Int J Clin Exp Pathol 2013;6(6):1051-1059
www.ijcep.com /ISSN:1936-2625/IJCEP1303045

Original Article

Solid-pseudopapillary neoplasm (SPN) of the pancreas: case series and literature review on an enigmatic entity

Nikolaos Vassos[1*], Abbas Agaimy[2*], Peter Klein[1], Werner Hohenberger[1], Roland S Croner[1]

[1]Department of Surgery, University Hospital, Erlangen, Germany; [2]Institute of Pathology, University Hospital, Erlangen, Germany. [*]Equally contributed.

Received March 19, 2013; Accepted April 23, 2013; Epub May 15, 2013; Published June 1, 2013

Abstract: Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare tumor which typically affects young women without significant clinical symptoms. SPN usually shows an indolent behavior and only rare cases recur and/or metastasize after complete resection. We report our experience with four cases of SPN of the pancreas. All four patients were female with an age range of 15-42 years (mean age: 24.5 years). Two patients presented with abdominal pain, one with abdominal mass and one with acute abdominal signs following blunt trauma. Tumor's size ranged from 1 to 16 cm (mean size: 5.5 cm). Two tumors were diagnosed preoperatively through percutaneous core needle biopsy and two underwent surgery without preoperative diagnosis because of high suspicion of SPN based on clinical and radiological findings. By immunohistochemistry, all cases stained strongly for vimentin, progesterone-receptor and beta-catenin (nuclear) and variably with pankeratin and neuroendocrine markers. The proliferation index (Ki-67) was <2% in all cases. After a median follow-up of 40 months (range: 24-57 months), all patients were alive with no evidence of recurrence or metastatic disease. In conclusion, SPN of the pancreas should be considered in the differential diagnosis of any solid and partly cystic pancreatic or upper abdominal mass, particularly in young females. SPN possesses a low malignant potential and complete surgical resection with clear margins is the treatment of choice. Following R0 resection, SPN has an excellent prognosis.

Keywords: Solid pseudopapillary neoplasm, Frantz tumor, pancreas, SPN

Introduction

Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare neoplasm, which represents 0.2-2.7% of pancreatic cancers [1-3]. The name of this entity dates back to 1959 when Virginia Frantz first described a "papillary cystic tumor of the pancreas" in the Armed Forces Institute of Pathology (AFIP) band on tumors of the pancreas. The patient was a 2-year-old boy who died during an attempted pancreatic-duodenectomy [4]. In 1970 Hamoudi et al described the ultrastructural features of the tumor, which led to its acceptance as a separate clinicopathological entity [5]. Until its inclusion in the World Health organization (WHO) classification of pancreatic tumors in 1996 as ''solid pseudopapillary tumor'' of the pancreas [6], this entity has been described by different names in the literature such as "papillary epithelial neoplasm of pancreas", "solid and cystic tumor of the pancreas", "adenocarcinoma of pancreas of childhood", "papillary-cystic tumor" and "solid and papillary epithelial neoplasm" [7], all reflecting histogenesis and biology of this lesion as well. In the current WHO classification [8], SPN is defined as a low-grade malignant neoplasm of the exocrine pancreas. The term SPN gained wide acceptance and is currently the most frequently used name for this entity [9].

To date, around 700 cases have been reported [1], more than two-thirds of them in the last 10 years [10, 11]. This probably reflects the increasing awareness of the clinicopathologic and radiographic features of SPN and the uniformity of the nomenclature used for SPN in the last years. However, the etiology and the differentiation status of SPN remained challenging and still enigmatic [9]. Herein, we present the clinical, histopathological, immunohistochemical and therapeutic characteristics of four SPN cases (**Table 1**) and discuss them together with a review of the literature.

Table 1. Clinicopathological features of 4 patients with SPN

Case	Age	Sex	Clinical presentation	Location (pancreas)	Size (cm)	Therapy	Recurrence Metastases	Follow-up (months)
1	23	F	abdominal pain	head	16	duodenal-panreatectomy	no	24
2	18	F	abdominal pain	head	2.5	distal pancreatectomy and splenectomy	no	28
3	15	F	pain following blunt trauma	corpus/tail	1	local excision	yes (local recurrence)	51
4	42	F	abdominal mass	head	2.5	duodenal-pancreatectomy	no	57

