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ORIGINAL ARTICLE

Pseudopapillary tumor in pediatric age: clinical and surgical management

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Abstract
Background Solid pseudopapillary tumors of the pancreas are rare exocrine pancreatic tumors. Through a review of pediatric cases in a single Institution, we present the clinical and surgical management of this neoplasm.
Methods We retrospectively reviewed the clinical charts of patients treated at our unit between 1995 and 2009 for SPT. Clinical and surgical management were analyzed and reported.
Results During the study period 11 patients underwent surgery for pseudopapillary tumor. Five patients were treated with duodenum-preserving pancreatic head resection and six patients with splenopancreasectomy with a Roux-en-Y pancreatic jejunostomy. Patients did not show recurrence and are currently disease free. Blood tests, Ultrasound, Computed tomography and Magnetic Resonance Imaging were not useful to preoperatively identify the nature of the pancreatic masses.
Conclusion Solid pseudopapillary tumor is a rare condition that should be taken into account for the differential diagnosis of pancreatic masses in pediatric age. Due to its favourable prognosis, surgical removal should be planned and done following the intraoperative findings.

Keywords Pediatric age · Solid pseudopapillary tumor · Pancreas

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Introduction

Solid pseudopapillary tumor (SPT) of the pancreas is a rare exocrine pancreatic tumor described for the first time by Franz in 1959 and is well known for its predilection for young women and its indolent biologic behaviour [1].

Clinical presentations range from asymptomatic "incidental" diagnosis to abdominal discomfort and pain, upto peritonitis caused by its rupture. In its first description, Franz reported four cases that had previously been misdiagnosed as non-functioning islet cell tumors. He considered this tumor as a new entity, which he called "papillary tumor of the pancreas". The tumor has since then been referred to using many different terms such as solid and cystic tumor, solid and papillary epithelial neoplasm, papillary-cystic neoplasm, papillary-cystic epithelial neoplasm, papillary-cystic tumor or Franz tumor.

Eventhough this condition is well known for its indolent biologic behaviour and low malignant potential, some patients with SPT develop metastases, mostly involving the liver, nodes or peritoneum but, despite the tumor advanced stage, usually with a favourable clinical course [2].

The prognosis of SPT after surgical resection is normally favourable with a survival rate at 5 years higher than 95% [3, 4].

Even if this condition is generally considered as rare, its occurrence in non-Caucasians is fairly high. A large number of cases have been reported in the Asian and

African-American population. In their study Morohoshi et al. stated that this neoplasm accounts for 2–3% of pancreatic neoplasms occurring at all ages [5, 6].

The aim of this study is to report the cases of SPT in pediatric age with different presentations and surgical treatments, focusing on the different clinical and radiological aspects of such a condition.

Materials and methods

We retrospectively reviewed the medical charts of pediatric patients treated at our Unit for SPT between 1995 and 2009. An interdisciplinary committee (Department of Surgical Sciences Research Committee) approved the review. Clinical presentation, management and surgical procedure were analyzed and compared. Inclusion criteria were patients with a pathological diagnosis of SPT.

All data were analyzed and compared per age at presentation and location (head, body, and tail). Radiological tests were reviewed and blood tests were correlated with the clinical presentation and diagnosis. Different surgical procedures were used during the study period and for this reason we decided to motivate all decisions. At present each patient is followed by an interdisciplinary team (pediatrician, pediatric surgeon, and oncological group). SPTs were divided into different groups, depending on tumor site. SPT was diagnosed following clinical, genetic and pathological criteria [5, 6].

The preoperative examination focused on the site of the lesions looking also for possible metastases. To determine the site of the tumor, physical examinations were performed in association with computed tomography (CT), ultrasonography, and magnetic resonance.

The surgical procedure to use in each case was decided after an interdivisional surgical meeting. Peri-pancreatic lymph nodes dissection was performed on all patients.

Results

Between 1995 and 2009, 11 patients were treated for SPT at the Authors' Pediatric Surgical Unit. Age range at diagnosis was 5–14 years; two patients were males and nine patients were females. All patients were Caucasian. In five cases the diagnosis was accidental (age range 10–14 years) and symptoms were present in six cases. In these cases there was a history of abdominal trauma during the previous 2 years without hospitalization (age range 5–11 years). The prevalent symptom at diagnosis for both groups was abdominal pain (70%); two patients had fever and nausea at diagnosis and none of the patients had jaundice. Two patients showed a palpable abdominal mass. SPT was located in the head in five cases (45%) and in the body/tail in the remaining cases.

