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Original Article General Surgery

Diagnosis and treatment of solid pseudopapillary tumor of the pancreas: A single center's experience

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ABSTRACT

OBJECTIVE: The present study reviews the records of patients with solid pseudopapillary pancreas neoplasm (SPT).

METHODS: A total of 13 patients diagnosed with SPT were included in the study. The criteria for SPT in the pathology specimens were the presence of cells with an oval round orthochromatic nucleus, with a thin chromatin structure and no nucleolus distinction, lined around a fibrovascular papilla in cystic areas.

RESULTS: The study included 11 female and two male patients, with a mean age of 33.07 (range: 16–73) years. All operated patients underwent open surgery, with five undergoing a subtotal pancreatectomy and splenectomy; one a distal pancreatectomy and splenectomy; four a spleen-preserving distal pancreatectomy; and one a pancreaticoduodenectomy. None of the operated patients developed recurrence during the long-term follow-up. The mean follow-up time of operable patients was 69.18 (range: 22–97) months, and none had metastasis at follow-up. The mean follow-up time for the malignant SPT patients was 2.75 (1.5–4) months.

CONCLUSION: SPTs are rare pancreatic tumors encountered more frequently today due to advances in imaging methods and have a low potential of recurrence and a good prognosis.

Keywords: Pancreas; pancreatic resection; pancreatic tumor; solid pseudopapillary tumor.

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Solid Pseudopapillary Tumor (SPT) of the pancreas is a rare entity first described by Frantz in 1959 [1]. Although most SPTs of the pancreas are benign, 10–15% exhibit malignant behaviors and are most often found in young women [2]. The prognosis is usually good after surgical resection. Postoperative recurrence in the presence of local infiltration and/or metastatic cases has been described in 10–15% of cases [3]. There are ongoing discussions about the pathogenesis of these tumors. However, it has been suggested that pancreatic ductal and acinar cells, endocrine cells or pluripotent stem cells may play a role in the etiopathogenesis [4, 5].

The present study evaluates the solid pseudopapillary tumor cases who underwent treatment in our clinic, assessing their clinical and radiological characteristics and long-term follow-up outcomes with a comparison with existing literature.

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MATERIALS AND METHODS

The study included patients who were operated on, consulted for treatment and identified with Solid Pseudopapillary Tumors based on a pathology report in the General Surgery Clinic of Cukurova University Faculty of Medicine Hospital between January 2012 and December 2019. This study was approved by the Cukurova University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (IRB No. 05.06.2020/100/27), and written informed consent was obtained from all participating in the study.

The study involved the retrospective collection and analysis of the demographic characteristics, clinical findings, pathology, imaging, and laboratory results of the patients. The file details were completed via phone. After a case-based assessment of the patients was concluded, Ultrasonography (USG), Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Endoscopic Ultrasonography (EUS), and Positron Emission Tomography (PET-CT) were used in the preoperative period as imaging methods. The study included cases detected in the histopathological examination to have solid and cystic areas, and cells with an oval, round, orthochromatic nucleus, aligned around a fibrovascular papilla, with a thin chromatin structure and without an apparent nucleolus in the cystic areas. These cases were confirmed to have low mitotic activity a Ki-67 proliferation index, and no necrosis or atypia. It was confirmed that the patients generally had Synaptophysin and Neuron Specific Enolase focal positivity and Chromogranin negativity. The criteria for pleomorphism, nuclear atypia, and abundant mitosis were confirmed in tumor cells with diffuse stratification in the histopathological assessment of the malignant SPT cases. Disease recurrence was determined based on Carcinoembryonic Antigen (CEA), Carbonic Anhydrase 19-9 (CA 19-9), CT and MRI. The patients were assessed at postoperative month 6 and annually after that.

Statistical Analysis

Statistical analyses were carried out using SPSS for Windows, version 17 (SPSS, Chicago, IL, USA). Categorical measurements were expressed as numbers and percentages, while continuous measurements were expressed as mean and standard deviation (with median and minimum–maximum where required).

Highlight key points

- Solid pseudopapillary tumors are more frequently encountered tumors today due to the increase in the use of imaging methods and technological advances in imaging methods.
- It is a tumor seen especially in young female and women patients.
- Although its frequency is said to be increased, it is a rare tumor.
- SPTs are pancreatic tumors with a low probability of recurrence and a good prognosis. For this reason, the treatment of patients with SPT as a result of histopathological evaluation should be aimed at R0 resection with more aggressive treatments, if possible.

