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Malignant Potential of Solid Pseudopapillary Tumours: Case Report and Literature Review

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Abstract

Solid pseudopapillary tumours of the pancreas (SPTs) are low-grade malignant potential tumors of the exocrine pancreas comprised of homogeneous, poorly adherent epithelial cells with solid-cystic elements. SPN mostly affects young females, the tumour mainly located in the body and tail of the pancreas (67%) and the head (32%). SPTs are asymptomatic until they get large and are found to be locally aggressive and infiltrate surrounding tissues, metastatic spread to the liver, peritoneum, and distant organs such as the lungs are detected. Despite of their malignancy, R0 and en bloc surgical resection have been demonstrated to enhance overall survival and disease-free survival. The surgical technique for SPTs is influenced by the location of the tumour. An excellent prognosis with a 5-year survival rate of up to 97% after surgical excision. Significant lymphadenectomy is not considered required because of the low risk of lymph node metastases of such tumor cells. Late recurrences have been recorded; long-term surveillance is recommended.
Keywords: solid pseudopapillary neoplasms, pancreas, clinical features, morphological study

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Злокачественный потенциал солидных псевдопапиллярных опухолей: клинический случай и обзор литературы

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Резюме

Солидные псевдопапиллярные опухоли поджелудочной железы (СПО) представляют собой высокодифференцированные потенциально злокачественные опухоли экзокринной части поджелудочной железы, состоящие из гомогенных эпителиальных клеток с солидно-кистозными элементами. СПО чаще поражают молодых женщин, локализуются в основном в теле и хвосте (67%), головке (32%) поджелудочной железы. Развитие СПО протекает бессимптомно до тех пор, пока опухоли не увеличиваются в размере настолько, что инфильтрируют окружающие ткани, вовлекают в процесс печень, брюшину, метастазируют в отдаленные органы, такие как легкие. Было продемонстрировано, что, несмотря на их злокачественный потенциал, R0 и хирургическая резекция единым блоком увеличивают общую выживаемость и выживаемость без признаков заболевания. Хирургическая техника удаления СПО зависит от локализации опухоли. После хирургического лечения 5-летняя выживаемость составляет до 97%, что является хорошим прогнозом. Расширенная лимфодиссекция не считается необходимой из-за низкого риска метастазирования СПО в лимфатические узлы. Для регистрации возможных поздних рецидивов рекомендуется длительное наблюдение.
Ключевые слова: солидная псевдопапиллярная опухоль, поджелудочная железа, клинические особенности, морфологическое исследование

■ INTRODUCTION

Solid pseudopapillary neoplasms of the pancreas is low-grade malignant comprised of homogeneous, poorly adherent epithelial cells that form solid and pseudopapillary morphologies [1]. Virginia K. Frantz initially described it in 1959 as a papillary cystic tumour of the pancreas in a 2-year-old male patient [1–3]. These tumours have been referred to by a number of names, including Hamoudi's tumour, solid and papillary epithelial neoplasm, papillary cystic carcinoma, solid cystic tumour, and papillary cystic tumour [1, 2].

It represents for 1–3% of exocrine pancreatic tumours, 5% of cystic pancreatic tumours, and 2–3% of all primary pancreatic tumours at any age [3]. Pancreatic SPTs are usually considered to be benign disorders, although up to 10% to 15% of instances are allegedly aggressive. Some SPNs are discovered to be locally aggressive and infiltrate surrounding tissues, whilst others are malignant and spread to the liver and peritoneum, as well as more distant organs such as the lungs. Regardless of their malignancy, surgical resection with R0 and en bloc have been shown to improve overall survival and disease-free survival [4, 5]. Although after full resection of SPTs recurrence was documented. One patient (3%) had a recurrence after a median follow-up of 4.8 years in a single institution study of 37 patients with SPTs [6]. Final research included 26 patients, with 2 (8%) recurrences recorded at 6- and 7-years following resection and no disease-specific mortalities observed after 73 months of follow-up [7]. This uncommon clinical pathologic disorder that primarily affects women. The vast majority of patients are young females, and the tumour is found in the pancreas's body and tail (67%) and head (32%), most tumours are asymptomatic until they can get large. Degenerative cystic changes are and the presence of a capsule is common [8]. Few cases were reported that SPN is associated with familial adenomatosis polyposis (FAP) [9, 10]. However, the FAP pattern of inheritance increases the susceptibility to SPN formation [9]. FAP is caused by APC gene mutations, with APC gene loss of function linked with intracellular B-catenin build-up, which leads to B-catenin/Wnt signalling pathway activation. Same pathway happens in pancreatic pseudopapillary tumour. The primary determinant of SPN tumorigenesis is transcriptional activation of the WNT signalling pathway via oncogenic mutation of CTNNB1 gene [11]. It is intriguing that beta-catenin abnormalities are detected in both SPN and FAP, however their role in carcinogenesis remains unknown. The surgical approach for SPNs depends on the tumour location. Distal pancreatectomy with/without splenectomy is for tumours located in the tail of the pancreas, and pancreaticoduodenectomy for pancreatic head tumours.

