Int J Clin Exp Pathol 2020;13(2):248-253
www.ijcep.com /ISSN:1936-2625/IJCEP0105421

Case Report

Solid pseudopapillary neoplasm (SPN) of the pancreas presenting with ascites misdiagnosed as pancreatic tuberculosis: a case report and literature review

Ben-Jian Gao[1], Jia Luo[2], Ying Liu[1], Fu-Rui Zhong[1], Qing-Xi Guo[3], Fang-Yi Peng[1], Xiao-Li Yang[1], Song Su[1], Bo Li[1]

Departments of [1]Hepatobiliary Surgery, [2]Oncology, [3]Pathology, The Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan Province, P. R. China

Received November 25, 2019; Accepted January 23, 2020; Epub February 1, 2020; Published February 15, 2020

Abstract: Introduction: Solid pseudopapillary neoplasm (SPN) is a rare pancreatic tumor that mainly affects young women. It is a low-grade malignant neoplasm, with an excellent prognosis after surgical treatment. We report herein a case of SPN presenting with ascites that was misdiagnosed as pancreatic tuberculosis (TB). Case report: A 16-year-old female initially presented with a large volume of ascites. Contrast-enhanced ultrasound and computed tomography found a heterogeneous lesion in the pancreatic body, which had slight contrast enhancement on the arterial phase. Analysis of ascites showed it was exudative. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of the mass only revealed a few blood clots. The diagnosis was highly suggestive of a pancreatic TB. However, after 6 months of anti-TB therapy, the pancreatic lesion remained essentially unchanged. Subsequently, magnetic resonance imaging indicated a mixed solid and cystic lesion with a well-defined margin in the pancreatic body. Further EUS-FNA showed monomorphic neoplastic cells with papillary architecture and immunohistochemical analysis revealed that the tumor cells were positive for β-catenin, CD10, vimentin, cytokeratin, and synaptophysin. These findings were consistent with SPN. After distal pancreatectomy with splenectomy, postoperative pathology and immunohistochemical staining confirmed the diagnosis of SPN. Conclusion: Clinicians should consider the possibility of SPN for pancreatic heterogeneous masses. Multiple diagnostic imaging modalities and EUS-FNA may contribute to the preoperative diagnosis of this disease.

Keywords: Pancreas, solid pseudopapillary neoplasm, pancreatic tuberculosis, ascites

Introduction

Solid pseudopapillary neoplasms (SPNs) of the pancreas were initially described by Frantz in 1959 [1]. The World Health Organization (WHO) classified them as solid pseudopapillary tumors (SPTs) in 1996 and named them as SPNs in 2010 [2]. The WHO classification describes SPN as a borderline tumor of the exocrine pancreas with low-grade malignancy and an overall excellent prognosis [1]. It is a rare pancreatic tumor, and accounts for only 1%-2% and 0.17%-2.7% of pancreatic exocrine tumors and all pancreatic tumors, respectively [2, 3]. It occurs predominantly in young women, with median age about 25-35 years. The clinical signs are usually insignificant: patients may complain of slight, epigastric pain, discomfort, or it may be asymptomatic and detected incidentally by imaging examinations [3-6]. SPN typically presents as a solitary, well-defined mass, which can have a purely solid, mixed cystic and solid, or completely cystic appearance on abdominal imaging [7]. Because of its rarity and nonspecific characteristics, early and accurate discrimination is usually difficult. In this context, we report a case of SPN initially presenting with ascites that was misdiagnosed as pancreatic tuberculosis (TB).

Case report

A 16-year-old previously healthy female presenting with mild abdominal distension for one week was admitted to our hospital. She had no history of abdominal pain, vomiting, jaundice, fever, loss of appetite and weight, no past medical history of TB nor relevant family history.

