Solid pseudopapillary tumor of the pancreas: A review of 553 cases in Chinese literature

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Abstract

AIM: To sum up the clinical and pathological characteristics of solid pseudopapillary tumor (SPT) and the experience with it.

METHODS: A total of 553 SPT patients reported in Chinese literature between January 1996 and January 2009 were retrospectively reviewed and analyzed.

RESULTS: The mean age of the 553 SPT patients included in this review was 27.2 years, and the male to female ratio was 1:8.37. Their symptoms were non-specific, and nearly one third of the patients were asymptomatic. Computed tomography and ultrasonography were performed to show the nature and location of SPT. Most of the tumors were distributed in the pancreatic head (39.8%), tail (19.5%). Forty-five patients (9.2%) were diagnosed as malignant SPT with metastasis or invasion. None of the clinical factors was closely related to the malignant potential of SPT. Surgery was the main therapeutic modality for SPT. Local resection, distal pancreatectomy and pancreatoduodenectomy were the most common surgical procedures. Local recurrence and hepatic metastasis were found in 11 and 2 patients, respectively, after radical resection. Four patients died of tumor progression within 4 years after palliative resection of SPT. The prognosis of SPT patients was good with a 5-year survival rate of 96.9%.

CONCLUSION: SPT of the pancreas is a rare indolent neoplasm that typically occurs in young females. It is a low-grade malignancy and can be cured with extended resection. The prognosis of such patients is good although the tumor may recur and metastasize.

Key words: Pancreatic neoplasm; Solid pseudopapillary tumor; Diagnosis; Treatment; Prognosis

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Yu Pf, Hu Zh, Wang XB, Guo JM, Cheng XD, Zhang YL, Xu Q. Solid pseudopapillary tumor of the pancreas: A review of 553 cases in the Chinese literature. World J Gastroenterol 2010 March 14; 16(10): 1209-1214 Available from: URL: http://www.wjgnet.com/1007-9327/full/v16/i10/1209.htm DOI: http://dx.doi.org/10.3748/wjg.v16.i10.1209
INTRODUCTION

Solid pseudopapillary tumor (SPT) of the pancreas, first reported by Frantz in 1959[1], is an uncommon but distinct pancreatic neoplasm with a low malignancy, accounting for 1%-2% of all pancreatic tumors[2]. Different names of this tumor were reported until it was defined by the World Health Organization (WHO) in 1996 as a “solid pseudopapillary tumor” of the pancreas[3]. SPT occurs mainly in young women and can be treated with surgical resection. SPT patients have a relatively favorable prognosis after surgical resection. With the widespread availability of high-quality imaging systems and a better understanding of its pathology, the number of such patients reported in the literature has been steadily increased. Papavramidis has summarized 718 SPT patients in English literature, mainly from USA, Europe, and Japan[4]. In this study, the cases of SPT reported in current Chinese literature were reviewed and analyzed.

MATERIALS AND METHODS

SPT-related literatures covered in the Chinese biology and medicine database (CBMD) and the China hospital knowledge database (CHKD) between January 1996 and January 2009 were retrieved. Indexing terms used for the retrieval were SPT, solid cystic tumor, papillary cystic tumor, papillary epithelial neoplasia, solid and papillary epithelial neoplasia, papillary epithelial tumor, Frantz’s tumor, solid and papillary tumor, solid and cystic papillary epithelial neoplasia, benign or malignant papillary tumor of the pancreas. A total of 241 articles were searched. Each article was carefully studied to avoid the repetitive adoption of the saved material. A database of the characteristics of these patients was developed, including age, gender, symptoms, tumor location (data were from radiological investigations or surgical record) and size (data were from radiological investigations or surgical record and finally confirmed by pathology), metastasis or invasion of adjacent tissues (data were from radiological investigations or surgical exploration, and finally was confirmed by pathology), treatment (data were from the record of therapy, including the types of surgery), and follow-up. Each case with at least 6 of these characteristics was defined as well-documented. Thus, a total of 117 articles describing 553 well-documented cases of pancreatic SPT were included in our review and analysis. All statistical analyses were performed using the SPSS 15.0 for Windows (Chicago, Illinois).

RESULTS

Of the 553 patients, 59 were men and 494 were women with a male to female ratio of 1:8.37. Their mean age was 27.2 years (range 6-71 years).

