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Solid and Pseudopapillary Tumor of the Pancreas in Saudi Patients: Clinicopathological and Immunohistochemical Evaluation

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Abstract. Solid pseudopapillary tumor of the pancreas is a rare low-grade malignancy that has distinct clinicopathological features. It occurs at a young age and almost exclusively in females. Five patients with this rare pancreatic neoplasm excised at two referral hospitals in the western province of Saudi Arabia; King Faisal Specialist Hospital and Research Center and King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between 2001 and 2006. The clinical and pathological findings were reviewed. A specific panel of immunohistochemistry analysis was performed. All five patients were females whose ages ranged between 18 and 23 years. Three patients presented with abdominal pain/discomfort and two patients with abdominal mass. The tumor size ranged between 6 and 12 cm. All five cases were positive for vimentin, CD56, CD10, neuron-specific enolase and beta catenin. All patients were treated surgically and all of them are in good health with a follow–up period between 1-4 years. Solid pseudopapillary tumor of the pancreas should be considered in the differential diagnosis of any solid or partly cystic pancreatic mass, particularly in young females. Pathologists should be aware of the classic morphological features of solid pseudopapillary tumor of the pancreas. Adequate surgical intervention is associated with an excellent prognosis.

Keywords: Solid pseudopapillary tumor, Neoplasm of pancreas, Solid cystic papillary tumor.

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Introduction

Solid pseudopapillary tumor of the pancreas (SPTP) is a distinctive and relatively uncommon clinicopathological entity that was first described by Frantz (1959)[1]. SPTP accounts for about 1-3% of all pancreatic tumors[2-4]. One possible explanation for the increase in diagnosis recently is greater awareness of the tumor, as well as a better understanding of its pathologic and radiographic features[5]. We diagnosed and reported 5 cases of SPTP in Saudi patients.

Methods

A retrospective review and analysis were done in patients who had pancreatic neoplasm excised at King Abdulaziz University Hospital and King Faisal Specialist Hospital and Research Center, Jeddah, Kingdom of Saudi Arabia (KSA), from 2001 to 2006. We identified 5 cases of SPTP that were surgically treated. The slides were reviewed and immunohistochemistry analysis was performed on archived material; the panel included Pankeratin, CK7, CK20, vimentin, CD10, CD56, alpha-1-antitrypsin, alpha-1-antichymotrypsin, neuron-specific enolase, synaptophysin, beta-catenin, progesterone and estrogen receptors.

Results

We described 5 cases of SPTPs diagnosed in Saudi patients. Summary of the clinical findings of the cases is demonstrated in Table 1.

Table 1. Summary of the clinical findings of the cases of SPTP.

Case	Age/sex	Clinical presentation	Location in pancreas	Evidence of metastasis	Other findings
1	19 year/Female	Abdominal pain	Pancreas, body	No	–
2	23 year/Female	Abdominal pain	Pancreas, body	No	–
3	21 year/Female	Abdominal mass	Pancreas, tail	No	Associated mature cystic teratoma
4	18 year/Female	Abdominal pain	Pancreas, tail	No	–
5	22 year/Female	Abdominal mass	Pancreas, body	No	–

All five patients were females who ranged in age between 18 and 23 years. Three patients presented with abdominal pain/discomfort and two patients presented with abdominal mass. The tumor size ranged between

6 and 12 cm. All of the cases were well circumscribed and two of them showed focal areas of hemorrhage (Fig. 1). All of the cases showed the classic microscopic appearance of SPTP. They were composed of sheets of medium-sized relatively uniform round to oval cells with clear to eosinophilic cytoplasm and central ovoid nuclei with occasional nuclear grooves. There were no prominent nucleoli or increase in mitotic figures in any of the cases. All of the cases showed papillary structures covered by epithelium (Fig. 2). Two cases (Cases 2 and 3) showed prominent areas of hemorrhage with foam cells, giant cells and cholesterol clefts. Immunohistochemistry showed that all five cases were positive for vimentin, CD56, CD10, alpha-1-antichymotrypsin, NSE and beta catenin (Fig. 2). Two were focally positive for synaptophysin. All were negative for pankeratin and chromogranin. Patient 3 also had associated ovarian mature cystic teratoma. All patients were treated surgically and all of them are in good health with a follow-up period between 1-4 years.