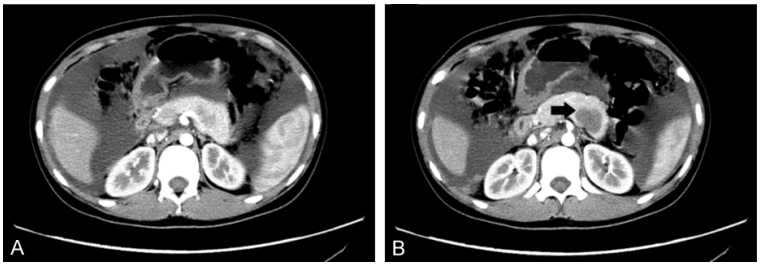

Figure 1. Contrast-enhanced computed tomography (CT) revealed a large volume of ascites (A), and a well-circumscribed mass (black arrow) in the pancreatic body, which showed mildly contrast enhancement on arterial phase (B).

On physical examination, an abdominal bulge was noted. Laboratory investigations showed no abnormalities excluding serum cancer antigen 125 (CA-125) 292.82 IU/mL (normal range, 0-35 IU/mL), C-reactive protein (CRP) 17.61 mg/L (normal range, 0-5 mg/L). Electrocardiogram and chest radiography found no specific manifestation. Contrast-enhanced computed tomography (CT) of the abdomen showed a large volume of ascites, omental inflammation, thickened peritoneum, multiple enlarged retroperitoneal and mesenteric lymph nodes, and a 3.1-cm mass in the body of the pancreas. The mass was well-circumscribed, slight hypodense to normal pancreatic parenchyma, and showed mild contrast enhancement on the arterial phase. It was suggestive of pancreatic neoplasm (**Figure 1**). Abdominal contrast-enhanced ultrasound (CE-US) found a heterogeneous, hypoechoic, and slightly enhancing lesion at the pancreatic body region. The possible diagnosis with CE-US included a pancreatic TB, or a pancreatic tumor (**Figure 2**). She underwent abdominal paracentesis and analyses of ascitic fluid revealed a predominance of mononuclear cells count of 91%, a high protein level of 50.8 g/L, and a lactate dehydrogenase (LDH) level of 178.4 U/L. The results of Ziehl-Neelsen staining, exfoliative cytologic examination, and ascitic-fluid culture for mycobacterium tuberculosis were negative. A test for tuberculosis-interferon gamma release assay (TB-IGRA) was positive. She then underwent endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of the lesion, revealing a few blood clots. Based on the imaging findings and the characterization of ascites, the principal provisional diagnosis of the lesion was pancreatic TB with tuberculous peritonitis, and a pancreatic tumor was not excluded. The Department of Infectious Diseases was consulted, and then she received anti-TB medication, including isoniazid, ethambutol, pyrazinamide and rifapentine. She was followed up monthly after discharge.

Ascites gradually decreased and completely disappeared after 6 months of anti-TB treatment, but the pancreatic lesion remained roughly unchanged in size. Subsequently, she underwent a magnetic resonance imaging (MRI) showing a 4×3 cm mixed solid and cystic lesion with well-defined margin located in the pancreatic body. The mass was predominantly hypointense on T1-weighted images and hyperintense on T2-weighted images. On contrast-enhanced dynamic MRI, the lesion showed peripheral and progressive enhancement, but slightly less than the normal pancreatic parenchyma (**Figure 3**). It was suggestive of solid pseudopapillary neoplasm of the pancreas or other tumors. During this hospital course, she underwent EUS-FNA of the lesion again. Pathology showed monomorphic neoplastic cells with papillary architecture. Immunohistochemical analysis indicated that the tumor cells were positive for β-catenin, CD10, vimentin, cytokeratin, and synaptophysin (**Figure 4**). The patient was diagnosed with a SPN of the pancreas.

A distal pancreatectomy with splenectomy was performed under general anesthesia, because the lesion was closely related to splenic vessels. No evidence of tumor spread was noted intraoperatively. On gross examination, the tumor located at the pancreatic body measuring 3.5×3×2.5 cm, and the cut section of the tumor showed a well-circumscribed, capsulated, gray-white colored, mixed solid and cystic appearance (**Figure 5A**). On postoperative pathology, the tumor showed mixed solid and pseudopapillary architectures with a predominantly solid component and intermixed areas of hemorrhage. The proximal pancreatic margins and spleen were negative for tumor (**Figure 5B** and **5C**). Immunohistochemical result: β-catenin, CD10, vimentin, cytokeratin, and synaptophysin were positive, CgA, E-cadherin, and P53 were negative, Ki-67 (+, <1%) (**Figure 5D-F**). These results were consistent with pancreatic