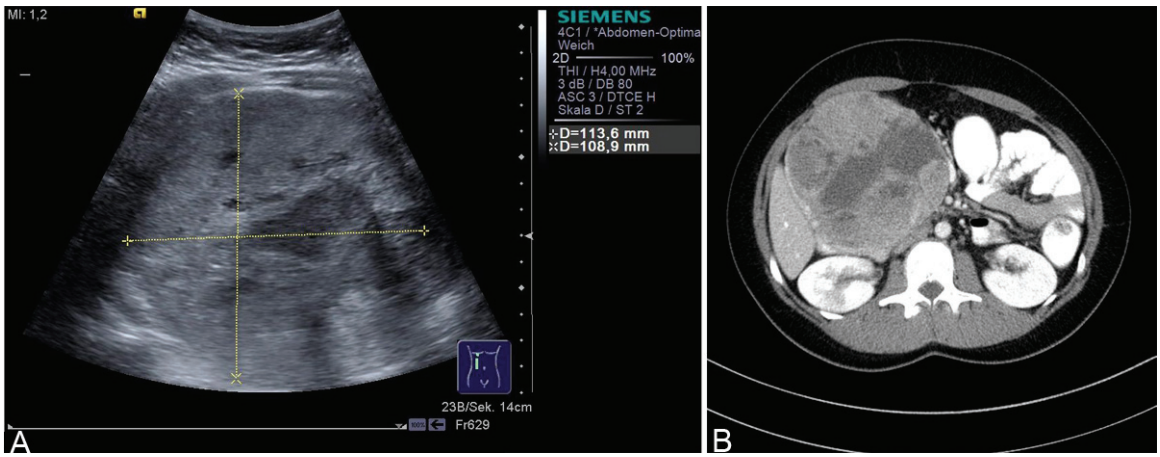

Figure 1. A. Ultrasonography of abdomen showing a circumscribed encapsulated tumor of the upper abdomen. B. Computed tomography of abdomen demonstrating a well-encapsulated, heterogenous mass with solid and cystic lesions arising from the head of pancreas.

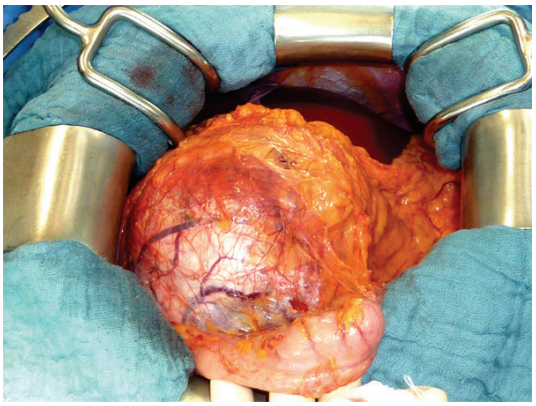

Figure 2. Laparotomy revealing a tumor arising from the head of pancreas.

Case descriptions

Case 1

A 23-year-old woman presented with upper abdominal swelling for 2 months. She was admitted to hospital due to an acute onset of pain. On physical examination, a 10 cm well defined, non-tender, non-pulsatile mass was palpable in the epigastrium and right hypochondrium. Apart from a slightly elevated white cell count, haematological and biochemical studies were unremarkable. The tumor markers (CA19-9, CEA and AFP) were normal. Abdominal ultrasound (US) (**Figure 1A**) and computed tomography (CT) (**Figure 1B**) showed a circumscribed encapsulated heterogeneous mass with solid and cystic areas arising from the head of pancreas, measuring 12 x 12 x 13 cm. No lymphadenopathy or other pathological findings were seen. US-guided percutaneous core needle biopsy was consistent with SPN of the pancreas. The immunohistochemistry was positive for vimentin, progesterone-receptor, beta-catenin (nuclear/cytoplasmic) with variable mostly focal expression of pankeratin, synaptophysin and neuron-specific enolase (NSE). The staining for Islet-1 und TTF1 was negative. The Ki67 index was <2%. Laparotomy confirmed a pancreatic head tumor (**Figure 2**) without evidence of intraabdominal metastasis. The patient underwent a Kausch-Whipple operation