The features of 473 SPT patients (85.5%) are listed in Table 1. The symptoms were non-specific, and coexistence of two or more symptoms was usually found. Nearly one third of the patients were asymptomatic, with the tumor found at routine physical examination. The tumor was localized in 507 patients (91.7%). The most common sites of the tumor were the pancreatic head (39.8%), tail (24.1%), body and tail (19.5%), body (11.2%), and neck (3.6%). SPT was found in extra-pancreatic tissues of retroperitoneum, mesenterium, and left adrenal gland in 9 patients (1.8%). The tumor sizes in 512 cases (92.6%) were provided. The mean diameter of the tumor was 7.87 cm (range 1-25 cm).

CT, US and magnetic resonance imaging (MRI) were performed for the evaluation of 460 (83.2%), 337 (60.9%) and 43 patients (7.8%), respectively. Preoperative fine needle aspiration cytology (FNAC), endoscopic ultrasounds (EUS), and endoscopic retrograde cholangiopancreatography (ERCP) were seldom performed. Of the 325 patients (75.0%) diagnosed before operation, only 77 (23.7%) were diagnosed as or suspected of SPT. The misdiagnosis rate for pancreatic adenocarcinoma, cystadenoma, cystadenocarcinoma, islet cell tumor, pancreatic cyst, neuroendocrine tumor, teratoma, and cystic tumor was 24.6%, 10.7%, 3%, 13.2%, 7.3%, 8.6%, 1.9%, and 7%, respectively. The masses were shown on cross-sectional imaging as heterogeneous (n = 300, 60.12%), cystic (n = 78, 15.63%), or solid (n = 121, 24.25%).

Of the 491 patients (88.8%) with metastasis or invasion, 45 (9.2%) were diagnosed as malignant SPT. The liver, portal/splenic vein/superior mesenteric vein, spleen, diaphragmatic muscle, omentum or peritoneum, duodenum, stomach, colon, and left kidney were involved in 6, 11, 4, 1, 7, 7, 3, 2 and 1 patients, respectively. Enlarged lymph nodes and lymph node metastasis were detected in 10 and 3 patients, respectively. The level of tumor markers, including α-fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9, CA125 and CA242, was slightly increased in 11 patients, but only two were diagnosed as malignant SPT. Other clinical factors, including sex, age, symptoms, and tumor size, location and characteristics, were analyzed in some reports. However, none of the features was found

| Symptoms | Patients (n) | %   |
|----------|-------------|-----|
| Abdominal pain | 178 | 37.63 |
| Abdominal mass | 170 | 35.94 |
| Abdominal discomfort | 155 | 32.77 |
| Asymptomatic | 150 | 31.70 |
| Vomiting | 25 | 5.29 |
| Post-trauma | 23 | 4.86 |
| Nausea | 19 | 4.01 |
| Back pain | 17 | 3.59 |
| Jaundice | 17 | 3.59 |
| Anorexia | 11 | 2.33 |
| Weight loss | 9 | 1.90 |
| Fever | 7 | 1.48 |
| Other symptoms | 5 | 1.06 |

SPT: Solid pseudopapillary tumor.

Table 1  Symptoms of SPT patients (n = 473)
to be closely related with the malignant potential of SPT in our study.

At present, radial resection is the main treatment of choice for pancreatic SPT. Local resection, distal pancreatectomy, and pancreaticoduodenectomy were the most commonly used surgical procedures for the 315 patients included in our study (Table 2). Resection of a cuff of the portal vein was performed in 3 patients with a vein graft repair and palliative operation was performed in 10 patients as the tumor was adhered to the adjacent tissues or its metastasis was not resectable. Of the 6 patients with liver metastasis, 1 underwent liver operation, 2 had liver biopsy for the metastasis followed by dehydrated alcohol injection and transarteral chemoembolization (TACE), and 3 received γ-radiation therapy, chemotherapy and radiofrequency, respectively. The most common complication after operation was pancreatic fistula which occurred in 17 cases (5.4%). Other complications including pancreatitis, steatorrhea, wound infection, biliary fistula, prolonged gastric emptying, gastrointestinal bleeding, diabetes mellitus, and ileus were observed in 3 (0.95%), 3 (0.95%), 3 (0.95%), 2 (0.63%), 2 (0.63%), 2 (0.63%), 1 (0.32%), and 1 (0.32%) patients, respectively.