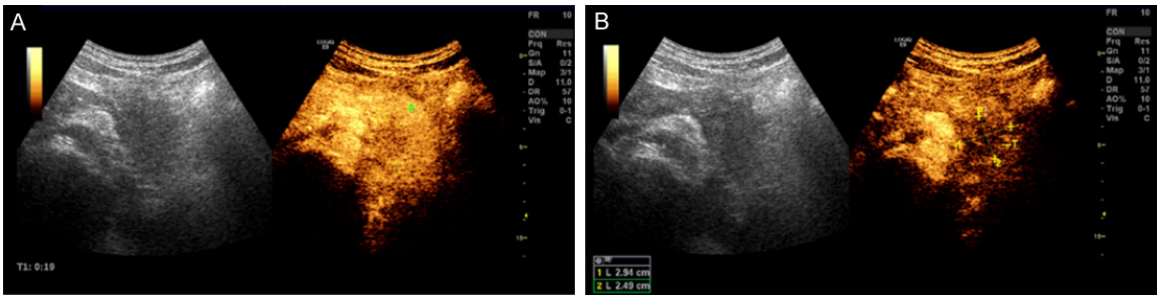

Figure 2. Contrast-enhanced ultrasound (CE-US) found a heterogeneous, hypoechoic, and slightly enhancing lesion at the pancreatic body region (A); lesion measured 2.9×2.5 cm (B).

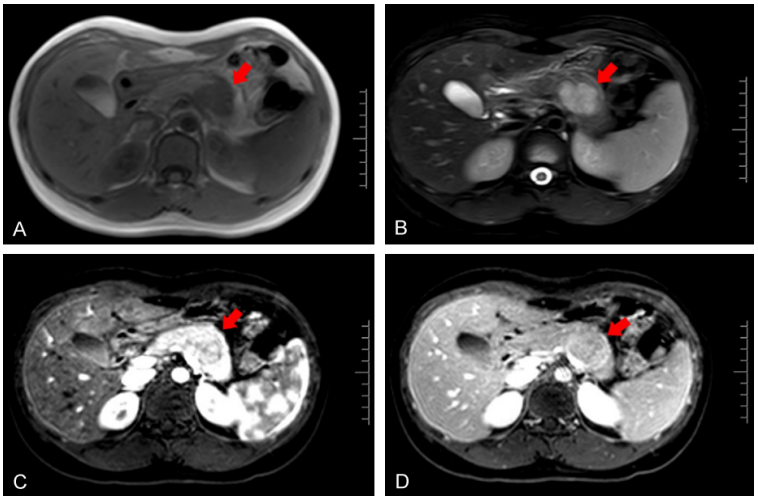

Figure 3. The mass (red arrows) was well-defined, predominantly hypointense on T1-weighted magnetic resonance imaging (MRI) (A), and hyperintense on T2-weighted image (B). Contrast-enhanced dynamic MRI showed a lesion with peripheral and progressive enhancement, but slightly less than the normal pancreatic parenchyma (C, D).