RESULTS

The study included 13 (0.93%) cases identified with SPT from among 1,385 pancreatic cancer cases who were followed up or operated on for pancreatic masses during the study period (Table 1). The study included 11 female and two male patients, with a mean age of 33.07 (range: 16–73) years. The patients presented with abdominal pain (n=10), nausea (n=3), palpable mass (n=2), and distention (n=2). Some cases had multiple symptoms, and one patient was asymptomatic. The mean tumor diameter was 6.72 (range: 2.2–16) cm. The tumor localizations and operational characteristics of the patients are presented in Table 1. Of the total, 11 cases were evaluated as benign SPT and underwent surgery. All operated patients underwent open surgery, with five undergoing a subtotal pancreatectomy and splenectomy; one a distal pancreatectomy and splenectomy; four a spleen-preserving distal pancreatectomy; and one a pancreaticoduodenectomy (Whipple procedure).

A multiple organ metastasis was identified in one case with a CA 19-9 level of 227 U/ml (normal value <37 U/ml), and this case was accepted as a non-operable malignant SPT. All patients' CEA, amylase and lipase values were within normal limits in the preoperative period. Only one patient had a high AFP level of 8.8 (patient 1, normal value: 0–6 IU/ml). Another patient was considered non-operable due to the presence of mediastinal metastatic multiple lymph nodes and multiple organ metastases. The pathological surgical margin was intact in all of the operated patients, and an R0 resection was performed. There was no postoperative mortality among these patients. None of the operated patients developed recurrence during the long-term follow-up. The mean follow-up time was 59.18 (range: 2–87) months, and

Table 1. Demographic characteristics, tumor localization and characteristics, preoperative findings, type of operation and follow-up findings of patients

	Sex/ age	Site	Preoperative symptoms	Size (cm)	Treatment/non-operability criteria	Follow-up /months	Tm recurrence
Patient 1	44/F	Corpus	Abdominal pain	5	SP+S	97	Aned
Patient 2	41/F	Corpus	Abdominal pain	2.2	SP+S	94	Aned
Patient 3	16/F	Distal	Distention, palpable mass	16	DP	85	Aned
Patient 4	29/F	Distal	Abdominal pain	7.2	DP+S	22	Aned
Patient 5	17/F	Uncinate	Distention, palpable mass	12	Whipple	71	Aned
Patient 6	20/F	Distal	Nausea	5	DP	65	Aned
Patient 7	17/F	Body-tail	Abdominal pain	6	SP+S	49	Aned
Patient 8	66/F	Head, Body	Abdominal pain (through the back)	7	Left kidney metastasis SMV invasion Pulmonary lymph node metastasis (inoperable)	1.5	Exitus
Patient 9	22/F	Corpus	Abdominal pain+nausea	2	SP+S	29	Aned
Patient 10	73/M	Head, uncinate	Abdominal pain	12	Right kidney invasion liver metastasis, left inguinal lymph node metastasis, metastatic lymph nodes in both lungs, SMA invasion (inoperable)	4	Exitus
Patient 11	45/F	Distal	Abdominal pain	5	DP	92	Aned
Patient 12	18/M	Distal	Abdominal pain	3	DP	60	Aned
Patient 13	22/F	Corpus	Abdominal pain, nausea	5	SP+S	97	Aned

A-ned: Alive with no recurrence; DP: Distal pancreatectomy; SP: Subtotal pancreatectomy; S: Splenectomy.

none of the patients had metastasis at follow-up. The preoperative imaging method was USG in nine patients, CT in 10 patients, MRI in eight patients, PET-CT in five patients, and EUS in two patients, as presented in Table 2 (Fig. 1, 2). Of the total, five (38.4%) developed postoperative complications. Wound site infection developed in one patient, pancreatitis in one patient, Grade A pancreatic fistula in two patients and Grade B pancreatic fistula in one patient, according to the International Study Group for Pancreatic Fistula (ISGPF) [6], and pleural effusion in the left lung.