■ METHODS AND PATIENTS

This article summaries the literature review with pathogenesis and malignant potential as well as presents our experience with a single-institution accepted study. It included four patients with pathologically proven pancreatic SPTs. Data were gathered through routine check-ups at our consultation polyclinic between August 2020 to May 2022. The confirmed cases of solid pseudopapillary tumour of the pancreas treated in our institution N.N. Alexandrov National Cancer Centre, Republic of Belarus, Minsk. Patients were assembled, one of them has been operated in 2014 and now had a recurrence in the head of the pancreas. The final diagnoses were confirmed histopathologically along with the expression of immunohistochemistry findings. All patients were operated by the same surgical oncology team in our centre. Although R0 resection was our fundamental goal, the precise location and size of the tumour were considered to determine the best surgical approach.

■ PATIENT A

A 33 years old female diagnosed with pancreatic tail pseudopapillary tumour in Minsk regional clinical hospital in 2014, underwent for distal pancreatectomy with splenectomy. She denied any history of symptoms except for epigastric discomfort, after that she was clinically followed up. Surgical history was for cesarean section in 2019. In February 2022

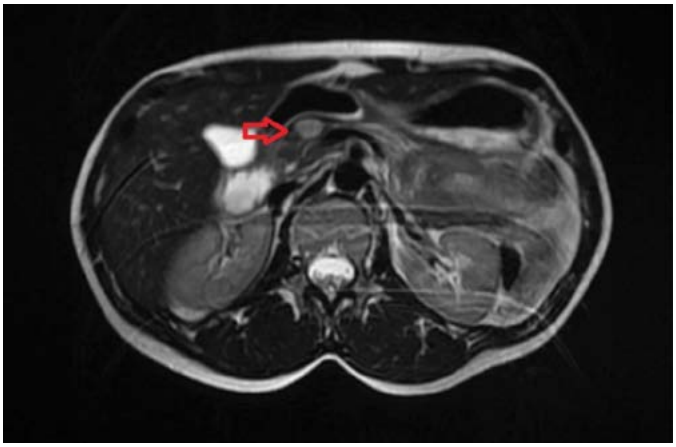

Fig. 1. Residual SPN in the uncinate process of the pancreas for patient A

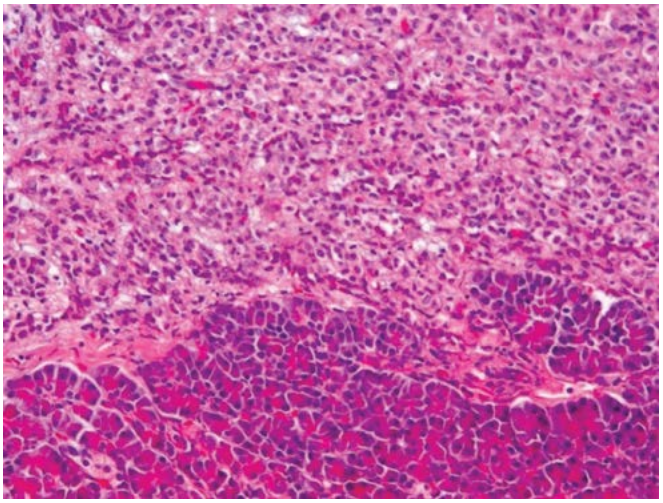

Fig. 2. Histopathology of the solid pseudopapillary tumour for patient A, HE, ×

referred to our hospital with a small tumour in the uncinate process of the pancreas. Magnetic resonance imaging was done confirmed a local recurrence near the resection site (Fig. 1).