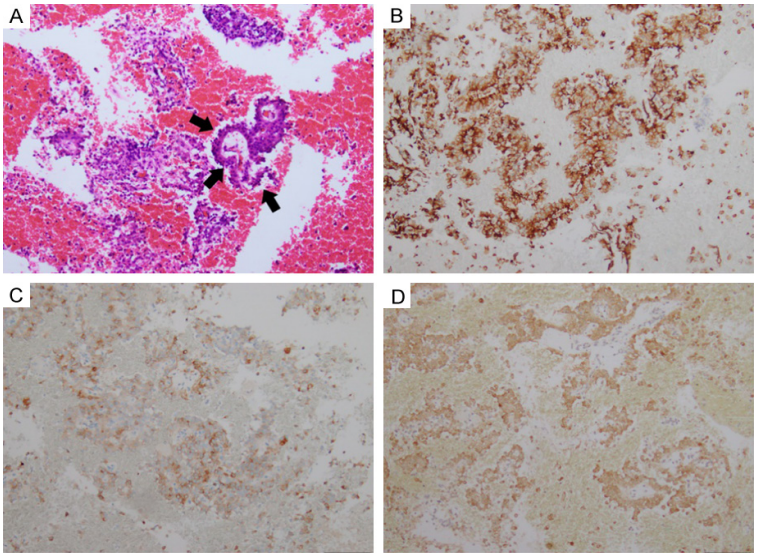

Figure 4. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) findings: pathology showed monomorphic neoplastic cells with papillary architecture (highlighted by black arrows) (A). H&E×100. Immunohistochemical staining of the tumor cell was positive for Vvimentin (B), CD10 (C), β-catenin (D). H&E = hematoxylin-eosin.

SPN. The patient recovered uneventfully after surgery. At the end of 3 months follow-up, she was disease-free and showed no signs of recurrence.

Discussion

Since the first description as "papillary tumor of the pancreas, benign or malignant" in 1959, various names have been used to describe this rare tumor, such as solid-cystic tumor, solid-cystic acinar tumor, papillary-cystic tumor, solid-papillary epithelial neoplasm and Frantz's tumor [4, 8]. Until 2010, the WHO defined it as SPN, and depicted it as low-grade malignant neoplasm made up of loosely cohesive monomorphic epithelial cells forming solid and pseudopapillary structures [2].

SPN is an uncommon pancreatic tumor, comprising approximately 0.17%-2.7% of all pancreatic tumors [2]. Due to its rarity, the natural course regarding this disease is currently limited. Although the hypotheses of its origin include endocrine cells, ductal cells, acinar cells, neurosecretory cells, and

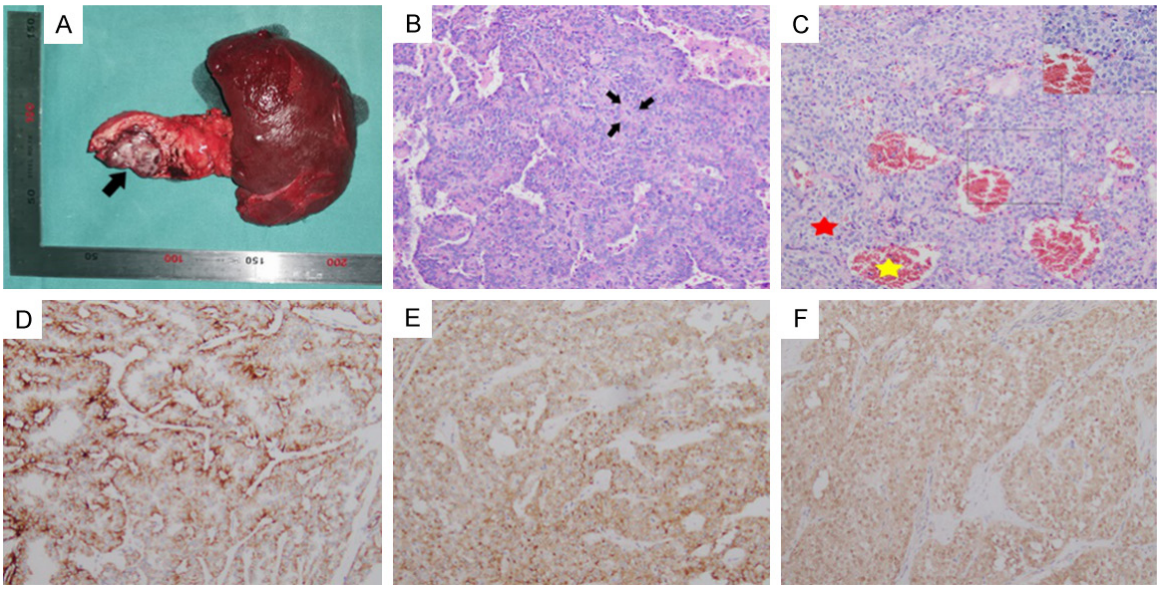

Figure 5. Gross picture of the specimen included the pancreatic body and tail containing the tumor (black arrow, measuring 3.5×3×2.5 cm), and the spleen. The cut section of tumor showed a well-circumscribed, capsulated, gray-white colored, mixed solid and cystic appearance (A). Postoperative histopathology revealing: pseudopapillary architecture (black arrows) (B); solid structures (red star) with intermixed areas of hemorrhage (yellow star) (C). H&E×100. The immunostaining was positive for vimentin (D), CD10 (E), β-catenin (F). H&E = hematoxylin-eosin.