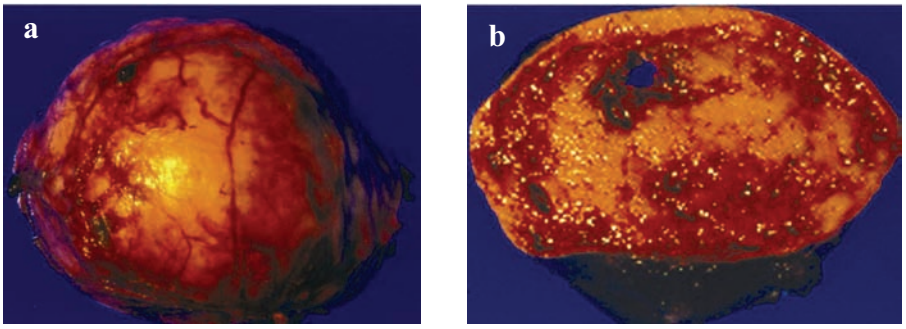

Fig. 1. (a) Gross image of one of the SPTP cases (Patient 3) shows the well-circumscribed large tumor (12 cm). (b) Cross section of the above described tumor reveals area of hemorrhage.

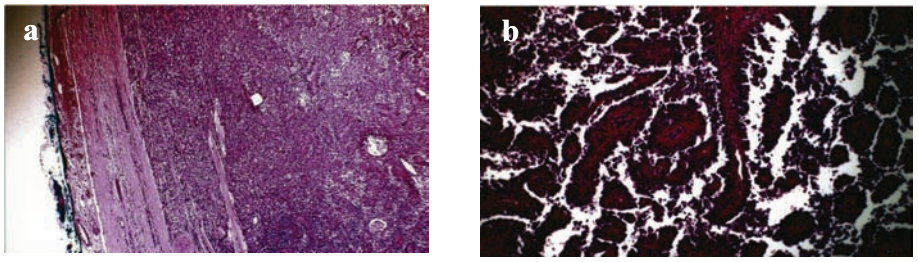

Fig. 2. (a) Microscopic section of one of the SPTP tumors shows a classic picture composed of pseudopapillary structures covered by monotonous bland looking cells (Hematoxylen and eosin stain, original power ×200). (b) Higher power shows pseudopapillary structures (Hematoxylen and eosin stain, original power ×400).

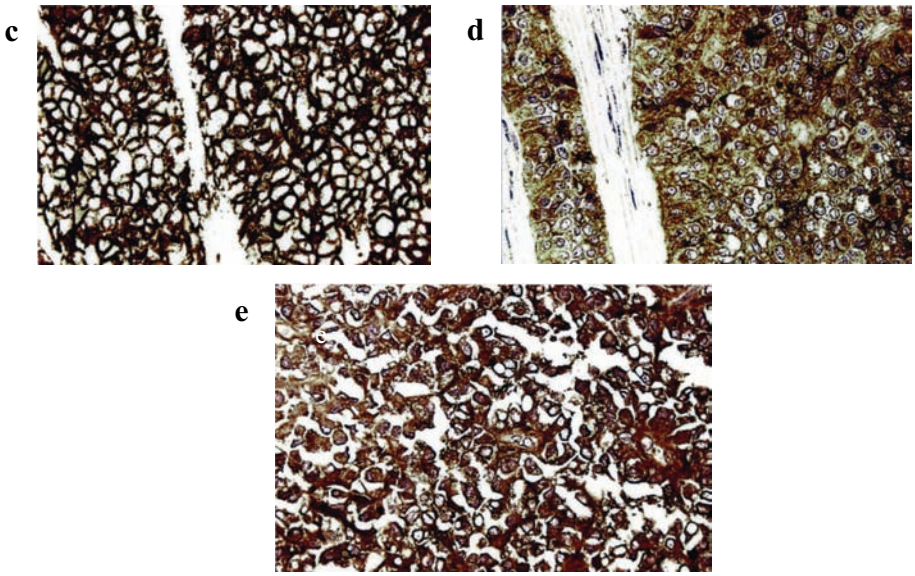

Fig. 2. (c) Immunohistochemical study shows positive staining for CD56.
(d) Immunohistochemical study shows positive staining for CD10.
(e) Immunohistochemical study shows positive staining for alpha-1-antichymotrypsin.