The patient underwent for complex tumour enucleation. The histopathology of the tumor is shown in the fig. 2.

Total pancreatectomy was contraindicated due to her age and poor quality of life after such operation. Since the operation the patient is on follow up. Complication was eventful she underwent for relaparotomy for bleeding and after that she suffered from post operative pancreatitis and fistula.

■ PATIENT B

A 2 years old female complains about 1-month of epigastric pain and episodic vomiting she was admitted to hospital after physical and clinical examination, general condition was normal, abdomen was soft no swelling, was sensitive to palpation in the epigastrium more on the left upper quadrant, no peritoneal symptoms was noted. After computed tomography CT revealed a solid appearing mass measuring 4.2×3.9 cm in the tail of the pancreas (Fig. 3).

She underwent for splenic sparing distal pancreatectomy. Specimen and pathohistology of the tumor is shown in the fig. 4 and 5.

Postoperative complications were only for pancreatic Grade A fistula (biochemical fistula) and was treated conservativity. Since the operation the patient is on follow up.

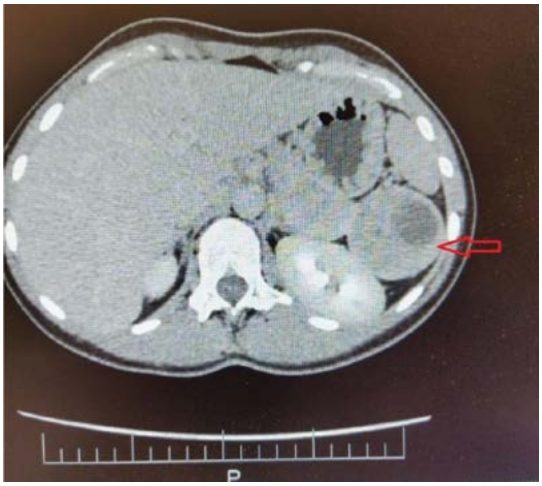

Fig. 3. CT scan shows a tumour in the pancreatic tail with solid and cystic components