totipotent primordial cells, the histogenesis and pathogenesis remain obscure [8]. SPN may affect both sexes, with a young female predominance [4]. Besides, Keiji et al. found that women seemed to have an early occurrence of SPN, and the average tumor diameter was significantly larger in female patients [2]. It can be located anywhere in the pancreas, mainly in the pancreatic tail and head [5, 6]. In extremely rare cases, SPN may also occur in extrapancreatic areas, like omentum, adrenal or mesentery [4]. Clinical symptoms of SPN are nonspecific. Abdominal pain is the most frequent symptom, followed by abdominal discomfort, palpable mass, indigestion, and back pain. Some patients are completely asymptomatic, and the lesions are found incidentally by imaging examinations [3-5, 9]. Physical examination is usually normal except for the possible appearance of an epigastric mass. Likewise, the results of laboratory analysis including liver function, serum amylase, tumor markers, and endocrine level are often within the normal ranges [8].

Imaging findings are useful and important modalities for preoperative diagnosis of SPN. On abdominal ultrasound (US), it usually presents as a well-encapsulated, mixed echogenicity, and heterogeneous cystic and solid mass, and sometimes with peripheral calcifications [10]. CT commonly reveals a heterogenous, well-defined lesion with intermixed solid and cystic components. After contrast enhancement, enhanced solid areas are typically noted peripherally [7, 10]. Compared with CT, MRI can better display a capsule and intratumoral hemorrhage [8]. Typically, SPN is visualized as low intensity on T1-weighted images and high intensity on T2- and diffusion-weighted images. Therefore, MRI has the potential to improve the diagnostic accuracy of SPN [7, 8]. EUS-FNA could also be used to increase the accuracy of diagnosis, and provide biopsy with the possibility of preoperative pathologic diagnosis [11, 12]. The cytomorphology finds a three-layered papillary architecture composed of a central capillary layer, a middle layer of myxoid stroma, and an outer layer of monomorphic neoplastic cells. In immunohistochemistry of EUS-FNA specimen, the protein markers, including vimentin, β-catenin and CD10, are highly positive, which are specific to SPN [2, 6]. Because of the limited specimens and technical difficulties of EUS-FNA, the preoperative accuracy was not consistent among different studies. Jani et al. and Joanna et al. reported that the diagnostic accuracy of EUS-FNA for SPN were 75% and

82.4% in their studies, respectively [6, 12]. However, due to its invasiveness and the possibility of peritoneal seeding, we should carefully consider indications for EUS-FNA [11].

The definitive diagnosis depends on pathologic examination and immunohistochemical analysis, although a combination of multiple diagnostic imaging modalities is important. Histologically, randomly mixed solid, pseudopapillary, or hemorrhagic pseudocystic structures is considered as a typical pathological feature of SPN [4, 5, 11]. Commonly, the tumor cells are monotonous, roundish with a uniform nucleus and amphophilic cytoplasm. The immunostaining is positive for β-catenin (nuclear and cytoplasmic), vimentin, CD10, synaptophysin, progesterone receptor (nuclear), CD56, NSE (neuron-specific enolase), and E-cadherin (loss of membrane and nuclear) [6, 13, 14].