Laboratory tests were not useful for diagnosis; all patients received abdominal ultrasounds and computed tomography or magnetic resonance (Table 1).

Head tumors

Five cases were treated; all the patients were females and had a previous history of abdominal trauma (bicycle trauma) without hospitalization. Age range at diagnosis was 5–12 years. The patients received blood tests and an abdominal ultrasound scan (US). Laboratory tests revealed leukocytosis (>12 $\times$ 10^9/L, reference range: 4–10 $\times$ 10^9/L) with pancreatic and hepatic values within normal ranges. On US, a round shaped mass with a clear edge without any features of malignancies was detected in the head of the pancreas; blood tumor markers (CEA, β-HCG, CA19-9; NSE), urinary vanilmandelic acid, and homovanilic acid did not show increased values. No signs of liver or gastrointestinal tract injuries were noted. On abdominal CT, all cases showed a well-circumscribed round shaped mass of mixed attenuation (>5 cm of diameter) in the head of the pancreas. On MRI (Fig. 1), unenhanced T1-weighted imaging showed a round, well-circumscribed, hypointense mass in the enlarged pancreatic head just anterior to the common bile duct. The mass was slightly hyperintense at T2-weighted imaging. On laparotomy, it was decided to perform a duodenum-preserving pancreatic head resection (Beger procedure) [7].

Table 1 Relevant demographic, clinical, and radiological features of 11 Patients of SPTs

Group	Head	Body	Tail
%	45	45	10
Number of patients	5	5	1
Gender	F	4F 1M	M
Age range	5–12	10–14	12
Symptoms			
Pain	++	+	−
Fever	−	−	−
Anorexia	+	+	−
Vomiting	++	+	−
Weight loss	−	−	+
Bowel changes	+	+	−
Bleeding	−	−	−
Abdominal mass	−	++	+
Incidental diagnosis	+	+	−
Jaundice	−	−	−
History of trauma	+++	+	−
Diameters (cm)	5–12	6–16	6–14

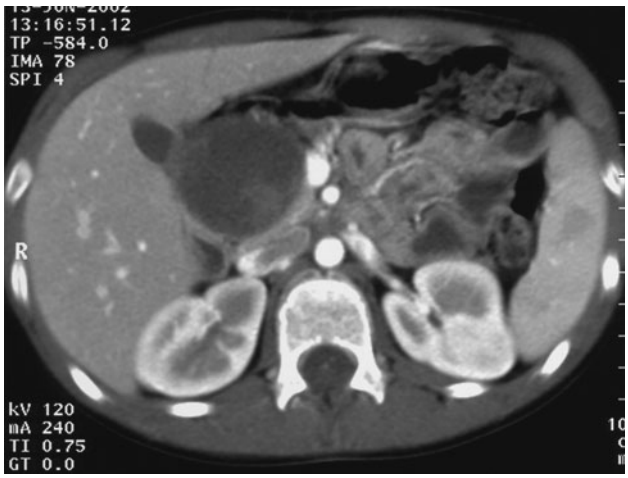

Fig. 1 Transverse abdominal MRI T1-weighted imaging demonstrating a round, well-circumscribed, hypointense mass in the enlarged pancreatic head just anterior to the common bile duct

Upto now none of these patients has shown any sign of diabetes with a good sugar balance.

Body/Tail tumors

Of the 6 cases (four females and two males) five cases had abdominal pain and one patient had nausea and vomiting. Age range at diagnosis was 10–14 years. Hematological and biochemical examination revealed no abnormalities. Serum tumor markers (carcinoembryonic antigen, alpha-fetoprotein, human chorionic gonadotropin, CA 19-9, IAP, elastase 1, neuron-specific enolase), urine vanilmandelic acid, and homovanilic acid were all within normal values. Ultrasonography showed a clearly demarcated round mass with a diameter >10 cm comprising a mixture of solid and cystic components in the upper left quadrant of the abdomen. In all cases, MRI revealed that the solid portion of the tumor showed low signal intensity on T1-weighted MR and high intensity on T2-weighted images. A firm well-encapsulated mass in the pancreas body and tail was found at super-umbilical transverse laparotomy. The masses consisted of a solid area with hemorrhage and a cystic area surrounded by an inflammatory tissue that also infiltrated the splenic hilar vessels. All patients received splenopancreasectomy using a Roux-en-Y pancreatic jejunostomy.