A tumor capsule was found in all specimens, assessed postoperatively. There was capsular invasion in two cases, calcification in one case and vascular invasion in three cases, while none had a perineural invasion (Fig. 3). The mean follow-up time for the malignant SPT patients was 2.75 (1.5–4) months. One patient died 1.5 months after diagnosis, and another patient died 4 months after diagnosis. Both had declined chemotherapy and/or radiotherapy (Table 1). The tumor characteristics of the patients are indicated in Table 3.

DISCUSSION

SPT of the pancreas is rare (1–3%), although the detection rate has gradually increased due to advances in imaging methods. It is more common in adolescents and young women, although cases have also been reported in the elderly, men, and children [7, 8]. In the present study, the mean age of the patients was 33.07 (range: 17–73) years and the female: male ratio was 11:2.

Most SPTs of the pancreas grow very slowly and may not be symptomatic until they reach a certain size. Cases are often detected incidentally during abdominal imaging intended for screening or other purposes. When a tumor grows sufficiently, it may pressure the adjacent organs and result in associated clinical symptoms [9]. In the present study, 10 patients had abdominal pain, three

Table 2. USG, CT, MRI, PET-CT, EUS findings

	USG (n=9)	CT (n=10)	MRI (n=8)	PET (SUV_{max} mean 20.22) (n=5)	EUS (n=2)
Patient 1	Solid Mass	Suspected neuroendocrine tm	No	Mass (7.02)	No
Patient 2	No	Hypodense lesion	No	Mass (5.4)	No
Patient 3	Solid mass	Solid mass	No	No	No
Patient 4	No	No	Solid cystic mass	Mass (8.3)	No
Patient 5	Cystic lesion	No	Solid cystic mass	No	No
Patient 6	Solid cystic mass	No	Solid cystic mass	No	No
Patient 7	Solid cystic mass	Hypodense mass	No	No	No
Patient 8	Solid cystic mass	Solid cystic mass	No	Lobular mass (54.7)	GIST (SMV invasion)
Patient 9	No	Solid pseudopapillary tumor	Solid Mass	No	Hypo-isoechoic mass
Patient 10	No	Solid lesion	GIST	Hypodense mass (25.69)	No
Patient 11	Solid cystic mass	Solid lesion	Solid cystic mass	No	No
Patient 12	Cystic lesion	Solid cystic mass	Solid cystic mass	No	No
Patient 13	Cystic lesion	Cystic lesion	Cystic lesion	No	No

USG: Ultrasonography; CT: Computed tomography; MRI: Magnetic resonance imaging; EUS: Endoscopic ultrasonography; PET: Positron emission tomography; GIST: Gastrointestinal stromal tumor.

patients had nausea, two patients had distention and two had palpable masses, while one asymptomatic patient was detected incidentally.

Serum amylase levels and tumor markers such as CA19-9, CEA, and AFP are usually within normal limits in patients with SPT [10]. In a study by Dong-Li et al. [10] evaluating 34 SPT cases, normal amylase and CEA levels were found in all cases, while the serum lipase level was elevated in three cases, CA19-9 in four cases, and AFP in one case. The present study identified an elevated CA19-9 level in one malignant SPT case and an elevated AFP level in one non-malignant SPT case. CEA, amylase, and lipase levels were within normal limits in all study patients.

SPT is identified as an encapsulated solid mass with well-defined borders and with cystic and hemorrhagic degeneration on CT imaging [11]. It is low-grade with low malignant potential and tends to have a better prognosis than other pancreatic tumors, even in the presence of a metastatic disease [12, 13]. Metastases occur in the liver, peritoneum, omentum and regional lymph nodes;

Table 3. Tumor characteristics of patients

	n
Tumor size (cm)	6.72 (range: 2.2–16)
Tumor location	
Corpus	4
Tail	5
Uncinate	1
Uncinate+head	1
Head+corpus	1
Corpus+tail	1
Metastasis	2

most metastatic patients are male. The link between tumor size and malignancy potential is controversial [12, 13]. In the present study, 11 patients were operated on, two patients had multiple metastatic foci, one patient had left kidney metastasis and another had right kidney invasion, both of whom were detected to have pulmo-