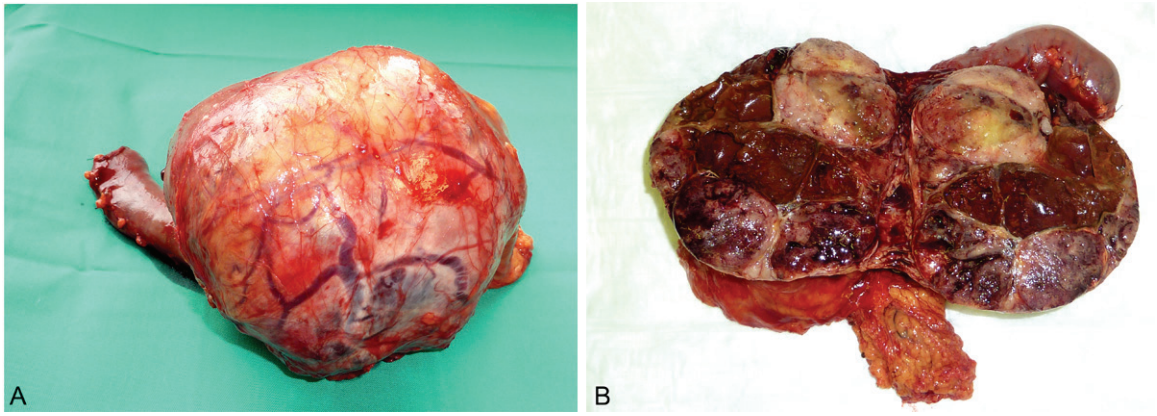

Figure 3. A. Intraoperative specimen. B. Cross section of specimen, showing a tumor composed of mixed cystic and solid components, with haemorrhagic areas.

(**Figure 3A**). The resection margins were free of tumor and none of the 11 lymph nodes recovered was positive for malignancy. On cross section, the tumor measured 16 cm in maximum diameter. It was composed of cystic and solid components with haemorrhagic areas (**Figure 3B**). The final histological report confirmed SPN (**Figure 4**). The patient is currently disease-free 24 months after surgery.

Case 2

A 18-year-old girl, in a good overall health, presented with a history of abdominal pain of 6-month duration. She reported nausea, diarrhoea and headache. Her past medical and surgical history was unremarkable. Clinical examination revealed no fever, pallor, icterus, lymphadenopathy or a palpable mass. All laboratory investigations including tumor markers were within normal limits. Gastroduodenoscopy, coloscopy, electroencephalography and magnetic resonance imaging (MRI) of the cranium (performed because of her headache) showed no abnormalities. Initial abdominal ultrasound was inconclusive. On abdominal CT, a solid mass, 2 cm in diameter, was observed in the pancreatic body and tail, with no evidence of invasion into surrounding tissues but with irregular peripheral calcifications. There was no evidence of abdominal lymph node metastases. On MRI, the mass was well-delineated, mainly solid but with cystic components and had a low signal intensity on T1 and a high intensity on T2. Under the clinical/radiological diagnosis of ''probable Frantz tumor'', decision was made for immediate tumor resection without a preoperative biopsy. A left pancreatectomy and splenectomy was performed. The lesion was 2.5 cm in size and it was removed with clear margins (R0). Seven biopsied lymph nodes were negative for tumor. Histological and immunohistochemical findings were similar to Case 1. Necrosis, vascular invasion and perineural invasion were absent. She is currently disease-free 28 months after surgery.

Case 3

A 15-year-old girl was initially admitted to a peripheral hospital for acute epigastric pain, presented after a fall. The MRT scan showed an intraabdominal hematoma, involving the pancreas. A diagnostic laparoscopy revealed a necr otic tumor in the upper abdomen between lesser curvature and lobe of the liver. Because a needle biopsy could not be performed and the organ primarily involved was not clear, a laparotomy was performed with local excision (enucleation) of the tumor from the pancreatic head. Pathologic examination of the specimen confirmed SPN with positive margins (R1). Five months later, MRI scan demonstrated a 3.5 x 2.4 cm encapsulated cystic and solid tumor of low and high signal intensity on T1 and T2, respectively. The pancreatic duct was dilated. Endosonography confirmed these findings. An explorative laparotomy was carried out and a distal pancreatectomy combined with splenectomy was performed. Histological review of the specimen revealed multiple recurrent SPN nodules, measuring from 0.5 to 1.5 cm in diameter, which were removed in toto (R0). There were no mitoses, atypia, vascular invasion or lymph

