IMAGES IN CLINICAL MEDICINE

Solid Pseudopapillary Pancreatic Tumor - Tumor of Frantz

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ABSTRACT

The solid cystic pseudopapillary tumour, known also as the tumour of Frantz, is a rare primary neoplasm of the pancreas with unknown etiology, occurring predominantly in young females. It is characterized by a paucity of clinical symptomatology and can reach large sizes before final diagnosis. Degenerative cystic changes and haemorrhagic areas are typical, and the most common clinical manifestation is a cystic pancreatic tumour, palpable mass and uncharacteristic abdominal pain. Although resection of the tumour provides a 5-year survival rate of almost 90%, local recurrence or distant metastases can occur in a significant number of patients. Patients with solid pseudopapillary cystic tumours have a much better prognosis, therefore it is important to distinguish it from other pancreatic neoplasms.
Key words: solid pseudopapillary pancreatic tumour, tumour of Frantz; pancreatic resection, immunohistochemistry, prognosis

INTRODUCTION

The solid pseudopapillary tumour (SPT) is a rare pathological entity of the pancreas (accounting for 1 – 2% of primary tumors), characterized by a low malignant potential and still uncertain cellular origin. It is most commonly found in young females. This type of tumour was first described by Frantz in 1959, when he reported three cases. Although SPT is classified as an epithelial pancreatic tumuor, in many of the cases cytokeratin production is not observed, but neuroendocrine differentiation is characteristic.

'Tumours of Frantz', 'solid cystic tumor', 'papillary and solid epithelial neoplasms', are some of the other designations given to SPT. The term SPPT (solid pseudopapillary pancreatic tumour) was introduced in 1996 by the WHO for the International classification of tumours of the exocrine pancreas. Despite the increasing recognition of this tumour during the last two decades, its pathogenesis and apparent therapeutic algorithm still remain uncertain.

CLINICAL CASES

Case 1.

A 25-year old female patient was admitted in our Clinic with a

presumed diagnosis of neuroendocrine tumor of the pancreas. The clinical signs symptoms at admission had been present for 3 months and consisted of pain in the upper quadrants of the abdomen, with consistent irradiation in the back, discrete swelling of the face and hands, multiple episodes of subfever (37.6°C), and hyperhidrosis.

Imaging studies (US and CT scan - *fig. 1*) revealed a well-encapsulated hypodense formation in the neck of the pancreas, with varying solid and cystic components owing to haemorrhagic degeneration, with a diameter of 67/60/45 mm. Following contrast administration, enhanced solid areas (with a density of about 50 XE) are typically noted peripherally, whereas cystic spaces (density XE 18-20) are more centrally located. Slightly extended d. Wirsungianus. FNA /performed under CT control/ - data suggestive for neuroendocrine tumour of the pancreas.

Intraoperatively, an oval tumour was noted, with a diameter of 8.5 / 6 / 4.5 cm. At macroscopic examination of the specimen, the cut surface appeared motley (gaily-coloured), with whitish, yellowish areas and bleeding. A radical resection of the midportion of the pancreas, including the tumour (*fig. 2* – operative specimen), was performed. The right resection margin was approximately 1 cm from the duodenum, while to the left a 4.5 – 5.0 cm long stump of the pancreatic tail was left. A stented pancreato-gastric anastomosis was performed. There were no postoperative complications and the patient was discharged. She is symptom and recurrence free 44 months after the operation.

Case 2.

A 31 year-old woman who had presented for slight upper abdominal discomfort was admitted with an intra-abdominal mass, located in the body of the pancreas. She was afebrile, with a normal pulse and blood pressure. No history of hepato-biliary or pancreatic disease or other malignancy in her family was noted. There was mild upper/left abdominal tenderness on palpation. Abdominal US (*fig. 3*) and CT scan showed a well-defined encapsulated heterogeneous mass, located in the head/body of the pancreas.

Intraoperatively, a rounded 6/5 cm tumour was noted. A radical resection of the mid portion of the pancreas was performed, with a pancreato-gastric anastomosis. The patient is symptom free 38 months after the procedure.

