Solid Pseudopapillary Neoplasm of the Pancreas: Report of a Case after a 10-Year Follow-Up and Review of the Literature

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Abstract
A solid pseudopapillary neoplasm (SPN) is an extremely rare tumour of the pancreas that frequently occurs in young females and is mostly benign. SPN is a low-grade malignant tumour that may evolve years before symptoms start. However, the pathogenesis of this tumour remains unclear and there are no adequate reports of long-term results to evaluate the management and the long-term surgical control. We describe a new case of SPN with a 10-year follow-up, and review the world literature that accounts for approximately 322 cases. Moreover, a review of the current management and surgical tendencies in the treatment of SPN is considered. An SPN pancreatic tumour occurred in a 24-year-old female who complained of episodic mild abdominal pain sustained by a palpable epigastric mass. The tumour mass was detected by ultrasound and computer tomography and was localised at the tail of the pancreas adherent to the spleen. The preoperative diagnosis was uncertain and en-block distal pancreatectomy and splenectomy were performed. The size of the mass which weighed 300 g was 11 × 12 × 8 cm, and the tumour was strictly adherent and invaded the splenic hilum. Histologic examination confirmed a complete resection of the primary SPN that locally invaded spleen. The postoperative period was uneventful and after a 10-year follow-up the patient is free of symptoms. SPN should be considered in the differential diagnosis of large pancreatic masses, especially in young females. Radical resection, where technically feasible, should be considered the therapy of choice as it is a safe and effective control of the disease.

Introduction
Solid pseudopapillary neoplasm (SPN) is an unusual pancreatic tumour that mostly affects young females as a large asymptomatic epigastric mass. Since the original description by Frantz [1] in 1959, approximately 322 cases have been reported in the literature [2–16]. SPNs are generally to be considered as neoplasia with a low-malignant potential, although they are usually benign even in the rare case with metastases. They occur predominantly in young women in their second or third decade of the life. SPN is a low-grade malignant tumour that may evolve years before symptoms start. However, the patho-
genesis of this tumour remains unclear and there are not enough reports to evaluate the long-term results of these young patients after surgical management.

Among the 322 cases reported to date in the world literature, 41 cases (12.7%) were recognised as malignant with invasion of adjacent organs or metastases [17–40]. There was a recurrence rate of 11.6% (in 5 cases), and in 24.4% (10 cases) the tumour was partially resected or was unrectectable. Only for 17 patients (5.3%) are there reports of 5-year follow-ups after surgical treatment: 8 were alive without disease, 5 were alive with disease, and 2 died of the disease [17–26]. Four patients with a follow-up of <5 years were alive with the tumour [27–29]. One patient died of the disease within the first 5 years after operation [21], and 2 patients with tumour died of unrelated causes [18]. In this article we report a new case of SPN with a 10-year follow-up and review the literature, discussing the current surgical management in the treatment of SPN and whether surgical therapy is the optimal and definitive therapy to achieve the best long-term prognosis. Furthermore, we review the world literature to evaluate the surgical control, the long-term results, the potential malignancy and recurrence rate of the tumour.

Case Report

A 24-year-old female was admitted to the University Hospital of Herakleion, Crete, Greece, 10 years ago. The patient complained of episodic epigastric abdominal pain associated with episodes of nausea and vomiting and a history of dyspepsia, fatigue and weight loss of approximately 2 kg in the previous 3 months. Imaging investigations including ultrasonography and computer tomography scan (CT) and laboratory analyses were performed. An unclear cystic mass in the tail of the pancreas was detected which was strictly adherent to the splenic hilum. Surgery consisted of distal pancreatectomy with splenectomy.

On admission the patient had a flat non-tender abdomen with a palpable mass. Ultrasonography and CT showed a large predominantly cystic abdominal mass in the tail of pancreas which was strictly adherent to the hilum of the spleen (fig. 1a). Laboratory analysis including haematological and hepatic tests and oncomarkers (CEA, αFP, Ca19-9) were in the normal range, and oestrogen receptors of the tumour were negative. Laparotomy was performed and a large tumour mass originating from the body and tail of the pancreas and adhering strictly to the splenic vessels and hilum was found (fig. 1b).