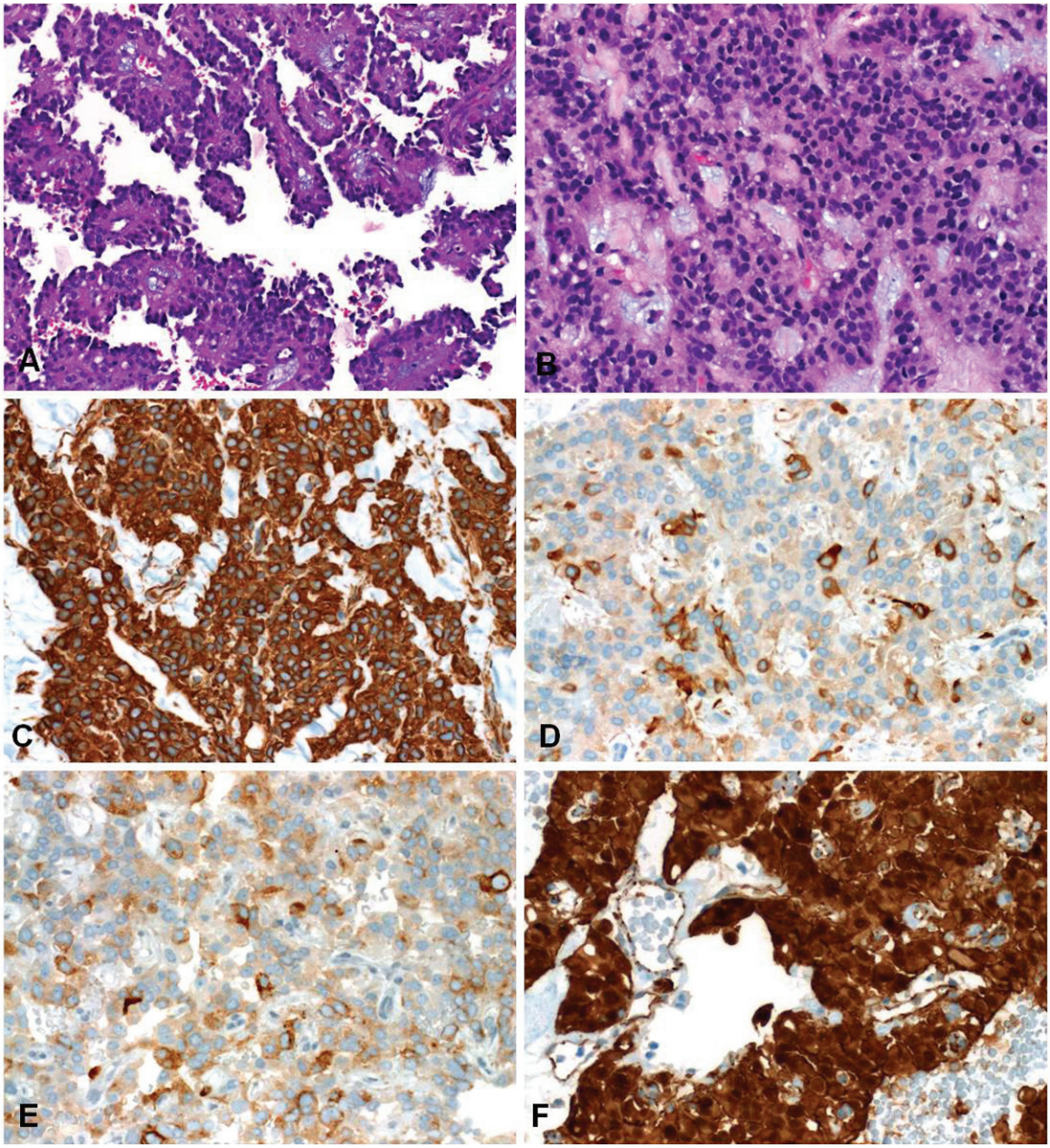

Figure 4. Pathological features of SPN. A. the tumors showed papillary structures with intervening cyst-like spaces. B. solid areas showed monotonous cell population with myxohyline stroma. Immunohistochemistry revealed strong and diffuse expression of vimentin (C), scattered positivity for pankeratin (D) and chromogranin A (E) and strong nuclear and cytoplasmic reactivity for beta-catenin (F).

node metastasis (0/22). On immunohistochemical study, the tumor cells showed similar marker profile as other cases. The patient remains disease free at last follow-up 51 months after surgery.

Case 4

A 42-year-old woman presented with a mass in the upper abdomen since 2 months, which has been gradually increasing in size. There was a previous history of biliary pancreatitis and a cholecystectomy due to cholecystitis. All laboratory investigations, including tumor markers, were within the normal ranges. CT-guided percutaneous core needle biopsy was consistent with SPN of the pancreas. Pancreaticoduodenectomy was performed by a Kausch-Whipple procedure. The lesion measured 2.5 cm and showed a yellowish cut-surface with hemor-

rhagic and necrotic areas admixed with solid areas. There was no invasion into the peripancreatic fat or involvement of regional lymph node (0/11). The surgical margins were free of tumor tissue. Histological and Immunohistoc hemical findings were similar to other cases. The postoperative course was uneventful. The patient is currently alive without evidence of disease 57 months after surgery.

Discussion

The spectrum of cystic and solid and cystic neoplasms of the pancreas is wide and encompasses at least 14 different tumor types [12]. However, the most commonly encountered cystic neoplasms of the pancreas may be classified into five categories: serous microcystic adenoma, mucinous cystic neoplasms (cystadenoma or cystadenocarcinoma), intraductal papillary mucinous neoplasm (IPMN), cystic neuroendocrine neoplasms and solid pseudopapillary neoplasm of the pancreas (SPN). Among these uncommon pancreatic tumors, SPN represents an exceedingly rare entity.