The histopathological examination of the operative specimens revealed an encapsulated tumour, made up of solid areas, surrounding vessels and connective
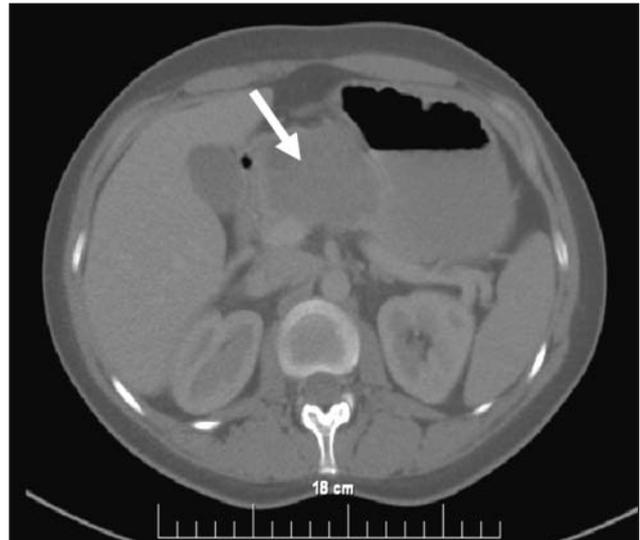

Figure 1 – D.V. 25 years CT scan - Tu mass in pancreas

Figure 2 – Postoperative specimen – heterogeneous appearance – solid, cystic and haemorrhagic areas

Figure 3 – P.N. 31 years US – Tu mass in pancreas

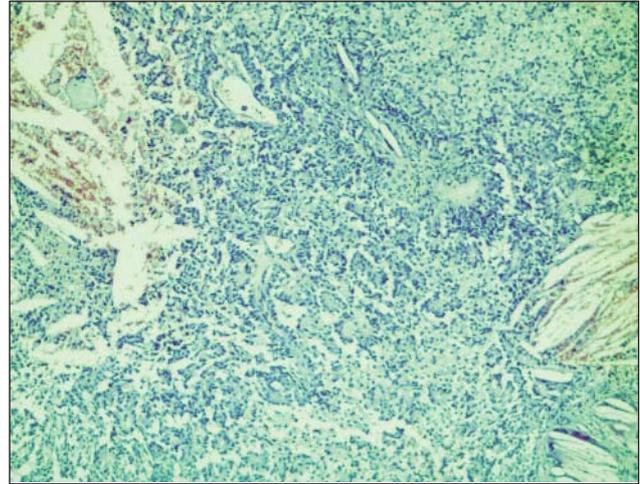**Figure 4 – Pseudopapillary tumour of the pancreas**

Figure 5 – Pseudopapillary structures

tissue, with disorganization and pseudocystic transformation (*fig. 4*), forming pseudopapillary structures (*fig. 5*) of medium-sized polygonal, rounded and elongated cells with oval nuclei. Some of the cells had a bright peripheral cytoplasm and nucleus. Microscopic examination found clusters of macrophages, large deposits of cholesterol and giant cell granulomatous reaction and calcification. In the periphery of the expansion unit there was a 3-cm sharply distinct nodule with a homogeneous structure and strands of small trabecules, a monotonous appearance of endocrine cells, thin-walled vessels and soft fibrous strands. IHH typing revealed weak expression of Chromogranin, mainly in the nodule, expression of S-100 in antigen presenting cells, as well as weak expression of Pancytokeratin mainly in the neuroendocrine component. There was also diffuse expression of Vimentin (*fig. 6*), nuclear expression of Progesterone (*fig. 7*) and low (under 10%), Ki nuclear activity.

Case 3.

A 46-year-old woman was admitted with complaints of pain in her upper abdomen, nausea and vomiting. She had a history of hypothyroidism, ischaemic heart disease, hysterectomy and bilateral adnexectomy for ovarian cancer over 8 years previously. The physical examination was unremarkable bar pain in the right upper quadrants at deep palpation.

The abdominal ultrasound and CT imaging revealed a body-tail tumour with an approximate size of 50/30 mm with hyperehogenic content, which exerted a mass effect on the pancreatic duct. The latter was dilated to a diameter of c. 4 mm. Intraoperative – findings
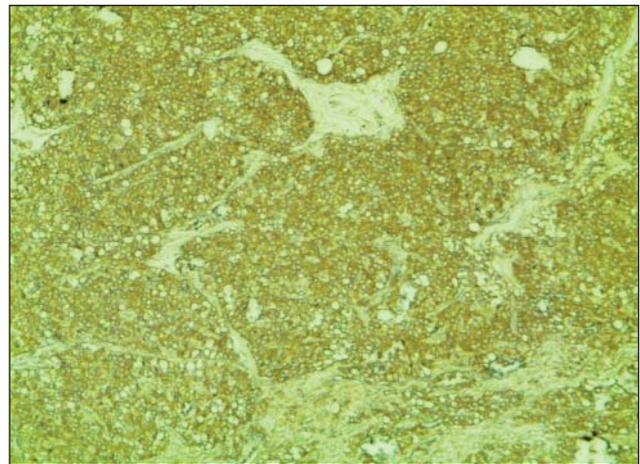