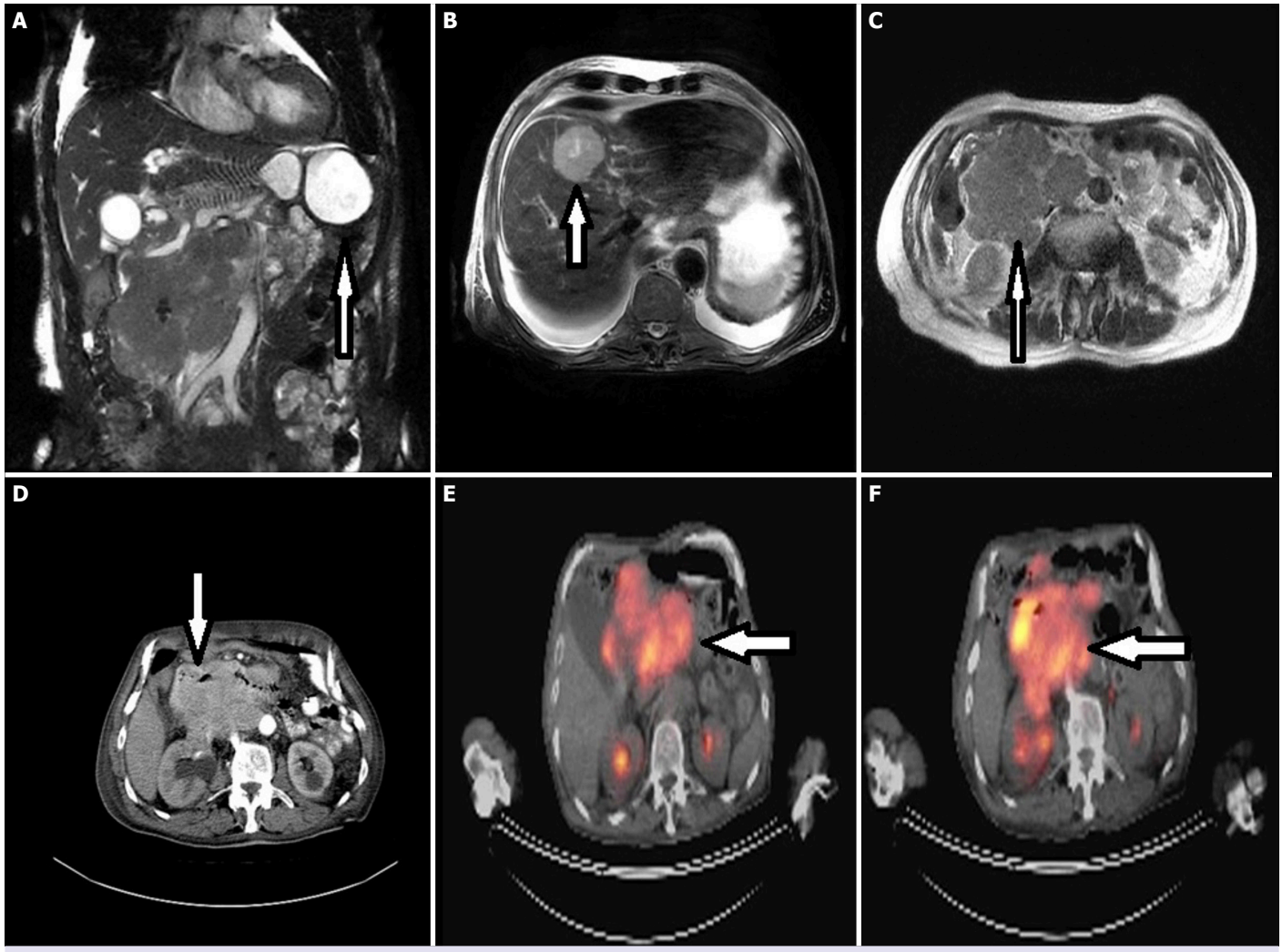

Figure 1. Patient 10 (malignant SPT) preoperative imaging, **(A)** MRI Cor Fiesta imaging, pancreas, **(B)** MRI T2-weighted imaging, Liver metastasis, **(C)** MRI T2-weighted imaging, liver metastasis, **(D)** CT imaging, pancreas, **(E, F)** PET-CT imaging.

nary lymph node metastases. No lymph node metastasis was observed in any of the operated patients. No invasion of the adjacent organs was observed in the operated patients. Genetics-related studies may serve to explain the more aggressive nature of SPT in the male gender.