Discussion

Since it has been described, various other names have been used for this type of tumor, including Frantz's tumor, solid and papillary epithelial neoplasm, solid and cystic tumors, papillary - cystic tumor and solid pseudopapillary tumor of the pancreas. The last entity is the most recent terminology used (WHO, 1996). This current study shows that all five patients were females who ranged in age between 18 and 23 years. Three patients presented with abdominal pain/discomfort and two patients with abdominal mass. SPTPs were reported in the literature as case reports and a few large series[6-8]. More than 90% of the patients were young females. In previous studies, follow-up data indicated that this tumor is a low-grade malignant neoplasm found primarily in young women[6,9,10]. The only available report from KSA described a case of a 12-year-old boy having a solid-pseudopapillary tumor of the pancreas presenting with a tender upper abdominal mass following a slight trauma[11]. The presenting features of SPTP are relatively non-specific. Because of patients' lack of obvious symptoms, this tumor is sometimes diagnosed accidentally by abdominal examination, ultrasound, CT scan, or MR

imaging of the abdomen[12]. The tumors are usually found incidentally, and they generally cause mild abdominal symptoms such as abdominal discomfort or chronic, acute pain and rarely causes weight loss, nausea, vomiting[13-15]. Physical examination might show a palpable mass and epigastric tenderness[16]. SPTP usually arises in the tail, the body, or occasionally in the head of the pancreas[17,18]. Rarely are these tumors found due to hemoperitoneum from rupture of the tumor[16,19]. Laboratory investigations provide little additional information[20]. Elevated serum tumor markers (CEA, CA19-9) have not been described with SPTP[21]. The origin and histogenesis of this tumor is controversial and little is known about it[16,22,23]. The overall features suggesting an origin from pluripotent stem cells are probably of ductal origin. Due to the prevalence of this tumor in females, it has been suggested that the sex hormones play a role in its growth, but not its genesis[24]. In the present study's cases, the tumor size ranged between 6 and 12 cm. All of the cases were well circumscribed and two of them showed focal areas of hemorrhage. The neoplasm was generally encapsulated and was well demarcated from the remaining pancreas, measuring 8-10 cm on average[21]. The cut surface revealed lobulated, light brown solid areas mixed with a zone of hemorrhage and necrosis, as well as cystic spaces filled with necrotic debris[23]. SPTP histologic appearances are very distinctive and diagnostic. It has mixed histological features including: a solid monomorphous pattern with variable sclerosis, a pseudopapillary, trabecular and microcystic patterns[25]. All of these cases showed the classic microscopic appearance of SPTP; they were composed of sheets of medium-sized cells with papillary structures covered by relatively uniform round to oval cells with clear to eosinophilic cytoplasm and central ovoid nuclei with occasional nuclear grooves. There were no prominent nucleoli or increase in mitotic figures in any of the cases. Two cases (Cases 2 and 3) showed prominent areas of hemorrhage with foam cells, giant cells and cholesterol clefts. Immunohistochemistry showed that all five cases were positive for vimentin, CD56, CD10, alpha-1-antichymotrypsin, NSE and beta catenin. Two were focally positive for synaptophysin oestrogen, and progesterone receptors have been demonstrated by biochemical assays in four solid-pseudopapillary tumors[26]. Immunohistologically, some studies fail to detect nuclear oestrogen receptors[27]. All of the study's cases were positive for beta catenin. Almost all SPTP harbored alterations in the The adenomatous polyposis coli (APC)/beta-catenin pathway. Nuclear accumulation of

beta-catenin protein was present in 95% (19 of 20), and activating beta-catenin oncogene mutations were identified in 90% (18 of 20) of the SPTP[28,29]. Markers like vimentin, alpha-1-antitrypsin, NSE and the progesterone receptor were present in more than 90% of SPTP[23,27]. Few case reports suggested that the preoperative diagnosis of SPTP is possible by using fine needle aspiration (FNA), especially in clinically typical examples[15,22,30]. On CT scan, SPTP appeared as sharply circumscribed, well-encapsulated, heterogeneous and hypodense lesions[14,18,31]. MRI offers good visualization of hemorrhagic areas[30]. On MRI, SPTPs were sharply demarcated and had areas of high signal intensity corresponding to foci of hemorrhage[15]. Studies have shown that the solid areas that were enhanced after contrast administration were noted predominantly at the periphery, whereas the cystic components were more centrally located[6,10,12]. There may be calcification at the periphery of the mass and also intravenous contrast enhancement[32]. However, none of these radiological features were diagnostic. The accuracy of CT scan in characterization of cystic pancreatic masses was about 60% in one series[30]. Based on the radiological findings, the differential diagnosis of SPTP includes any cystic and/or solid pancreatic process such as: hemorrhagic pseudocyst, parasitic hydatid cyst, and other common cystic neoplasms of the pancreas, such as serous cystadenoma or cystadenocarcinoma, mucinous cystic neoplasms[12,18,33,34]. Patient 3 also had associated ovarian mature cystic teratoma. All patients were treated surgically and all of them are in good health with a follow-up period between 1-4 years. Complete resection is the treatment of choice for SPTP[20], and the standard therapy should involve complete removal of the tumor, the associated lymph nodes, the involved pancreas and any adjacent involved organs. Local invasion, recurrence, or limited metastases should not be considered contraindications to resection[35,36].