SPN usually affects young women at an average age of 28 years with a female: male ratio of 10:1 [13]. About 20-25% of the cases are seen in pediatric patients [1]. One of our patients (case 4), presented at a relatively higher age (42 yrs) compared to most reported cases [9]. However, sporadic rare cases in men and in the elderly have also been reported [9, 14]. Certainly, our case series illustrates many of the salient features of this tumor, such as higher frequency in females, indolent clinical course and potential curability after complete surgical removal (R0).

The clinical presentation of SPN is nonspecific. Most of patients present with non-specific symptoms including abdominal discomfort, mild abdominal pain or palpable abdominal mass [15]. Due to its slow growth, SPN often remains asymptomatic, until the tumor has enlarged considerably. Accordingly, many are detected incidentally on diagnostic imaging for unrelated diseases or after a blunt abdominal trauma [16] - as presented in our case 3. Other uncommon clinical symptoms are poor appetite and nausea, loss of weight, vomiting and (very rarely) jaundice and hematemesis [15, 17].

The most common localization of SPN is the tail of the pancreas, followed by the head and the body. Unusual presentations include multicentric tumors in the pancreas and extrapancreatic sites, such as the mesocolon, retroperitoneum, omentum, liver and duodenum, possibly representing synchronous tumor spread [1, 14].

SPN has been postulated to arise from primitive pancreatic cells (e.g. acinar cells, ductal epithelium or endocrine cells) [18] or from cell lines of the female genital bud [2]. The key histological hallmarks are solid and pseudopapillary proliferation of homomorphous cells without increased mitoses or cytological atypia [19, 20]. Beta-catenin mutations, alterations of the wnt pathway and disorganisation of E-cadherin have been implicated in the development of SPN [21, 22]. CyclinD1, a downstream transcriptional target of Beta-catenin, is over expressed in most cases [20]. The common expression of progesterone receptor and the strong predilection for females suggest that it might be a hormone-dependent tumor [23]. However, estrogen receptors have not been demonstrated. Another hypothesis is an extrapancreatic origin from genital ridge anlage-related cells [19, 20].

Concerning diagnostics, routine laboratory parameters and tumor markers are of no help. Ultrasound and CT/MRI-scans typically show a large well-circumscribed, heterogeneous mass with varying solid and cystic components, generally demarcated by a peripheral capsule and occasional calcification. MRI is superior to CT in distinguishing certain tissue characteristics, such as haemorrhage, cystic degeneration or the presence of a capsule and may suggest correct diagnosis [24]. Angiography usually demonstrates an avascular or hypovascular tumor and may help delineate the mass from other involved adjacent structures [24]. Given the good prognosis after adequate resection, preoperative diagnosis would be helpful in surgical planning. The diagnosis can be confirmed by an endoscopic ultrasound scan (EUS) with fine-needle aspiration (FNA) biopsy [25, 26] or percutaneous core needle biopsy with ultrasound or CT-guidance [27]. The latter method was used in 2 of our four patients without any complications and definite preoperative diagnosis could be made in these cases.

Histologically, SPN are commonly well-circumscribed and -encapsulated with irregular degen-

erative cystic cavities and hemorrhages. The tumor contains a mixture of solid, cystic, and pseudopapillary patterns in various proportions [28]. The diagnosis can be confirmed by immunohistochemical analysis [28-30]. In some cases, reactivity with epithelial markers and S-100 was described [28], but the expression of epithelial markers (AEI/AE3, CAM 5.2) is usually focal and weak. SPN cells may also reveal focal immunoreactivity for synaptophysin and other neuroendocrine markers. abnormal nuclear and cytoplasmic beta-catenin expression and presence of progesterone receptor are fairly common features of SPN. In addition, SPN express galectin-3 and CD10, all of which are useful in differentiating SPN from pancreatic neuroendocrine tumors. APC/ beta-catenin pathway and cyclin-D1 alterations are observed in over 90% of cases [30]. The low Ki-67 index (≤5%) indicates a slow growth of the tumor.

The differential diagnosis of SPN is wide and includes in particular solid and cystic lesions such as serous microcystic adenoma, cystadenocarcinoma, mucinous cystic neoplasms, cystic neuroendocrine tumors, cystic acinar cell carcinoma, teratoma, pancreatoblastoma as well as a variety of congenital and acquired dysontogenetic, post-inflammatory and infectious cysts [31]. However, the typical constellation of a pancreas-associated solid and cystic upper abdominal mass with or without calcifications in a young woman should always alert to the possibility of SPN.