An SPT morphology on US, CT or MRI is usually identified as thick-wall cystic entity or a well-defined, large mass involving solid components with cystic elements. Contrast-enhanced CT plays an important role in the diagnostic assessment of cystic neoplasms, and is typically viewed on CT as an encapsulated, heterogeneous lesion with variously distributed solid and cystic components. Compared to MRI, CT has natural limitations, displaying characteristics such as hemorrhage, cystic degeneration or capsule presence. MRI plays an important role in the detection of SPT due to its superior contrast resolution. On MRI, high-signal intensity areas are observed in hemorrhagic zones, and the capsule is usually defined as a thin, hypoechoic, intense tissue. MRI may also provide information on tumor resectability, which is of great importance for proper patient management [14]. In the present study, the patients underwent USG (n=9), CT (n=10), MRI (n=8), PET-CT (n=5) and EUS (n=1), and all imaging methods revealed cystic or solid lesions in the pancreas. Serous microcystic adenoma, mucinous cystic neoplasm, islet cell tumor, pancreatoblastoma and calcified hemorrhagic pseudocyst should be considered in a differential diagnosis [15–17]. In the present study, one of the SPT cases was defined as a neuroendocrine tumor on CT, one as a gastrointestinal stromal tumor (GIST) on MRI and one as GIST on EUS. CT was the most commonly used imaging meth-

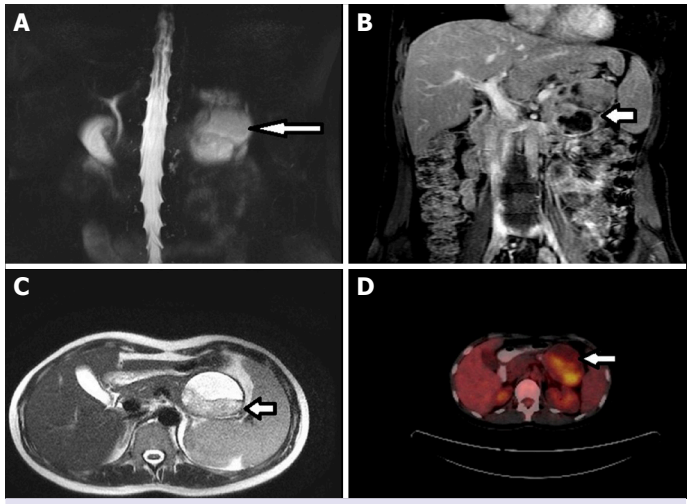

FIGURE 2. Patient 4 preoperative imaging, **(A)** MRCP asset imaging, **(B)** Coronal MRI imaging, **(C)** MRI T2-weighted imaging, **(D)** PET-CT imaging.

od (n=10, 76.9%) in the present study, revealing a mass in all patients. Differential diagnosis may be challenging in the presence of small, solid lesions, in unilocular cysts or in male patients. EUS-guided fine-needle aspiration biopsy (FNAB) has recently been suggested as a diagnostic tool. The diagnostic accuracy of EUS-FNAB in SPT detection was found to be 75% by Jani et al. [18] in their multicenter experience. The present study evaluated two patients considered non-operable after imaging with a diagnosis based on EUS-FNAB. The role of PET-CT in SPT has yet to be clearly described. In the study by Beltrame et al. [19], 10 patients with SPT underwent PET-CT and a significant 18-FDG uptake was observed in seven cases, although no correlation could be established between SUV_{max} and disease behavior. In the present study, five patients underwent PET-CT, and the mean SUV_{max} was 20.22. The highest SUV_{max} was 54.7 in one malignant SPT case, and 25.69 in the other malignant SPT case. For the benign SPTs, the mean SUV_{max} was 6.9 (median 7.02). Prospective randomized studies involving more extensive case series, and comparing the SUV max values of malignant and non-malignant SPTs, would significantly contribute to the literature.