Because of the unclear diagnosis and the young age of the patient, en-block distal pancreatectomy and splenectomy with complete resection of the primary tumour were performed. The tumour size was 11 × 12 × 8 cm and the weight was 300 g (fig. 1b). The histological examinations showed a solid papillary neoplasm of the pancreas with invasion of the spleen. The tumour was circumscribed with a thick fibrous capsule and had macroscopically detectable solid and cystic components, as well as areas of haemorrhage and necrosis. The solid tumour areas showed sheets and cords of cells arranged around delicate fibrovascular septa, but in non-cohesive areas the creation of spaces between cells resulted in a rare papillary pattern (fig. 2). Trabecular patterns with hyalised collagen surrounding blood vessels were common. The central part showed evidence of marked degenerative changes with cyst formation, haemorrhage, and foamy macrophages. Severe degrees of nuclear atypia and pleomorphism were uncommon, and mitotic figures were rare (fig. 2). The capsule was often incomplete, however, overt capsular invasion was demonstrated only toward the spleen and vascular invasion by tumour cells.
was not seen. There were no postoperative complications. The patient was strictly followed up with clinical examinations, imaging investigations and laboratory analyses every 6 months for the first 5 years, thereafter once a year. After the 10-year follow-up the patient is free of symptoms.

Discussion

Pancreatic tumours show great diversity and many morphologic varieties have been described. SPNs of the pancreas are rare, accounting for only 0.17–2.7% of all non-endocrine tumours of the pancreas [41, 42]. SPN was first described by Frantz [1] in 1959, but has received greater recognition during the past 2 decades following the report of Hamoudi et al. [43] in 1970. A recent review identified a total of 292 cases published to date [2]. Thereafter, along with the current report, another 30 cases have been described [3–16]. Because of the macroscopic and histological features, SPN has been called a solid and papillary epithelial neoplasm, a solid and cystic tumour papillary epithelial neoplasm and a papillary epithelial tumour [44]. Some authors believe that the tumour is not rare but frequently misdiagnosed [23]. Pathologic examination requires differentiation from an islet cell tumour, cystadenoma, cystadenocarcinoma, acinar cell tumour, pancreaticoblastoma, and adenocarcinoma of the pancreas [45].

Here we report the case of a young female in keeping with the literature with the peak incidence during the second and third decade of life. The clinical presentation is usually a mildly symptomatic upper abdominal mass with symptoms from the upper gastrointestinal system such as nausea, vomiting and dyspepsia; however, cases of patients who complained of severe abdominal pain have been described [46].

Haematologic laboratory investigations provided little additional information in our patient, although hyperamylasaemia, elevated hepatic enzymes, and leukocytosis have been described [45, 47]. Radiologic studies are important in the preoperative evaluation. Abdominal roentgenograms may demonstrate displacement of the stomach, colon, or spleen by an extrinsic mass [32]. Calcification within the large mass is seldom encountered. When present, however, calcifications are peripheral and curvilinear, as compared with the sunburst pattern described in microcystic adenomas [48]. SPNs appear on CT and ultrasonographic imaging as well-circumscribed lesions, but of variable internal architecture. They are most commonly of mixed cystic and solid components, but may be almost entirely solid or else cystic with thick walls. The cystic areas may represent haemorrhage or necrosis [49]. CT is an accurate means of assessing not only the primary mass but also the status of the liver. The main features on magnetic resonance imaging are a well-demarcated rim enclosing a multiloculated mass and the presence of internal structures consistent with tumour nodules [50]. Selective visceral angiography has been reported to be helpful in cases with hepatic metastases, where resection is being considered, or for evaluation of the portal vein with large lesions in the pancreatic head and neck [33]. Improved imaging with contrast enhancement has made CT angiography obsolete. Endoscopic retrograde cholangiopancreatography (ERCP) evaluation has been reported to be helpful for evident displacement of the pancreatic duct, without duct invasion or leak. It
may be helpful to differentiate SPN from invasive neoplasms showing duct obstruction and from pseudocysts with duct disruption or features of chronic pancreatitis. Warshaw et al. [51] described similar findings of either a normal pancreatic duct or non-specific bowing of the duct around the mass on ERCP in most cases. The differential diagnosis of SPN is varied, including congenital pancreatic cysts, pseudocysts, parasitic hydatid disease, and other more common cystic neoplasms of the pancreas, such as serous cystadenoma or carcinoma, mucinous neoplasms, cystic islet cell tumours, or mucinous duct ectasia [51]. In fact, our patient was also originally misdiagnosed as probably having a hydatid cyst and only during surgery was the correct diagnosis made. There are reports of cases managed by cystogastrostomy for a misdiagnosed pancreatic cyst [46]. During laparotomy, the unusual papillary architecture of the tumour and the spleen invasion forced us to perform a radical resection of the tumour en bloc with the invaded spleen. Biopsy of the cyst wall confirmed the correct diagnosis and the tumour was totally excised.

A preoperative diagnosis of SPN can be made by fine-needle aspiration (FNA) cytology. Bondeson et al. [52] first described a preoperative FNA cytological diagnosis under ultrasound guidance, and other authors have confirmed their findings [44, 53, 54]. Smears show highly cellular patterns, with many branching delicate papillary fronds composed of central fibrovascular stalks covered by a single or several layers of tumour cells [44]. We have not used preoperative FNA cytology because of the potential risk of the supposed hydatid cyst spillage, and it is a contradiction that could compromise surgical cure.