Unlike most other pancreatic tumors, SPN usually behaves in an indolent fashion, but certainly has a low malignant potential with generally excellent prognosis. Malignant behavior is observed in about 10-15% of the cases; some of them have been treated with aggressive resection. Metastases were described in regional lymph nodes, liver and peritoneum/ omentum [1]. Given their low malignant potential and the excellent overall prognosis, surgical resection has been the standard of care in the management of SPN [32]. Tumor enucleation and incomplete excision should be avoided due to the risk of tumor dissemination, development of a pancreatic fistula [33] and the higher recurrence rare, as shown in our case 3. Extensive lymphatic dissection or resection of adjacent structures is not warranted since lymph node metastasis are found in <2% [9, 34]. In our cases, all histologically examined lymph nodes were negative for metastatic disease. Tumor size should not be regarded as a predictor of unresectability because lesions as large as 30 cm may be resected without problems [35]. Unlike other pancreatic tumors, the stage of the disease does not play any role for the treatment of SPN [9]. If veins are infiltrated, vascular en-bloc resection and reconstruction with vein grafts has been proposed and the results were encouraging [9].

Other therapeutic options such chemotherapy and radiotherapy have been applied in some cases [36], but they basically have no place with this entity The role of neoadjuvant chemotherapy is described in a case of advanced disease with invasion of the superior mesenteric vein with good response [37], which is however a clear sign of non-indicated treatment. To avoid this kind of overtreatment, preoperative core needle biopsy should be taken, which is a safe procedure in an experienced center and clearly enables the true diagnosis of this entity Certainly, there is no need for neoadjuvant chemotherapy like some experimental regimes which have been used including 5-fluorouracil, doxorubicin, streptozocin, cisplatin, topotecan, iphosphamide and etoposide, however without significant clinical response [9]. A favorable response to radiotherapy in locally advanced unresectable disease has also been reported [38]. Fried et al observed substantial shrinkage of an unresectable tumor after 6 weeks of radiotherapy [36].

Overall 5-year survival approaches 97% in patients undergoing surgical resection [9, 39]. Death ascribed directly to the tumor is rare and long-term survival (years to decades) has been described even in the presence of asymptomatic disseminated disease [39]. Clear-cut criteria of malignancy have not been established and it is difficult to predict the behavior of SPN on histomorphological grounds. The Ki-67 index has been suggested as a potential indicator of malignant potential and poor outcome of SPN [29]. Features that may indicate an aggressive clinical behavior are venous invasion, diffuse infiltrative growth pattern, extensive tumor necrosis, significant nuclear atypia, high mitotic count, nuclear pleomorphism, dedifferentiation, DNA aneuploidy, double loss of X chromosomes, trisomy of chromosome 3 and unbalanced translocation between chromosomes 13

and 17 [28, 29]. SPN affecting elderly males have been associated with increased likelihood of malignancy [20, 40].

Conclusion

In conclusion, SPN is a rare pancreatic neoplasm of unclear histogenesis that typically affects young females without significant symptoms. Appearance on imaging is fairly characteristic and may suggest diagnosis, but in unclear cases preoperative diagnosis should be accomplished by percutaneous CT-guided core needle biopsy in order to avoid not indicated preoperative chemotherapy or radiotherapy. Complete surgical resection of the tumor is the only effective treatment option. Whenever possible, surgery seems to be justified for local recurrence or metastasis. SPN should be considered in the differential diagnosis of any solid and partly cystic pancreatic or upper abdominal mass, particularly in young females.

Conflict of interest

All authors have declared no conflicts of interest.

Address correspondence to: Dr. Nikolaos Vassos, Department of Surgery, University Hospital Erlangen, Krankenhausstraße 12, D-91054 Erlangen, Germany. Tel: +49-9131-85-33296; Fax: +49-9131-85-36294; E-mail: nikolaos.vassos@uk-erlangen.de

References

[1] Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in the English literature. J Am Coll Surg 2005; 2: 965-72.

[2] Tang LH, Aydin H, Brennan MF, Klinstra DS. Clinically aggressive solid pseudopapillary tumor of pancreas: A report of cases with components of undifferentiated carcinoma and a comparative clinicopathologic analysis of 34 conventional cases. Am J Surg Pathol 2005; 29: 51-2.

[3] de Castro SM, Singhal D, Aronson DC, Busch OR, van Gulik TM, Obertop H, Gouma DJ. Management of solid-pseudopapillary neoplasms of the pancreas: a comparison with standard pancreatic neoplasms. World J Surg 2007; 31: 1129-34.

[4] Frantz VK. Tumors of the pancreas. In: Bumberg CW, editors. Atlas of Tumor Pathology, VII. Fascicles 27 and 28. Washington, DC: Armed Forced Institute of Pathology 1959; pp: 32-33.