In our case, this patient initially presented with a large number of exudative ascites, which is rare in SPN. Combined with the imaging findings and the negative results of the first EUS-FNA, the pancreatic lesion was thought to be a pancreatic TB, which is also rare. Similarly, the clinical presentations of pancreatic TB are nonspecific and diverse, as vague epigastric pain, loss of appetite and weight, ascites, low-grade fever and night sweats [15-17]. Frequently, pancreatic TB appears as a hypoechoic, focal, and parenchymal pancreatic lesion on US and as a focal hypodense lesion with an irregular border, or a solitary heterogenous lesion with peripancreatic enlarged lymph nodes on CT. Moreover, MRI usually demonstrates the lesion with hypointense on T1-weighted images, and hyperintense on T2-weighted images; occasionally dilatation of the bile and the pancreatic ducts, vascular invasion, and diffuse pancreatic enlargement may be noted [18, 19]. The similarities of the imaging findings and clinical features of this case to a pancreatic TB may have led to the misdiagnosis.

However, patients with pancreatic TB may have a past history of tuberculosis, or present with extrapancreatic lesions, especially in the lung and ileocecal region [15]. EUS-FNA is a useful modality for the diagnosis of pancreatic TB, and the presence of granulomas is the most common histologic finding, while it is nonspecific and may occur in other diseases like Crohn's disease, sarcoidosis, and other infectious diseases [16, 18]. By contrast, the presence of mycobacterium tuberculosis DNA obtained by polymerase chain reaction (PCR) and the evidence of tuberculosis acquired by the Ziehl-Neelsen staining or culture in the EUS-FNA specimens provide specific clues to the diagnosis of pancreatic TB [18]. Furthermore, most patients respond well to anti-TB therapy, and there is improvement in clinical symptom and radiologic findings [17].

In general, SPN has an indolent course, but malignant transformation is possible [2, 8]. Surgery is the preferred treatment for SPN, and the outcome of resected SPN is excellent, with a 5-year survival rate of approximately 96.9% [1, 3, 4]. Due to its indolent behavior, function-preserving surgery is recommended to maintain the function of pancreas and improve the postoperative quality of life [3, 5]. However, local recurrence or distant metastases after surgical resection can occur in a few patients. In those cases, second surgery or adjuvant therapy, such as chemotherapy or radiotherapy, may be an option, although the efficacy of adjuvant therapy has been undefined [3, 11]. Some studies had found that a large mass (>8 cm), microscopic malignant features, peritoneal seeding, and distant metastasis were factors for predicting tumor recurrence [9, 11]. Therefore, long-term follow-up is necessary in patients with high risk of recurrence.

In conclusion, SPN is a rare pancreatic tumor with low malignant potential and nonspecific clinical features, and mainly affects young females with imaging indicating a mixed cystic and solid lesion in the pancreas. Therefore, this disease should be considered in the differential diagnosis of pancreatic heterogeneous masses, especially in young women. Multiple diagnostic imaging modalities, particularly MRI, could increase the accuracy of preoperative diagnosis, and EUS-FNA is recommended for difficult cases. Surgical resection is the mainstay treatment for SPN, with an overall favorable prognosis. However, close follow-up must be maintained in patients with high risk of recurrence.

Acknowledgements

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Bo Li, Department of Hepatobiliary Surgery, The Affiliated Hospital of Southwest Medical University, Luzhou 646000, Sichuan Province, P. R. China. Tel: +86-135183-71998; E-mail: liboer2002@126.com

References

[1] Law JK, Ahmed A, Singh VK, Akshintala VS, Olson MT, Raman SP, Ali SZ, Fishman EK, Kamel I, Canto MI, Dal Molin M, Moran RA, Khashab MA, Ahuja N, Goggins M, Hruban RH, Wolfgang CL and Lennon AM. A systematic review of solid-pseudopapillary neoplasms: are these rare lesions? Pancreas 2014; 43: 331-337.

[2] Hanada K, Kurihara K, Itoi T, Katanuma A, Sasaki T, Hara K, Nakamura M, Kimura W, Suzuki Y, Sugiyama M, Ohike N, Fukushima N, Shimizu M, Ishigami K, Gabata T and Okazaki K. Clinical and pathological features of solid pseudopapillary neoplasms of the pancreas: a nationwide multicenter study in Japan. Pancreas 2018; 47: 1019-1026.

[3] Liu M, Liu J, Hu Q, Xu W, Liu W, Zhang Z, Sun Q, Qin Y, Yu X, Ji S and Xu X. Management of solid pseudopapillary neoplasms of pancreas: a single center experience of 243 consecutive patients. Pancreatology 2019; 19: 681-685.