At macroscopic and microscopic evaluation the main pancreatic duct was not involved by the tumor.

Microscopic evaluations

All lymph nodes were free from disease. On microscopic pathological examination, it was possible to detect the following: a centrally located large area of coagulative necrosis composed of aggregates of ischemic-necrotized neoplastic "ghost cells" (6 cases); PAS-positive bodies within the neoplastic cells (all cases); abundant eosinophilic cytoplasms (5 cases); regular nuclei with low-grade atypia (6 cases). The percentage of proliferating cells was about 1% as measured by immunostaining for proliferation marker Ki67 (all cases). Rare atypical mitoses were also found (all cases). Immunohistochemistry revealed cytoplasmic positivity for Vimentin, CD56, PgP, beta-catenin and progesterone receptors were positive in all cases (Fig. 2).

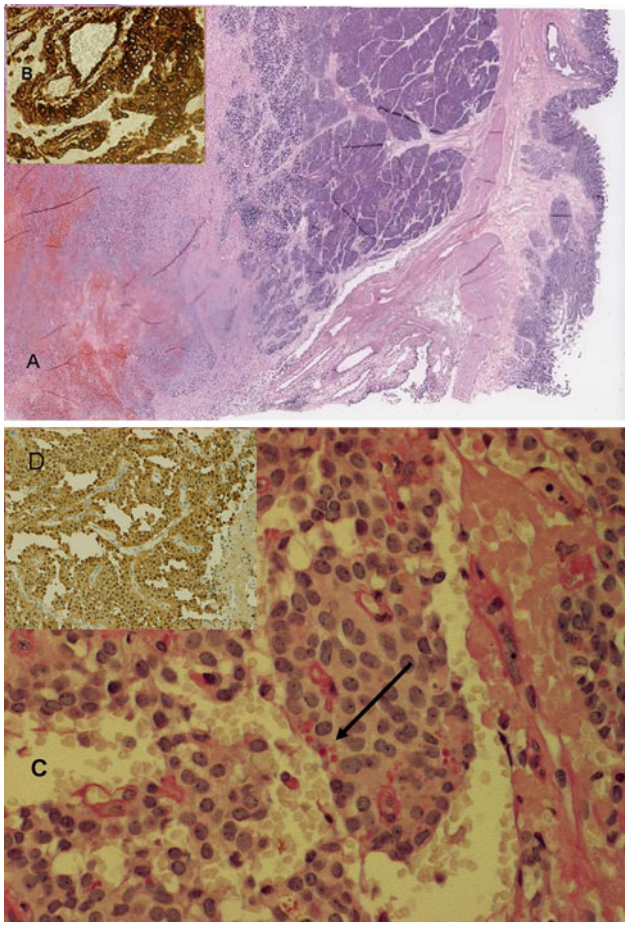

Fig. 2 **a** SPT with an extensive necrotic area at low-power magnification. **b** Strong positivity for Vimentin immunostain. **c** Eosinophilic bodies Pas+ (*arrows*). **d** SPT markedly positive for beta-catenin immunohistochemical marker

Discussion

This study shows how the presentation of SPT in pediatric age and adolescence could be different. In literature only few pediatric patients were correctly diagnosed preoperatively [7].

SPT of the pancreas predominates in adolescent girls and young women while it is uncommon in male subjects.

It was possible to observe only two cases of SPT in male patients with a body/tail pancreatic tumor. Although literature has shown no preferential localization within the gland, the pancreas head is the preferential site of this tumor, with an incidence rate of 42% (48% of the cases observed) [7].

The review of currently available literature revealed two main series of SPT cases: in 1995 Mao et al. reviewed 292 cases, and in 2005 Papavramidis and Papavrimidis reported 718 cases of SPT, with the tumor occurring predominantly in young Asian women between 15 and 35 years of age [8, 9].

The diagnosis of SPT is not often suspected until laparotomy is performed because specific laboratory tests are not currently available. Jaundice is rare, even with tumors originating from the head of the pancreas and there is usually no associated functional endocrine pathology. Very rarely these tumors are responsible for hemoperitoneum caused by rupture of the tumor. Radiographic studies are helpful in the preoperative evaluation although the findings are not definitive. Computed tomography and magnetic resonance imaging with contrast administration may help distinguish SPT from other pancreatic tumors: if these radiographic tests are suitably correlated with the clinical setting, the presence of an encapsulated solid and cystic mass with areas of "hemorrhagic degeneration" seems to be suggestive of SPT diagnosis [10, 11].