SPN occurs with an equal distribution between the tail, body and head with prevalence in the body-tail of the pancreas [2, 55] as in our case. Development of the tumour in ectopic sites of pancreatic tissue has also been described in the mesocolon [56], retroperitoneum [57] and liver parenchyma [58]. A multicentric neoplasm presenting with two distinct masses within the pancreas has been reported [59]. 86.7% of the patients presented with the disease limited to the pancreas, 6.2% with local peripancreatic infiltration or recurrence and 5.8% develop distant metastases [60]. Complications due to SPN are rare and usually reflect local compression of the surrounding structures rather than invasion. Reports highlight obstructive jaundice [9], invasion or compression of the portal vein [17, 20], other vessels [18, 34] and invasion of the duodenum [17, 20], stomach [29] or spleen [20, 30, 31] as in our case. Rupture of the tumour occurred in 2.3% of the reported cases. These included 1 traumatic rupture, 2 caused by malignancy [27, 28], and 5 without cause, an unusual spontaneous rupture that may have been caused by the haemorrhagic nature of the tumour [18, 23, 40, 61–62].

Surgical management has been tailored to the slow-growing non-invasive nature of the lesion. However, long-term reports in the literature on young patients affected by SPN do not contribute very much to the evaluation of the recurrence rate and the potential curability of the tumour after surgery [17–26]. Standard therapy involves complete removal of the tumour, the involved pancreas and any adjacent organs [45, 32, 34]. Local invasion, recurrence, or limited metastases should not be considered as contraindications to resection. Portal vein resection has also been advocated when there is evidence of tumour invasion [33]. With tumour involvement of the head of the pancreas, a pylorus-preserving pancreaticoduodenectomy was performed by some authors to avoid the dumping and diarrhoea associated with gastrectomy [46, 63]. Central pancreatectomy and re-implantation of the pancreatic remnant into the stomach, with the theoretical benefit of preserving the pancreatic parenchyma and spleen after SPN resection involving the neck or body of the pancreas, have been described [46]. We agree with other authors in recommending splenic conservation following distal pancreatectomy when possible and when there is no tumour splenic invasion, without compromising radical resection. However, when technically feasible, we recommend radical tumour excision without formal pancreatic resection, which may be a viable alternative to more extensive surgery and has not been associated with recurrence in different reports [46, 61]. The lesser procedure avoids the need for a pancreaticoduodenectomy, which may be technically demanding when the bile duct is small and the pancreatic remnant is soft with a small duct. Moreover, because of the potential low-grade malignancy of the tumour, radical tumoural excision should always be performed and the patient should be strictly followed up in case of a recurrence which should be promptly controlled. Little experience has accrued with non-surgical modalities of treatment. Matsuda et al. [25] reported a patient with multiple hepatic metastases who responded to chemoembolisation of the tumour. Fried et al. [35] observed substantial shrinkage of an unresectable tumour after 6 weeks of radiotherapy. The role of chemotherapy, radiotherapy, or embolisation has not been well established [2].

SPN is an indolent pancreatic tumour with low malignant potential. Attempts to define features predictive of aggressive behaviour have been unsuccessful [64]. Tumours occurring in older patients are more likely to
behave aggressively [21], but histologic features such as solid or infiltrating growth [65] and DNA aneuploidy [66] have not reliably predicted the malignant potential. No difference in the histologic appearance of the tumours with liver metastases has been found [46]. It is not clear why SPN occurs almost exclusively in women, most notably in the reproductive age. The obvious search for hormonal dependence has not shown conclusive results. In the past SPN may have been incorrectly diagnosed as a more aggressive type of pancreatic neoplasm. This may explain cases with a long survival after resection for apparent adenocarcinoma [20]. Based on immunocytochemical data, Kosmahl et al. [67] argued that, although SPN is a neoplasm with a complex immune profile, it is found to be related to the genital ridge/ovarian anlage cells which are attached during early embryogenesis to the pancreatic tissue. SPN should be considered in the differential diagnosis of large pancreatic masses, especially in young females. The clinical presentation and pathology of our patient suggest that the lesion is capable of local invasion and infrequently of malignant spread. Radical surgical removal is the treatment of choice, either of the primary tumour site or the potential metastases. Increased awareness of SPN should facilitate a surgical approach to this rare but curable tumour. Tumour size and the presence of metastases are not contraindications to resection. Where technically feasible, conservative surgical strategies without compromising radical resection are safe and effective. Because SPNs affect young patients with a reasonable long-term life expectancy they should be strictly followed up to confirm that this surgical lesion is potentially curable.

References