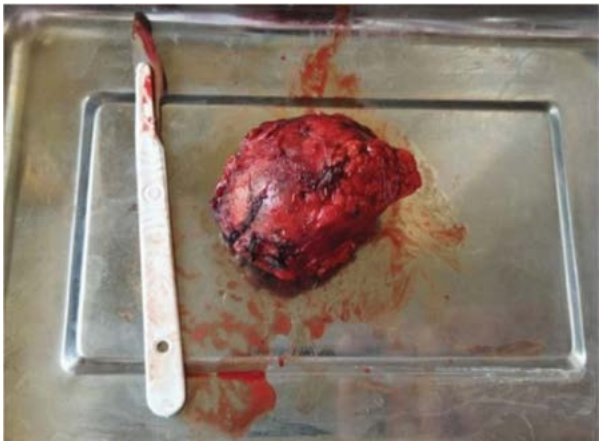

Fig. 4. Specimen with SPN with en bloc resection

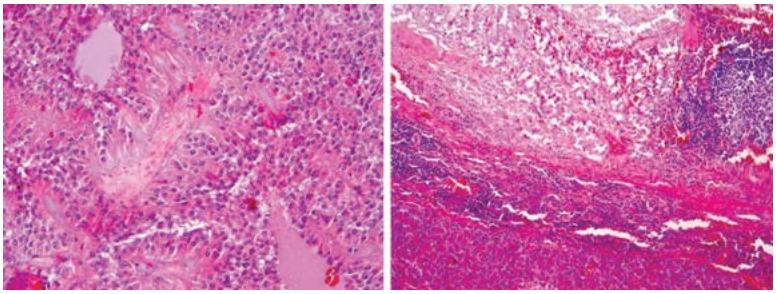

Fig. 5. Histopathology of the solid pseudopapillary tumour for patient B. HE, ×

■ PATIENT C

18 years old referred to our hospital for left upper quadrant mass detected by routine abdominal ultrasound. She dienes any symptoms, general examination was normal and abdomen was soft except for left upper flank mass was palpable. No abdominal abnormalities were noted, stool and diuresis were normal as well. A computed tomography (CT) scan revealed a mass involving the tail of the pancreas measuring about 12 cm × 8 cm × 2.5 cm, splenic vein compression was seen but invasion can't be excluded (Fig. 6). She underwent for open distal pancreatectomy with conventional splenectomy. The histopathology of the tumor is shown in the fig. 7.

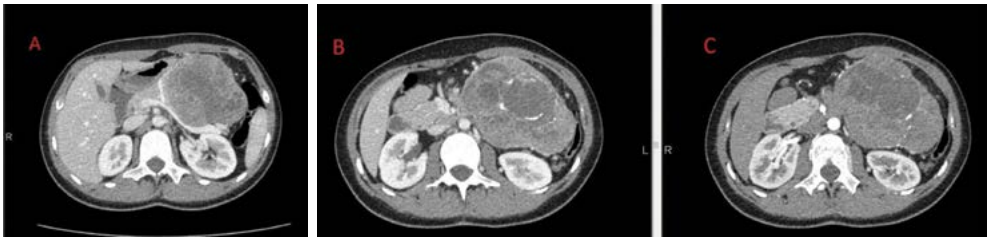

Fig. 6. CT scan with contrast shows a solid pseudopapillary tumour involving the body and tail of the pancreas: splenic vein is compressed by the tumour (A); solid cystic components of SPN with calcification (B and C)

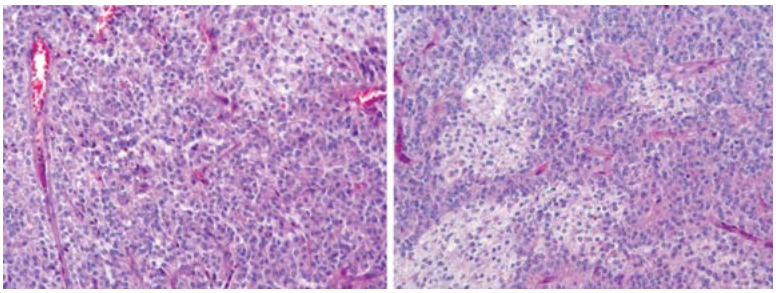

Fig. 7. Histopathology of the solid pseudopapillary tumour for patient C. HE, 20×

Since the operation the patient is on follow up. Postoperative complications were uneventful.

■ PATIENT D

24 years old female referred to our hospital for a tumour in the tail of the pancreas found accidently in routine ultrasound for kidney checkup. She was sent for CT scan (Fig. 8 A, B) and confirmed a solid appearing mass in the pancreatic tail measuring about 22.80 mm × 26.87 mm.

The patient underwent for s splenic sparing distal pancreatectomy. Specimen and pathohistology of the tumor is shown in the fig. 9 and 10.

Postoperative complications were remarkable, relaparotomy for bleeding from the pancreatic stump and also, she experienced episode of pancreatitis and fistula.

Table 1 presents the biomarkers of patients A, B, C and D.

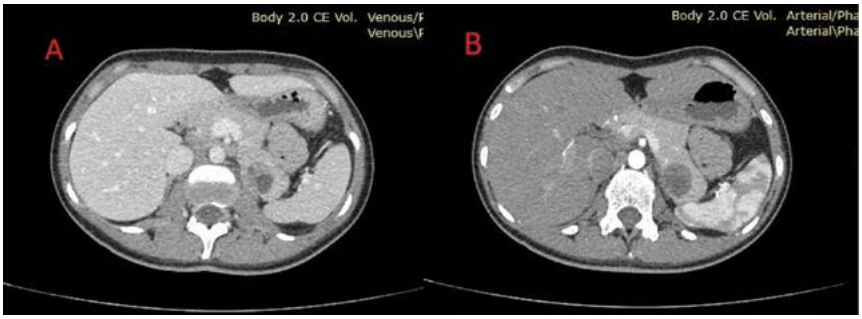

Fig. 8. Contrast enhanced CT scan with shows a solid-cystic tumour involving the pancreatic tail (A and B)