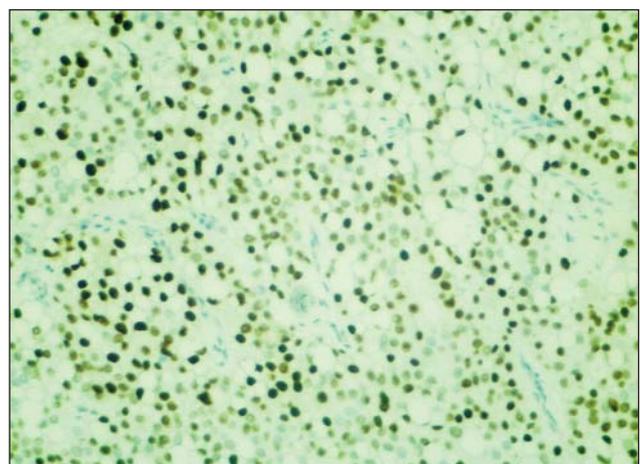**Figure 6 – Expression of Vimentin in SPTT**

Figure 7 – Progesterone expression in SPTT

consisted of increased pancreatic dimensions, with a cystic lesion in the body area and peripancreatic

inflammatory collection (abscess), with necrotic areas. Microbiological examination isolated Staphylococcus haemolyticus. A resection of the altered part of the pancreas was performed. There were no complaints 3 months after the operation.

DISCUSSION

Primary tumours of the exocrine pancreas are extremely rare in children. Warthin (1952) described an embryonic carcinoma in a 15 year-old boy, and later 8 more cases of cancer and two cases of lymphosarcoma of the pancreas in children. Frable described a specific type of pancreatic cancer in the young, which he called "papillary carcinoma of the childrens' pancreas."

SPPT was established by Frantz in 1959, when he described three patients with this disease and recognized the special characteristics of the tumour. More than 700 cases described in the English medical literature, were from Europe, USA and Japan (reviewed by Papavramidis et al.), while 550 cases were reported in Chinese literature (Peng-Fei Yu et al.). Hamoudi (1970) and Kloppel (1981) suggested its differentiation as a separate tumour. SPT accounts for 1 to 2% of all exocrine pancreatic tumours.

Clinical presentation of the tumor is usually non-specific, consisting of upper abdominal discomfort with uncharacteristic vague abdominal pain. SPPT can also be completely asymptomatic. The tumour can be found in any part of the pancreas, but is most commonly located in the body and tail. Obstructive jaundice is extremely rare, even if the tumour is located in the head of the pancreas. It is most commonly found in young females (especially between 20 and 30 years of age), and less frequently in older women or males. They are usually slow-growing and with an indolent course. A gradually enlarging palpable abdominal mass is one of the main clinical symptoms. In most cases this type of tumor is found after trauma caused bleeding from the tumor mass and/or abdominal discomfort. Acute manifestations are rare but should be kept in mind.

SPPTs are usually well-demarcated tumours, with a diameter ranging from 1.5 to 30 cm (average 10 cm). In our cases sizes were: 8.5 / 6.0 / 4.2 cm, 5.0/6.0 cm. and 5.0/3.0 cm, respectively (*fig. 1, 2, 3, 8*).

The tumour is soft, yellow-red in colour and contains solid and cystic areas. Areas of haemorrhage, cystic degeneration and irregular cystic walls can be observed. Microscopically, cells are characterized by the same polygonal shape, with eosinophilic and vacuolar cytoplasm, around an often grooved ovoid nucleus which contains a nucleolus and dispersed chromatin. The nuclei are round or wrinkled, sometimes enlarged and irregular. The stroma is vascularized with areas of bleeding hyalin aggregates of foamy histiocytes, cholesterol clefts, foreign body giant cells and haemorrhage. The most characteristic feature is the presence of pseudopapillary structures (*fig. 5*), covered by several layers of epithelial cells with pale eosinophilic cytoplasm and absence of glycogen and mucin. Pseudopapillary structures are formed by the disintegration of tumour cells in pseudocystic cavities. Quite often PAS - positive spherical cytoplasmic inclusions are found. Mitotic index and Ki67 are usually low, emphasizing the low malignancy rate of the tumour. Electron-microscopic appearance is characterised by signs of glandular, tubular and endocrine structures. The most striking ultrastructural feature is the presence of focally abundant, variably sized electron-dense granules. Another commonly documented feature is the presence of cytoplasmatic annulated lamellae.