In 2007, Salvia et al. reported the experience carried out at the surgical department of their institution on 31 consecutive patients affected by SPT. After describing the nature and clinical features of this condition, they concluded that even if SPT appears to be an indolent neoplasm with low-grade aggressiveness, surgical treatment is possible and efficient despite tumor location, size and presence of metastatic lesions [12].

Common pancreatic tumor markers are usually within normal values. SPT generally displaces the surrounding structures rather than invading them. Furthermore, because of its softness, SPT rarely causes bile or pancreatic duct obstruction, even when it is located in the head of the pancreas. Following the pathological examinations of this study, the larger the tumor, the more frequently the neoplasm is encapsulated within a cystic-necrotic structure; local invasion, recurrence, or limited metastases and size should not be considered contraindications to resection of the pancreas [13–18].

The pathology of solid pseudopapillary tumor of the pancreas was described for the first time by Hamoudi et al. in 1970. This tumor was considered as a distinct clinical entity by Kloppel et al. in 1981 [19, 20].

The pathologic diagnosis of SPT is mainly based on its well-defined solid and cystic structure and characteristic pseudopapillary features under the microscope. Histological features indicating a higher malignant potential of SPT include venous invasion, higher nuclear grade and more prominent necrobiotic nests [21].

The most important differential diagnosis during childhood is restricted to pancreatoblastoma, which is more aggressive and is usually found in younger individuals of either sex. Also cystic and/or solid pancreatic processes such as congenital pancreatic cysts or hemorrhagic pseudocysts should be taken into consideration [13].

Recently, it has been argued that these neoplasms are amenable to fine-needle aspiration using computed tomography-guided and endoscopic ultrasound-guided techniques. Cytological features of SPT include highly cellular smears in most cases with characteristic branching papillary fragments composed of central fibrovascular stalks. These are covered with one to several layers of tumor cells with an amorphous perivascular myxoid substance. Tumor cells are monomorphic with occasional intracytoplasmatic hyaline globules. Mitoses are rare or absent [22–24].

Immunohistochemical studies are frequently performed to confirm the diagnosis. SPT is typically positive for vimentin and antitrypsin, while it is negative for trypsin and chymotrypsin. SPT may also show focal immunoreactivity for neuron-specific enolase (NSE) and cytokeratin, beta-catenin and progesterone receptor (PgR) [24–27].

Prognosis of SPT is based on clinical follow-up: there are no significant differences in the survival rate depending on the resection technique used. After complete removal of SPT more than 95% of patients are cured. Surgical resection still plays a pivotal role in the treatment of patients with metastatic, locally advanced or recurrent diseases [13–30].

Surgical management

Surgical management has been tailored to the slow-growing, non-invasive nature of this tumor. Surgical treatment is chosen depending on SPT location. With an involvement of the head of pancreas the suggested treatment is a pylorus-preserving pancreaticoduodenectomy, while pancreas resection by central pancreatectomy and reimplantation of the pancreatic remnant in the stomach is reported for SPT involving the neck or body of the pancreas, with the theoretical benefit of preserving the pancreatic parenchyma and spleen. When the tumor is located in the pancreatic tail, body or in both the tail and the body of the pancreas, distal pancreatectomy with splenectomy is employed in many cases. Many authors recommend splenic conservation following distal pancreatectomy whenever this is possible. The use of a Roux-en-Y pancreatic jejunostomy is also recommended for body/tail pancreatic tumors (to prevent pseudocyst formation) [13].

As suggested by Dasgupta et al. demolitive pancreatic surgery in pediatric age should be planned with a different approach with respect to adult patients. It is necessary to carefully evaluate dimension and localization of the tumor and its prevalent benign nature. For this reason, as it happens at our institution, pancreatic surgery should be performed by expert multidisciplinary teams operating in high-volume institutions [31].

Conclusion

Since SPT is a rare condition the authors wish to emphasize the importance of a multidisciplinary approach when managing a pancreatic mixed mass in pediatric age. Surgical removal with tumor-free margins is necessary in order to have a good clinical course and outcome.

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