Generally, SPT tumors have a low malignancy potential. Although the 5-year survival rate is over 95% after resection, local recurrences or distant metastases may occur in rare cases [18]. Conditions with short disease survival can be used to estimate malignant cases [20, 21]. The link between tumor size and malignant potential is controversial [13, 16]. The study by Lubezky et al. [22]

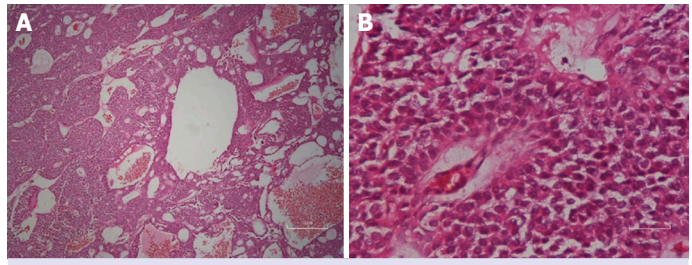

FIGURE 3. Histopathological imaging **(A)** Monotonous tumor with solid and cystic areas at small magnification, **(B)** Malignant tumor tissue with a hyperchromatic, oval, round nucleus, a narrow cytoplasm and sporadic mitotic activity at small magnification.

found tumor size to be the leading clinical characteristic related to metastatic disease and reduced disease-free survival. The mean tumor size was found to be significantly greater in metastatic cases than in those with disease-free survival. Vascular invasion, high-degree nuclear atypia, a high mitotic index and large necrotic clusters are criteria indicating high malignancy potential [22].

The study by Kim et al. [23] described a tumor size greater than 5 cm as predictive of high malignancy. The authors, therefore, argued that SPT patients with a tumor size greater than 5 cm should undergo lymph node dissection and curative surgery [23]. The present study found the mean tumor size of patients to be 6.72 (range: 2.2–16) cm and to be 9.5 (7–12) cm in two cases with malignant SPT. Even patients with metastatic liver and/or peritoneal disease may have long-term survival [23]. Local invasion, recurrence or limited metastasis are not contraindications to resection. There is general consensus that debulking should be performed in the presence of metastasis, in contrast to the oncological principles applied to other pancreatic malignancies. The two patients in the present study considered non-operable had widespread metastases that made R0 resection impossible. The SPT cases with malignancy potential had short survival times, as reported in literature. None of the operated patients developed recurrence or metastasis in long-term follow-up. The mean follow-up time of the two patients with malignant characteristics was 2.75 months. The follow-up time was 57.18 (range: 2–87) months for the operated patients, none of whom developed local recurrence or distant organ metastasis.

SPT may occur anywhere in the pancreas, but most frequently in the corpus and tail [2]. Lesions located in the pancreatic head are treated with a pancreaticoduo-

denectomy (Whipple procedure), while a distal pancreatectomy is used to treat lesions with corpus or tail localizations. A parenchymal preservation technique, such as a central pancreatectomy, may be considered for lesions located in the neck of the pancreas. Such a procedure has the advantage of preserving both the endocrine and exocrine functions of the pancreas. That said, such procedures are technically associated with a significantly high risk of such complications as pancreatic leaks [24]. In the present study, the Whipple procedure was performed on only one of the 11 operated patients due to tumor localization, while the other 10 patients underwent distal pancreatectomy or subtotal pancreatectomy procedures. Of the 10 patients who underwent distal/subtotal pancreatectomy, three (30%) developed a pancreatic fistula, which was managed with medical treatment.

The limitations of the present study include its retrospective design and small patient population. For the preoperative detection of SPT, prospective studies comparing imaging methods may provide insight into appropriate surgical/medical treatments and may prevent extended surgery. Genetics-based studies revealing the role of the male gender in tumor aggressiveness, and studies comparing the SUV_{max} of malignant and non-malignant SPT cases, will provide important information about this disease.

Conclusion

SPTs are rare pancreatic tumors encountered more frequently today due to advances in imaging methods. Recurrence during long-term follow-up after R0 resection is less likely, and the prognosis is good. R0 resection or debulking surgery is the most important step in SPT treatment.

Ethics Committee Approval: The Cukurova University Faculty of Medicine Non-interventional Clinical Research Ethics Committee granted approval for this study (date: 05.06.2020, number: 100/27).

Authorship Contributions: Concept – AGS, MOG, SG; Design – AGS, MOG, IA; Supervision – AGS, MOG; Materials – AU, AGS, ATA; Data collection and/or processing – AGS, MOG, SG, IA; Analysis and/or interpretation – AGS, MOG, SG, IA; Literature review – AGS, ATA, AU; Writing – AGS, MOG; Critical review – AGS, MOG, ATA, AU.

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