Aggressive attempts at complete resection seem to be warranted because recurrence has not been reported after complete resection of local disease[7,37]. The incidence of malignancy is thought to be about 15%. Even in the reported cases that were considered malignant, the survival of patients was prolonged after adequate surgical resection[7,8,12,25,38]. Prolonged survival in patients with residual disease after surgery, and in patients with unresectable tumors, are well reported in the literature[7,39]. Surgical debulking may help to reduce the tumor load and thereby prolong survival[8,36,40,41]. Matusuda *et al.* reported a

case of multiple hepatic metastases which responded to chemo-embolisation of the tumor[42]; Fried *et al.* observed substantial shrinkage of an unresectable tumor after 6 weeks of radiotherapy[10]. The use of radiotherapy has only been reported in one case, in which the tumor was deemed unresectable as it involved the porta hepatis[10]. The patient was free of disease at the 3-year follow up. Common sites of metastasis include liver (42%), peritoneum (42%) and lymph nodes (25%)[2,12,25,38]. The morphology of the metastases in most cases is similar to that of the primary tumor[3,27,36]. Although criteria of malignancy have not been clearly established[21], unequivocal perineural invasion or angioinvasion, cellular atypia with or without deep invasion into the surrounding tissue is taken to indicate malignant behavior[23,39]. In the current study we described 5 cases of SPTP resected from Saudi patients and we conclude that SPTP should be considered in the differential diagnosis of any solid or partly cystic pancreatic mass particularly in young females. Adequate surgical intervention is associated with an excellent prognosis.

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الورم الحليمي الجامد للبنكرياس ــ الصفات النسيجية والإكلينيكية والمناعية في المرضى السعوديين

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المستخلص. يعتبر الورم الحليمي الجامد للبنكرياس من الأورام النادرة ذات الدرجة الدنيا من السرطان والتي تتميز بصفات إكلينيكية والنسيجية مميزة. يحصل هذا الورم غالبا في النساء الصغيرات. تم تشخيص خمس حالات من هذا الورم وأزيلت جراحيا او تم مراجعة العينات النسيجية لها في مستشفيي جامعة الملك عبدالعزيز ومستشفى الملك فيصل التخصصي بجدة وذلك للفترة ما بين ٢٠٠١ و٢٠٠٦م تمت مراجعة الصفات الإكلينيكية والنسيجية وتم عمل مجموعة من الصبغات المناعية على العينات النسيجية لهذه الأورام . كل الحالات الخمس كانت في نساء تتراوح أعمارهن ما بين ١٨و ٢٣، سنة ثلاثة من المرضى، كانوا يشتكون من ألم في البطن، ومريضتان تشتكيان من ورم محسوس في البطن. يتراوح حجم الأورام ما بين ٦ إلى ١٢ سنتمترًا، كل الأورام كانت محددة الإطار، واثنان منها كانا يحتويان مناطق نزيف. أظهر التحليل الصبغي المناعي أن الحالات الخمس كانت إيجابية لـــ vimentin, CD56, CD10, NSE and beta catenin. كل المرضى استئصلت لهم هذه الأورام جراحيًا ويتمتعون بصحة

جيدة بعد مرور سنة إلى أربع سنوات. الورم الحليمي الجامد للبنكرياس يجب أن يؤخذ بالاعتبار ضمن التشخيصات لأورام البنكرياس بالذات في النساء الصغيرات، ويجب أن يكون أطباء علم الأمراض على دراية تامة بالصفات النسيجية لهذه الأورام. الإزالة الكاملة الجراحية للورم تصاحب عادة بنتائج ممتازة.