The data of immunohistochemical profile are listed in Table 3. SPT cells were typically positive for vimentin, α1-antitrypsin, α1-antichymotrypsin, and neuron specific enolase. Focal expression of synaptophysin, cytokeratin and chromogranin A was detected in a few tumors. The positive rate was higher for progesterone receptor than for oestrogen receptor, but usually variable. Immunohistochemical staining of Ki-67 was detected in 12 (0.32%) patients, respectively.

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### DISCUSSION

SPT of the pancreas is a rare neoplasm with a low malignant potential, usually affecting young women in the second or third decade of life. Its pathogenesis still remains unknown, although its tendency to affect young women is due to the involvement of sex hormones. However, no difference has been found in immunohistochemical staining for sex hormone-receptor proteins or in clinicopathologic characteristics attributable to gender alone. Sun *et al.* reported that 62.5% of SPT patients are infected with hepatitis B virus (HBV), which can induce over-expression of β-catenin in tumor cells, indicating that HBV infection may be involved in the pathogenesis of SPT, which, however, has not been confirmed.

Although the malignant potential of SPT is low, up to 15% of SPT patients develop metastasis. The most common sites of metastasis are the liver, regional lymph nodes, mesentery, omentum, and peritoneum. Local invasion of the duodenum, stomach, spleen or major blood vessels may also occur, as reported in our study. Washington *et al.* showed that the clinical and pathologic features of SPT, including diffuse growth, venous invasion, nuclear pleomorphism, mitotic rate, necrosis and dedifferentiation, are related to its aggressive behavior or metastatic potential. Other studies indicate that DNA aneuploidy, double loss of X chromosomes, trisomy for chromosome 3, unbalanced translocation between chromosomes 13 and 17 found in SPT patients are associated with its aggressive behavior and may be indicators of its possible metastatic potential. In our study, the clinical factors, including sex, age, symptoms,
and tumor size, location and characteristics were not closely related to its malignant potential. Four of the 5 patients positive for Ki-67 immunoreactivity were confirmed to have malignant SPT, which is consistent with the reported findings\cite{18}, suggesting that positive staining of Ki-67 may correlate with the malignant potential and poor outcome of SPT. However, there are some limitations in our study due to the available data, more SPT patients should be studied for Ki-67 and new biomarkers in order to better predict its malignancy.

The clinical presentation of SPT is usually unspecific. Most patients have unclear clinical features including abdominal pain or discomfort, poor appetite and nausea, which are related to tumor compression on adjacent organs. SPT is often diagnosed during complementary imaging investigations such as ultrasound or CT scan of the abdomen, usually showing a well-encapsulated complex mass with both solid and cystic components. Dynamic contrast-enhanced CT can show less enhanced tumor, typical cystic spaces in the center, and enhanced solid areas at its surroundings\cite{19}. MRI is better than CT in detecting the cistic or solid components of the tumor. If MRI reveals an encapsulated mass with solid and cystic components as well as hemorrhage without obvious internal septum, SPT of the pancreas should be highly suspected\cite{20}. Percutaneous or EUS-guided FNAC can help to distinguish SPT from other pancreatic tumors. However, reports are also available on seeding such as bleeding, pancreatic fistula and biliary fistula during the procedure\cite{21}. Despite the technological advances, preoperative diagnosis is still difficult and only 77 patients were diagnosed as or suspected of SPT in our series. The results of our study show that CT/MRI scans combined with age and gender should be sufficient for the decision to operate, and diagnostic interventions such as FNAC should be performed when radiology fails in diagnosing it.

At present, radical resection is the treatment of choice for SPT even with metastasis or local recurrence. Local resection or enucleation can be performed for small tumors with complete amicula. Distal pancreatectomy combined with or without splenectomy can be performed for pancreatic body and/or tail tumor, and pancreatectoduodenectomy for pancreatic head tumor. Intra-operative frozen section may help to ascertain the adequate resection of margins. Extensive lymphatic dissection is not warranted since lymph node metastasis was found in only 3 patients (0.61\%) in our study. Surgery should be performed for the tumor with local invasion or metastasis\cite{22}. Sperti et al\cite{22} have reported 17 patients who underwent vascular resection and reconstruction with no death occurred. In our study, the infiltrated portal veins were reconstructed with vein grafts after en-bloc resection and the patients had a long survival time. Martin et al\cite{22} reported that four patients underwent resection of liver metastasis and primary tumor, and two of them survived for at least 6 and 11 years, respectively. Other treatment modalities for liver metastasis, such as alcohol injection, TACE, ɣ-radiation therapy and even liver transplantation, have been reported\cite{11,22}. The role of chemotherapy and radiotherapy in treatment of SPT is poorly defined at present, since only few reports are available on them.