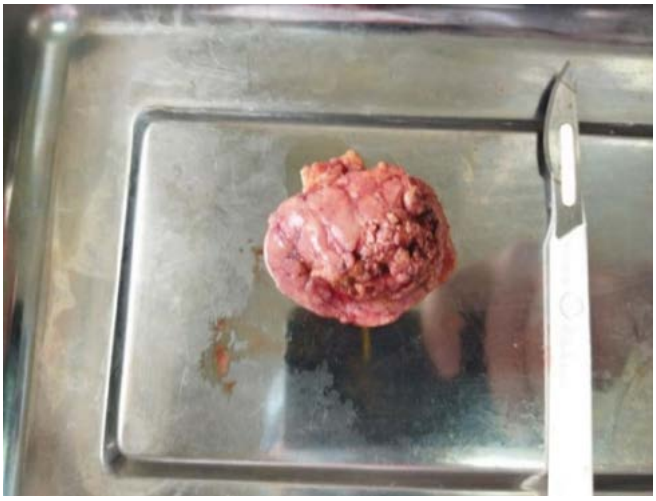

Fig. 9. Specimen with tumour and en bloc resection patient D

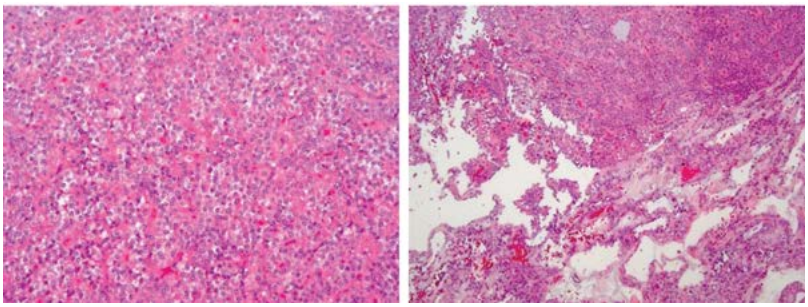

Fig. 10. Histopathologic view of the solid pseudopapillary tumour of the pancreas, HE, ×

Table 1
Tumour biomarkers

Biomarkers	Patient A	Patient B	Patient C	Patient D	Reference range
CEA	0.22 ng/ml	1.10 ng/ml	0.91 ng/ml	1.20 ng/ml	Up to 4.7 ng/ml
CA 19-9	3.4 U/ml	9.7 U/ml	5.9 U/ml	10.3 U/ml	Up to 35 U/ml
AFP	1.79 ng/ml	0.97 ng/ml	2.61 ng/ml	1.33 ng/ml	Up to 9 ng/ml
CA-125	12.15 U/ml	17.61 U/ml	14.1 U/ml	17.11 U/ml	Up to 35 U/ml
HE-4	36.71	39.05	34.20	22.40	Up to 60.5
ROMA	3.67%	4.32%	3.33%	4.70%	Up to 11.4%

■ PATHOGENESIS AND MALIGNANT POTENTIAL

SPN's cellular origin is still unknown. Beta-catenin signalling within the beta-catenin/Wnt pathway is required during proper pancreatic development, and this route is often significantly suppressed in the adult organ. The Wnt pathway is a signal transduction cascade that controls development and cellular proliferation over normal physiological conditions but has also been linked to a number of growth-related diseases and malignancies [12]. Mutations in the beta-catenin gene exon-3 somatic CTNNB1 activates Wnt signalling, which is critical in the development of SPN and its seen in about 85–90% and 10–15% having other exonal mutations [13]. Because of cell cycle dysregulation, cell cycle-associated proteins such as cyclin D1 and cyclin D3 are overexpressed in SPN [13]. Additional gene mutations of solid pseudopapillary neoplasms comprises an EWS/FLI-1 translocation t (11;22) (q24; q12), a translocation t (13;17) (q14; p11), derivation of chromosomes 1, 14, and 20, and trisomy 3 [14]. FLI-1 was detected in SPN; however, it was not associated with CD 34 positivity or EWS/FLI-1 translocation [13]. As a result, if the EWS/FLI-1 translocation is positive, the diagnosis of SPN becomes less likely. Chromosome 11 is prone to particular genetic alterations because it contains numerous genes for proteins that are overexpressed in SPN like (cyclin D1, FLI-1, progesterone receptor, and CD56) [15]. SPNs are regarded as hormone responsive because they explicit progesterone receptor. whilst P21, P27 and cyclin D1 expression is impacted by oestradiol and progesterone [16]. The significance of cyclin-dependent kinase inhibitors P21 and P27 in modulating the activated Wnt/beta-catenin signalling pathway explains the decreased tumour growth rate in SPN [13, 17, 18].

