrogen and/or progesterone receptors have been demonstrated by biochemical methods in four SCT (Ladanyi et al. 1987; Wrba et al. 1988; Carbone et al. 1989), but the results of these reports differ considerably with respect to receptor concentration and affinity as well as presence or absence of these receptors in normal pancreatic tissue. In addition, all but one study (De Lagausie et al. 1988) failed to detect nuclear oestrogen receptors by immunocytochemistry (Wrba et al. 1988; Miettinen et al. 1987; Carbone et al. 1989). Taken together, there is little evidence for a role of sex female hormones in the pathogenesis of SCT. Other factors that promote the growth of this peculiar tumour and are predominantly present in fertile women have therefore to be considered.

Most SCT are located in the head or the tail of the



2

Fig. 2. Solid-cystic tumour of the pancreas. Tumour tissue with cholesterol granulomas (*arrows*) and microcystic structures with vacuolated cells (*asterisk*). H & E, ×125



3a b

Fig. 3a, b. Solid-cystic tumour of the pancreas. **a** Characteristic pattern of alpha-1-antitrypsin immunostaining. ×125. **b** Immunostaining for vimentin reveals positivity in tumour cells as well as in vascular cells (*arrow*). ×250

pancreas (Kamisawa et al. 1987). In one of our two male patients, the SCT was found posterior to the head of the pancreas in close vicinity to the gall bladder, the left adrenal gland, and the kidney. Recently, a primary tumour of the liver with the features of a solid-cystic tumour of the pancreas has been reported (Kim et al. 1990). Although no pancreatic tissue was found near this tumour, origin from ectopic pancreas in the liver was discussed. As the extrapancreatic SCT seen in our patient showed some ductal structures in its fibrous capsule resembling pancreatic ducts, it is possible that this tumour originated from ectopic pancreatic tissue.

Immunocytochemical and electron microscopical results have thus far been inconclusive with regard to the cellular phenotype of SCT. Thus, support has been provided for ductular cell origin (Schlosnagle and Campbell 1981; Oertel et al. 1982; Lieber et al. 1987), acinar cell origin (Bombi et al. 1984) or pluripotential primordial cell origin (Miettinen et al. 1987; Matsunou and Konishi 1990). Our results do not clarify this issue further. They only confirm that SCT is characterized by a focal positivity for alpha-1-antitrypsin, accompanied by positive reactions for neuron-specific erolase (Chott et al. 1987), vimentin (Miettinen et al. 1987) and the broad spectrum keratin marker Lu-5 (Heitz et al. 1989). As in most other reported cases, our tumours were negative for keratin markers KL 1 and CAM 5.2, the neuroendocrine markers chromagranin A, Leu 7 and synaptophysin and also for the pancreatic hormones.

The long-term prognosis of SCT appears to be very good. Simple enucleation or resection of this tumour proved to be sufficient in the majority of patients. Recurrence or metastasis have been reported in a few patients (for review, see Cappellari et al. 1990), but even in these instances long-term prognosis seems to be favourable (for review, see Matsunou and Konishi 1990).

In conclusion, this report demonstrates that young men may develop SCT identical in morphology and biology to those seen in women.

Acknowledgments. The skillful technical help of Mrs. N. Buelens is gratefully acknowledged. We thank Mrs. V. Olmanst and H. Lox for secretarial work.

Addendum

Since this manuscript was submitted, another case report of an extrapancretic SCT has been published [Ishikawa et al. (1990) Am J Gastroenterol 85:597–601]. This tumour arose from an ectopic pancreas in the mesocolon.

References

Bombi JA, Milla A, Badal JM, Piulachs J, Estape J, Cardesa A (1984) Papillary-cystic neoplasm of the pancreas: report of two cases and review of the literature. Cancer 54:780–784

Cappellari JO, Geisinger KR, Albertson DA, Wolfman NT, Kute TE (1990) Malignant papillary cystic tumor of the pancreas. Cancer 66:193–198

Carbone A, Ranelletti FO, Rinell A, Vecchio FM, Lauriola L, Piantelli M, Capelli A (1989) Papillary cystic tumor of pancreas: a sex hormone-dependent tumor? (abstract) Pathol Res Pract 185:29

Choi BI, Kim KW, Han MC, Kim YI, Kim C-W (1988) Solid and papillary epithelial neoplasms of the pancreas: CT findings. Radiology 166:413–416