The diagnosis of this type of neoplasm can be easily established by US- or CT-guided FNA biopsy. If the biopsy material is obtained in this manner, the cytological diagnosis is often difficult in terms of differential diagnosis with pancreatic neuroendocrine tumors (as it was the case in our patients).

The origin of SPPT is still unknown and remains enigmatic. Most scientists believe it originates from multipotent primary stem cells. The immuno-histochemical profile of SPT is not similar to any of the pancreatic cells'. Vimentin expression is common - > 90% (*fig. 6*), suggesting that SPT might have a mes-

Figure 7 – Gross appearance of postoperative specimen – solid and haemorrhagic areas

enchymal origin, rather than being epithelial tumours of the pancreas. The expression of α1-antitrypsin, which is characteristic for pancreatic adenocarcinomas and NETs), is weak and nonspecific. Cytokeratin expression varies in different studies from 30% to 60%, making the assignment of SPPT epithelial tumours difficult. Increased activity of neuron specific enolase (NSE), the absence of hormone synthesis, as well the lack of any endocrine dysfunction whatsoever indicates that SPT cannot be defined as NET, although there is typical neuroendocrine differentiation. There is also an increased reactivity of specific markers for epithelial ductal carcinomas as CA 19-9 and CEA were not found in those patients. The results suggest that SPPT cannot be attributed to epithelial ductal carcinomas. It is assumed that during embryogenesis, nervous system forming cells come into contact with the pancreas and produce a new line of differentiation, leading to speculation that SPPT is derived from these cells.

Although the capsular, vascular and nervous invasion, as well as nuclear polymorphism and the presence of mitotic activity all suggest aggressive behaviour of the tumour, it is sometimes difficult to assign histopathological criteria suggesting malignant potential to SPPT. Nishihara et al. reported that venous invasion, diffuse growth pattern, extensive tumor necrosis, significant nuclear atypia and high mitotic rate are indicative of aggressive behaviour. Metastases are described in about 12-15% of the cases, occurring in the liver and peritoneum. Liver metastases occur in 7% - 9% of cases. The lungs and skin may also be affected by metastases. The recurrence rate is 2% to 6%, and is usually due to infiltration into adjacent organs and structures. Even in cases of metastases there is a long survival rate.

The curative treatment of SPPT is surgical: distal pancreatectomy (with or without splenic preservation), pancreaticoduodenectomy, local resection or enucleation are the most common procedures. Extensive lymphatic dissection is not indicated in most of the cases. For the metastases there is also general consensus that surgical debulking could be performed (in contrast to pancreatic cancer). Laparoscopic surgery seems to be a feasible option, especially in patients with distal location and small size of the tumour. In our patients we performed middle pancreatic resections with pancreato-gastric anastomosis. Local invasion, limited metastases or recurrence of the disease are not contraindications for resectional surgery.

Overall prognosis is good, even after limited resections, because of the tumour's indolent growth. Even in the presence of disseminated disease, the clinical course is usually protracted and overall 5-year survival rate is more than 65%.

Since a good prognosis is expected in patients with SPT, it is very important to differentiate between ductal adenocarcinoma and NETs. Typical macro-and microscopic features make this differential diagnosis quite easy. Ductal carcinoma (composed of tubules and gland structures) is more common in older men and is usually much smaller than SPPT. Neuroendocrine tumours usually present as a solid mass, and complications such as bleeding and pseudocysts are not typical. Microscopic nuclei are small, round, with smooth contours.

CONCLUSIONS

Solid pseudopapillary tumour of the pancreas is a rare primary neoplasm with unknown etiology, occurring most commonly in young females. It is characterized by a paucity of clinical symptomatology, and can reach large dimensions before final diagnosis. SPPT has a good prognosis, but potentially aggressive character. It is radically curable with surgery, easily distinguished from other tumours with similar location because of its characteristic clinical and histopathological features. Clinical experience with this disease published in the literature supports the concept that despite the large size and the tendency to local invasion, radical surgical resection offers the chance of cure and is beneficial in almost all of the patients. Even SPPT patients with metastatic disease can expect survivals ranging between 6 months and 15 years. The role of chemotherapy, radiotherapy, TAE, TACE, and radiofrequency in the multimodal treatment of this disease is still under scrutiny.

Conflict of interest

All author declare that they have no conflict of interest.

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