Grossly, SPT is well-encapsulated and usually well-demarcated from the pancreas, with large spongy areas of hemorrhage on its cut surface alternating with both solid and cystic degenerations. The tumor contains a mixture of solid, cystic, and pseudopapillary patterns in various proportions. The solid portions of the tumor are composed of uniform and polygonal epithelioid cells with well-vascularized stroma and a discohesive arrangement\cite{23}. Immunohistochemically, SPT is typically positive for vimentin (Vim), a-1-antitrypsin (AAT), a-1-antichymotrypsin (AACT), and neuron specific enolase (NSE)\cite{23}, which is consistent with the finding in our study. However, the unique immunohistochemical features with expression of CD56 and CD10 have not been reported\cite{11,22}. SPT cells may also reveal focal immunoreactivity for cytokeratin (CK) and synaptophysin (Syn), abnormal nuclear location of β-catenin, and presence of progesterone receptors (PR), and may express galectin-3, all of which are useful in differentiating SPT from endocrine pancreatic tumor\cite{22}.

The prognosis of SPT patients even with local recurrence and metastasis or invasion is good. SPT is limited to the pancreas in over 95\% of its patients and can be radically resected\cite{22}. Its local recurrence rate is less than 10\% and usually occurs within 4 years after surgery\cite{22}. Recurrence, local invasion, and limited metastasis are not the contraindications for resection,
and some patients with “unresectable” SPT may also have a long survival time\(^\text{[38]}\). It has been reported that the overall 5-year survival rate of SPT patients is about 95%\(^\text{[19]}\). Due to the favorable prognosis and long survival rate of SPT patients with local recurrence or metastasis, it is difficult to identify the predictive factors for their survival time.

Although this retrospective review has certain limits due to the available data, our results are consistent with the reported findings\(^\text{[4,11]}\). Further study should be based on the selective cases with more detailed information.

In conclusion, SPT, an infrequently-encountered tumor, typically affects young women without significant symptoms. Its behavior is relatively indolent and largely benign. Patients may survive a long time after radial resection of the tumor. Whenever possible, surgery is justified for local invasion or metastasis of SPT. The prognosis of SPT patients even with unresectable metastasis is good. The role of chemotherapy and radiotherapy remains to be studied.

**COMMENTS**

**Background**

Solid pseudopapillary tumor (SPT) of the pancreas is a rare neoplasm with a low malignant potential, usually affecting young women in the second or third decade of life. With widespread availability of high-quality imaging systems and a better understanding of its pathology, the number of cases reported in the literature has been steadily increased in recent years.

**Research frontiers**

The clinical and pathological characteristics of SPT are still not fully recognized. Although a variety of radiological investigations have been performed for the evaluation, its misdiagnosis rate is still high. The experience in management of SPT, especially with a malignant potential, is still not adequate enough.

**Innovations and breakthroughs**

In this study, the authors collected relatively comprehensive data from the published Chinese literature and found that SPT is potentially curable with extended resections. The prognosis of SPT patients even with recurrence or unresectable metastasis is good. In addition, the authors analyzed the potential relation between hepatitis B virus infection and pathogenesis of SPT. The positive staining of Ki-67 may correlate with the malignant potential and poor outcome of SPT.

**Applications**

The results of this study indicate that the behavior of SPT is relatively indolent and largely benign. However, surgical resection is warranted since patients can survive a long time after it.

**Peer review**

This is a retrospective study summarizing a considerable number of patients (553 patients) with SPT of the pancreas covered in two Chinese databases. The manuscript is consisted of a good description of the patients with their demographic data, symptoms, imaging studies, location and invasion, surgical data and complications, pathology, immunohistochemical profile and survival time provided.

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