Chott A, Klöppel G, Buxbaum P, Heitz PU (1987) Neuron specific enolase demonstration in the diagnosis of a solid-cystic (papillary cystic) tumour of the pancreas. Virchows Arch [A] 410:397–402

Cubilla AL, Fitzgerald PJ (1984) Tumors of the exocrine pancreas. In: Hartmann WH (ed) Atlas of tumor pathology, 2nd series, fascicle 19. Armed Forces Institute of Pathology, Washington, D.C., pp 201–207

De Lagausie P, Maillet B, Viala T, Sudan N, Monges G (1988) Un cas de tumeur papillaire du pancréas. Gastroenterol Clin Biol 12:965–967

Duff P, Greene VP (1985) Pregnancy complicated by solid-papillary epithelial tumor of the pancreas, pulmonary embolism, and pulmonary embolectomy. Am J Obstet Gynecol 152:80–81

Frantz VK (1959) Tumors of the pancreas. Atlas of tumor pathology, section 7, fascicles 27 and 28. Armed Forces Institute of Pathology, Washington, D.C. pp 32–33

Friedman AC, Lichtenstein JE, Fishman EK, Oertel JE, Dachman AH, Siegelman SS (1985) Solid and papillary epithelial neoplasm of the pancreas. Radiology 154:333–337

Heitz PU, Stolte M, Klöppel G (1989) Large pancreatic tumor in a young woman. Ultrastruct Pathol 13:589–592

Kamisawa T, Fukayama M, Koike M, Tabata I and Okamoto A (1987) So-called "papillary and cystic neoplasm of the pancreas". Acta Pathol Jpn 37:785–794

Kim YI, Kim ST, Lee GK, Choi BI (1990) Papillary cystic tumor of the liver: a case report with ultrastructural observation. Cancer 65:2740–2746

Klöppel G, Morohoshi T, John HD, Oehmichen W, Opitz K, Angelkort A, Lietz H, Rückert K (1981) Solid and cystic acinar cell tumour of the pancreas. A tumour in young women with favourable prognosis. Virchows Arch [A] 392:171–183

Ladanyi M, Mulay S, Arseneau J, Bettez P (1987) Estrogen and progesterone receptor determination in the papillary cystic neoplasm of the pancreas. With immunohistochemical and ultrastructural observations. Cancer 60:1604–1611

Lieber MR, Lack EE, Roberts JR, Merino MJ, Patterson K, Restrepo C, Solomon D, Chandra R, Triche TJ (1987) Solid and papillary epithelial neoplasm of the pancreas. An ultrastructural and immunocytochemical study of six cases. Am J Surg Pathol 11:85–93

Matsunou H, Konishi F (1990) Papillary-cystic neoplasm of the pancreas: a clinicopathologic study concerning the tumor aging and malignancy of nine cases. Cancer 65:283–291

Miettinen M, Partanen S, Fräki O, Kivilaakso E (1987) Papillary cystic tumor of the pancreas. An analysis of cellular differentiation by electron microscopy and immunohistochemistry. Am J Surg Pathol 11:855–865

Morohoshi T, Kanda M, Horie A, Chott A, Dreyer T, Klöppel G, Heitz PU (1987) Immunocytochemical markers of uncommon pancreatic tumors. Cancer 59:739–747

Oertel JE, Mendelsohn G, Compagno J (1982) Solid and papillary epithelial neoplasms of the pancreas. In: Humphrey GB, Grindey GB, Dehner LP, Acton RT, Pysher TJ (eds) Pancreatic tumors in children. Martinus Nijhoff, Den Haag, pp 167–171

Sanfey H, Mendelsohn G, Cameron JL (1983) Solid and papillary neoplasm of the pancreas: a potentially curable surgical lesion. Ann Surg 197:272–275

Schlosnagle DC, Campbell WG (1981) The papillary and solid neoplasm of the pancreas: a report of two cases with electron microscopy, one containing neurosecretory granules. Cancer 47:2603–2610

Wrba F, Chott A, Ludvik B, Schratter M, Spona J, Reiner A, Schernthaner G, Krisch K (1988) Solid and cystic tumour of the pancreas: a hormonal-dependent neoplasm? Histopathology 12:338–340