[4] Zalatnai A and Kis-Orha V. Solid-pseudopapillary neoplasms of the pancreas is still an enigma: a clinicopathological review. Pathol Oncol Res 2019; [Epub ahead of print].

[5] Papavramidis T and Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. J Am Coll Surg 2005; 200: 965-972.

[6] Jani N, Dewitt J, Eloubeidi M, Varadarajulu S, Appalaneni V, Hoffman B, Brugge W, Lee K, Khalid A and McGrath K. Endoscopic ultrasound-guided fine-needle aspiration for diagnosis of solid pseudopapillary tumors of the pancreas: a multicenter experience. Endoscopy 2008; 40: 200-203.

[7] Li DL, Li HS, Xu YK, Wang QS, Chen RY and Zhou F. Solid pseudopapillary tumor of the pancreas: clinical features and imaging findings. Clin Imaging 2018; 48: 113-121.

[8] Karatag O, Yenice G, Ozkurt H, Basak M, Basaran C and Yilmaz B. A case of solid pseudopapillary tumor of the pancreas. World J Gastroenterol 2006; 12: 6239-6243.

[9] Kang CM, Choi SH, Kim SC, Lee WJ, Choi DW and Kim SW; Korean Pancreatic Surgery Club. Predicting recurrence of pancreatic solid pseudopapillary tumors after surgical resection: a multicenter analysis in Korea. Ann Surg 2014; 260: 348-355.

[10] Xu M, Li XJ, Zhang XE, Pan FS, Tan Y, Huang TY, Hong Y, Huang GL and Xie XY. Application of contrast-enhanced ultrasound in the diagnosis of solid pseudopapillary tumors of the pancreas: imaging findings compared with contrast-enhanced computed tomography. J Ultrasound Med 2019; 38: 3247-3255.

[11] Kim CW, Han DJ, Kim J, Kim YH, Park JB and Kim SC. Solid pseudopapillary tumor of the pancreas: can malignancy be predicted? Surgery 2011; 149: 625-634.

[12] Law JK, Stoita A, Wever W, Weaver W, Gleeson FC, Dries AM, Blackford A, Kiswani V, Shin EJ, Khashab MA, Canto MI, Singh VK and Lennon AM. Endoscopic ultrasound-guided fine needle aspiration improves the pre-operative diagnostic yield of solid-pseudopapillary neoplasm of the pancreas: an international multicenter case series (with video). Surg Endosc 2014; 28: 2592-2598.

[13] Wright MJ, Javed AA, Saunders T, Zhu Y, Burkhart RA, Yu J, He J, Cameron JL, Makary MA, Wolfgang CL and Weiss MJ. Surgical resection of 78 pancreatic solid pseudopapillary tumors: a 30-year single institutional experience. J Gastrointest Surg 2019; [Epub ahead of print].

[14] Serra S and Chetty R. Revision 2: an immunohistochemical approach and evaluation of solid pseudopapillary tumour of the pancreas. J Clin Pathol 2008; 61: 1153-1159.

[15] Nagar AM, Raut AA, Morani AC, Sanghvi DA, Desai CS and Thapar VB. Pancreatic tuberculosis: a clinical and imaging review of 32 cases. J Comput Assist Tomogr 2009; 33: 136-141.

[16] Puri R, Thandassery RB, Eloubeidi MA and Sud R. Diagnosis of isolated pancreatic tuberculosis: the role of EUS-guided FNA cytology. Gastrointest Endosc 2012; 75: 900-904.

[17] Zacharia GS, Antony R, Kolassery S and Ramachandran TM. Isolated pancreatic tuberculosis masquerading as pancreatic cancer. Gastroenterol Rep (Oxf) 2014; 2: 154-157.

[18] Sharma V, Rana SS, Kumar A and Bhasin DK. Pancreatic tuberculosis. J Gastroenterol Hepatol 2016; 31: 310-318.

[19] Ibrahim GF and Al-Nakshabandi NA. Pancreatic tuberculosis: role of multidetector computed tomography. Can Assoc Radiol J 2011; 62: 260-264.