[5] Hamoudi AB, Misugi K, Grosfeld JL, Reiner CB. Papillary epithelial neoplasm of pancreas in a child. Report of a case with electron microscopy. Cancer 1970; 26: 1126-30.

[6] Kloppel G, Solcia E, Longnecker DS, Capella C et al. Histological typing of tumors of the exocrine pancreas. In: World Health Organisation International Histological Classification of Tumors. 2nd ed. Berlin, Heidelberg, New York: Springer 1996; pp: 8452/1.

[7] Solcia E, Capella C, Kloeppel G. Tumors of the pancreas. In: Atlas of Tumor Pathology, 3rd series, fasciale 20. Washington, DC: Armed Forces Institute of Pathology 1997.

[8] Klöppel G, Hruban RH, Klimstra DS, Maitra A, Morohoshi T, Notohara K, Shimizu M, Terris B. Solid-pseudopapillary tumor of pancreas. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, editors. World Health Organization Classification of Tumours of the digestive system. Lyon: IARC 2010; pp: 327-330.

[9] Martin RC, Klimstra DS, Brennan MF, Conlon KC. Solid-pseudopapillary tumor of pancreas: A surgical enigma? Ann Surg Oncol 2002; 9: 35-40.

[10] Cai H, Zhou M, Hu Y, He H, Chen J, Tian W, Deng Y. Solid-pseudopapillary neoplasms of the pancreas: clinical and pathological features of 33 cases. Surg Today 2013; 43: 148-54.

[11] Yang F, Jin C, Long J, Yu XJ, Xu J, Di Y, Li J, Fu de L, Ni QX. Solid pseudopapillary tumor of the pancreas: a case series of 26 consecutive patients. Am J Surg 2009; 198: 210-5.

[12] Kloppel G, Kosmahl M. Cystic lesions and neoplasms of the pancreas. The features are becoming clearer. Pancreatology 2001; 1: 648-55.

[13] 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 Chinese literature. World J Gastroenterol 2010; 16: 1209-14.

[14] Klöppel G, Maurer R, Hofmann E, Lüthold K, Oscarson J, Forsby N, Ihse I, Ljungberg O, Heitz PU. Solid-cystic (papillary-cystic) tumors within and outside the pancreas in men: report of two patients. Virchows Arch 1991; 418: 179-83.

[15] Reddy S, Cameron JL, Scudiere J, Hruban RH, Fishman EK, Ahuja N, Pawlik TM, Edil BH, Schulick RD, Wolfgang CL. Surgical management of solid-pseudopapillary neoplasms of the pancreas: a large single-institutional series. J Amer Coll Surg 2009; 208: 950-9.

[16] Mozaffar M, Abdollahi SM. Acute post-traumatic presentation of a solid-pseudopapillary tumor of the pancreas: a case report. Iran J Cancer Prev 2008; 1: 43-51.

[17] Apostolidis S, Papavramidis TS, Zatagias A, Michalopoulos A, Papadopoulos VN, Paramythiotis D, Harlaftis N. Hematemesis, a very rare presentation of solid-pseudopapillary tumors of the pancreas: a case report. J Med Case Reports 2008; 2: 271.

[18] Klöppel G, Morohoshi T, John HD, Oehmichen W, Opitz K, Angelkort A, Lietz H, Rückert K. Solid and cystic acinar cell tumor of the pancreas: a tumor in young women with favourable prognosis. Virchows Arch A Pathol Anat Histol 1981; 392: 171-83.

[19] Matos JM, Grützmann R, Agaram NP, Saeger HD, Kumar HR, Lillemoe KD, Schmidt CM. Solid pseudopapillary tumor neoplasms of the pancreas: A multi-institutional study of 21 patients. J Surg Res 2009; 157: 137-42.

[20] Geers C, Moulin P, Gigot JF, Weynand B, Deprez P, Rahier J, Sempoux C. Solid and pseudopapillary tumor of the pancreas-review and new insights into pathogenesis. Am J Surg Pathol 2006; 30: 1243-49.

[21] El-Bahrawy MA, Rowan A, Horncastle D, Tomlinson I, Theis BA, Russell RC, Stamp G. E-cadherin/catenin complex status in solid-pseudopapillary tumor of the pancreas. Am J Surg Pathol 2008; 32: 1-7.

[22] Tanaka Y, Kato K, Notohara K, Hojo H, Ijiri R, Miyake T, Nagahara N, Sasaki F, Kitagawa N, Nakatani Y, Kobayashi Y. Frequent beta-catenin mutation and cytoplasmic/nuclear accumulation in pancreatic solid-pseudopapillary neoplasm. Cancer Res 2001; 61: 8401-4.