Table 2
Immunohistochemistry results for SPN

IHC components	Patient A	Patient B	Patient C	Patient D
β-catenin	+	–	+	+
synaptophysin	–	–	+	–
chromograninA	–	–	–	–
cyclinD1	+	+	–	+
PR	–	–	+	–
CD56	+	–	–	–
CD99	–	–	–	–
E-cadherin	–	–	–	–
CK8/18	–	–	–	–
panCK	±	±	–	–
Ki67	0–1%	1–2%	~ 7%	1%

■ MACROSCOPIC AND MICROSCOPIC APPEARANCE AND IMMUNOHISTOCHEMISTRY

R0 resection was our key focus. All surgical specimens were pathologically evaluated by an expert pathologist. We established a clear margins in all four patients, according to the analysis under the microscope, it was found to be free of lymphovascular invasion and perineural invasion. The pathologic imaging results are shown in Fig. 2, 4, 5, 7 and the immunohistochemistry results are demonstrated in table 2.

■ DISCUSSION

Solid pseudopapillary neoplasms has very low malignant potential however, malignant transformation and metastatic disease was noted. It is the most frequent pancreatic tumor in the second decade of life, and mainly occurs in the second to fourth decade in young women [19] SPN's clinical presentation is typically nonspecific. The most common symptom is palpable abdominal mass, which is followed by abdominal pain, vomiting, and jaundice. There are no SPN-specific serum markers known for diagnosing SPN. In SPN patients, common serum markers such as alpha-fetoprotein, CEA, beta-human chorionic gonadotropin generally negative [20]. Usually CA 19-9, and CA 125 are normal but can be elevated. However, Mucin (ductal origin), enzymes (acinar origin), and hormones (endocrine origin) are consistently negative in SPN cells [20]. The female preponderance of SPN, combined with the appearance of progesterone receptors in many cases, points to a neuroendocrine origin [21]. Because the significant proportion of these tumour cells are positive for Beta-catenin, it is possible that SPN growth is mediated by the Wnt signalling pathway [22, 23]. A beta-catenin (CTNNB1) mutation could also play a significant role in SPN tumorigenesis. There are various reported cases of pancreatic SPN in the world literature we collected several cases with aggressive behaviour and recurrence. Morito et al reported a case of 71 years old woman underwent for distal pancreatic resection, first recurrence was discovered by CT scan in the liver segment S7-S8 four years after the first resection. Finally, 18 months after liver resection another recurrent liver metastasis also underwent for re-hepatic resection for metastasis. This was the same outcome as the previous surgery. The labelling index for Ki-67 was 3% [24]. Another review was reported by Piyush et al. to 42 years old male diagnosed by solid appearing mass measuring about 11.2×9.6 cm in the tail of the pancreas. He underwent for distal pancreatectomy with