[23] Morales A, Ruíz Molina JM, Estéves HO, Robles-Díaz G, Díaz-Sánchez V. Papillary-cystic neoplasm of the pancreas. A sex-steroid dependent tumor. Int J Pancreatol 1998; 24: 219-25.

[24] Cantisani V, Mortele KJ, Levy A, Glickman JN, Ricci P, Passariello R, Ros PR, Silverman SG. MR imaging features of solid pseudopapillary tumor of the pancreas in adult and pediatric patients. Am J Roentgenol 2003; 181: 395-401.

[25] Jani N, Dewitt J, Eloubeidi M, Varadarajulu S, Appalaneni V, Hoffman B, Brugge W, Lee K, Khalid A, McGrath K. Endoscopic ultrasound-guided fine-needle aspiration for the diagnosis of solid-pseudopapillary tumors of the pancreas: a multicenter experience. Endoscopy 2008; 40: 200-3.

[26] Voss M, Hammel P, Molas G, Palazzo L, Dancour A, O'Toole D, Terris B, Degott C, Bernades P, Ruszniewski P. Value of endoscopic ultrasound guided fine needle aspiration biopsy in the diagnosis of solid pancreatic masses. Gut 2000; 6: 244-9.

[27] Zamboni GA, D'Onofrio M, Principe F, Pozzi-Mucelli R. Focal pancreatic lesions: accuracy and complications of US-guided fine-needle aspiration cytology. Abdom Imaging 2010; 24: 362-6.

[28] Pettinato G, Manivel JC, Ravetto C, Terracciano LM, Gould EW, di Tuoro A, Jaszcz W, Alberes-Saavedra J. Papillary cystic tumor of the pancreas. A clinicopathologic study of 20 cases with cytologic, immunohistochemical, ultrastructural and flow cytometric observations and a review of the literature. Am J Clin Pathol 1992; 98: 478-88.

[29] Serra S, Chetty R. Revision 2: an immunohistochemical approach and evaluation of solid pseudopapillary tumour of the pancreas. J Clin Pathol 2008; 61: 1153-9.

[30] Chetty R, Serra S. Loss of expression of E-cadherin in solid pseudopapillary tumors of the pancreas. Pancreas 2009; 38: 338-9.

[31] Warshaw AL, Compton CC, Lewandrowski K, Cardenosa G, Mueller PR. Cystic tumors of the pancreas. Ann Surg 1990; 212: 432-45.

[32] Hashimoto M, Watanabe G, Matsuda M, Mori M. Serous cystic neoplasm of the pancreas-indications for surgery. Hepatogastroenterology 2006; 53: 950-2.

[33] Patil TB, Shrikhande SV, Kanhere HA, Saoji RR, Ramadwar MR, Shukla PJ. Solid pseudopapillary neoplasm of the pancreas: a single institution experience of 14 cases. HPB 2006; 8: 148-50.

[34] Yoon DY, Hines OJ, Bilchik AJ, Lewin K, Cortina G, Reber HA. Solid and papillary epithelial neoplasms of the pancreas: aggressive resection for cure. Am Surg 2001; 67: 1195-9.

[35] Vollmer CM, Dixon W, Grant DR. Management of a solid pseudopapillary tumor of the pancreas with liver metastases. HPB 2003; 5: 264-7.

[36] Fried P, Cooper J, Balthazar E, Fazzini E, Newall J. The role of radiotherapy in the treatment of solid and papillary neoplasms of the pancreas. Cancer 1985; 56: 2783-5.

[37] Das G, Bhuyan C, Das BK, Sharma JD, Saikia BJ, Purkystha J. Spleen-preserving distal pancreatectomy following neoadjuvant chemotherapy for papillary solid and cystic neoplasm of pancreas. Ind J Gastroenterology 2004; 23: 188-9.

[38] Matsunou H, Konishi F. Papillary-cystic neoplasm of the pancreas: a clinicopathologic study concerning the tumor aging and malignancy of nine cases. Cancer 1990; 65: 283-91.

[39] Tang LH, Aydin H, Brennan MF, Klinstra DS. Clinically aggressive solid pseudopapillary tumor of pancreas: A report of cases with components of undifferentiated carcinoma and a comparative clinicopathologic analysis of 34

conventional cases. Am J Surg Pathol 2005; 29: 512-9.

[40] Machado MC, Machado MA, Bacchella T, Jukemura J, Almeida JL, Cunha JE. Solid pseudopapillary neoplasm of the pancreas: distinct patterns of onset, diagnosis and prognosis for male versus female patients. Surgery 2008; 143: 29-34.