splenectomy and with lymph node dissection of the splenic artery. After four years proven recurrence was proved by biopsy the tumour was adhered to the splenic flexure and gastric fundus and was removed by a wedge gastrectomy and a partial colectomy. And also 4 cm nodule of tumour adhering to the diaphragm removed by superficial layer stripping and omentum was excised [25]. A 49-year-old woman diagnosed with SPN in the pancreatic head underwent for pancreaticoduodenectomy, six years after the first surgery, a well-defined tumour 15×15-mm in Couinaud segment VI of the liver, detected by routine follow-up CT scan. Pathology confirmed the presence of recurrent metastatic SPN after a partial hepatectomy. Additional metastatic lesions in the liver were detected 98 and 113 months following the first operation, necessitating recurrent partial hepatectomies. We discovered that the Ki-67 index increases with each metastasis, namely 1.88%, 7.38%, 5.53%, and 11.22%, respectively [26]. Last patient was 15-year-old female diagnosed with non-tender mass located in the left lower. An abdominal ultrasound revealed five left-sided abdominal tumours and a right ovarian cyst. an abdominal CT scan demonstrated a lesion inside the pancreatic tail, with peripheral solid components and calcifications. The patient had an exploratory laparotomy, distal pancreatectomy and splenectomy, omentectomy, excision of several intra-abdominal tumours, and right ovarian cystectomy with ovary preservation. Final pathology revealed confirmed SPN with lymphovascular involvement 4 out of 22 lymph nodes [27]. Our patient (patient C) has the same tumour aggressiveness as the last patient mentioned above but without distant metastases. None of our patients experienced any episodes of jaundice or pancreatitis preoperatively. The length of hospital stays and postoperative complications were documented. The criteria of complications used in this paper have already been described. briefly, three patients (A, B and D) experienced a postoperative pancreatic fistula (POPF) grade A (biochemical), PF characterizes as an abdominal drain fluid with amylase level three times higher than normal serum levels no specific treatment was recommended. Delayed gastric emptying (DGE) defined as the requirement for nasogastric intubation for 10 days or longer, or the inability to consume normal meals prior to or on the postoperative day (POD) 14, none of our patients had (DGE).

Two patients (A and D) they had relaparotomy for bleeding from the resected site and pancreatic stump 24 hours postoperatively, patient (D) suffered from postoperative pancreatitis (Table 4) according to presenting symptoms and lab tests, was treated conservatively. Because of the favorable prognosis even in the presence of big tumours

Table 3
Laboratory parameters pre-operatively

Analysis type	Patient A	Patient B	Patient C	Patient D	Reference range
Creatinine	76	66	56	62	58–96 μmol/L
Amylase	19	31	64	51	30–125 U/L
Glucose	7.36	10.56	7.57	5.35	4.1–5.9 mmol/l
CRP	–	1.6	–	0.6	0–5 mg/L
LDH	135	123	147	148	25–247 U/L
AST	20	19	15	21	5–40 U/L
ALT	12	21	8	23	5–40 U/L
ALP	72	43	80	46	30–120 U/L

Table 4
Laboratory parameters post-operatively

Analysis type	Patient A	Patient B	Patient C	Patient D	Reference range
Creatinine	71	70	62	50	58–96 μmol/L
Total protein	52.8	69	62.3	64.5	65–85 g/L
Albumin	29.4	38	33.2	31	35–52 g/L
Amylase	15	141	68	245	30–125 U/L
Glucose	7.66	7.08	5.14	5.85	4.1–5.9 mmol/l
CRP	132.1	60.4	176.5	186	0–5 mg/L
LDH	161	134	175	171	25–247 U/L
AST	20	18	27	22	5–40 U/L
ALT	14	14	12	41	5–40 U/L
ALP	46	40	33	63	30–120 U/L

or progressive diseases, surgical removal is the definitive treatment of SPNs. the low risk of lymph node metastases of such tumour, significant lymphadenectomy is not considered required. Chemotherapy (gemcitabine-based therapy) is not recommended in patients undergone for full resection, margins negative and no distant metastasis. SPT has an excellent prognosis, with a 5-year survival rate of up to 97% after surgical excision. Because late recurrences have been reported, long-term observation is advised. SPTs has an excellent prognosis, with a 5-year survival rate of up to 97% after surgical excision [27, 28]. Because late recurrences have been reported, long-term follow up is advised [29].

■ CONCLUSION

Solid pseudopapillary neoplasms have a minimal malignant potential, malignant transformation and metastatic invasion have been reported. Surgical resection with negative margins in the primary goal of the treatment modality. Solid pseudopapillary tumours have an excellent prognosis with 5-years survival rate 96% after successful surgical resection. Chemotherapeutic agents are not recommended in localized non-metastatic tumour. Further investigation and interval imaging should be considered to detect future recurrence.

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