CASE REPORT

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Solid Pseudopapillary Neoplasm of the Pancreas: Radiological, Clinical, Histopathological and Prognostic Features of 5 Patients

Pankreasın Solid Psödopapiller Neoplazmı: 5 Hastanın Radyolojik, Klinik, Histopatolojik ve Prognostik Özellikleri

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ABSTRACT
Solid pseudopapillary neoplasms of the pancreas are rare lesions, classified as borderline malignant tumors. They predominantly affect younger females and have more favorable outcomes compared to other pancreatic tumors. While patients may present with non-specific symptoms, the use of imaging modalities has led to an increase in incidental cases. These neoplasms are typically diagnosed using radiological imaging methods due to their characteristic features. Unlike pancreatic adenocarcinomas, surgical treatment results in lower morbidity rates and disease-free survival rates above ninety percent. This study aims to report the clinical, histopathological, and prognostic features of five cases of solid pseudopapillary neoplasms of the pancreas and review the current literature.

ÖZET
Pankreasın solid psödopapiller neoplazmaları nadir lezyonlardır ve borderline malign tümor olarak sınıflandırılır. Daha çok genç yaştaki kadınlarda görülürler ve pankreasın diğer tümörlerine kıyasla daha iyi prognoza sahiptirler. Hastalar spesifik olmayan semptomlarla başvurabilir, ancak insidental vakaların sayısı son yıllarda görüntüleme yöntemlerinin yoğun kullanımının bir sonucu olarak artmıştır. Tümörlerin karakteristik özellikleri ile çoğunlukla radyolojik görüntüleme yöntemleri ile teşhis edilirler. Pankreas adenokarsinomlarından farklı olarak cerrahi ile morbidite oranları daha düşüktür ve hastalıksız sağ kalım oranları yüzde doksanın üzerindedir. Bu çalışmada beş pankreas solid psödopapiller neoplazi olgusunun klinik, histopatolojik ve prognostik özelliklerini sunmayı ve literatürün güncel durumunu gözden geçirmeyi amaçladık.

Keywords:
Pseudopapillary tumor
Pancreas
Incidental tumors

Anahtar Kelimeler:
Psödopapiller tümör
Pankreas
Insidental tümörler

INTRODUCTION

Solid pseudopapillary neoplasms of the pancreas (SPNs) are rare lesions, accounting for 1-2% of all exocrine pancreatic tumors. They are classified as borderline malignant tumors (1–3). SPNs predominantly affect young women in their 4th and 5th decades of life (2, 4–6). Patients typically present with non-specific upper abdominal discomfort or incidentally discovered abdominal masses on imaging (2,4). These lesions can occur anywhere in the pancreas but are most commonly found in the corpus or tail. They present as solitary, well-circumscribed masses with cystic/solid components and peripheral calcifications (7,8). Although SPNs have a low potential for metastasis and are usually limited to the pancreas, more aggressive tumors have been reported in males (5). Approximately 10-15% of cases present with metastatic disease, commonly involving the liver, regional lymph nodes, and peritoneum (3,9). Depending on tumor location, treatment usually involves conservative resection to preserve as much of the pancreas as possible (2,3,7). Surgical outcomes show lower morbidity rates and disease-free survival rates exceeding 95%, unlike pancreatic adenocarcinomas (2,7). This study aims to report the clinical, histopathological, and prognostic features of five SPN cases diagnosed between January 2012 and January 2021 and review the current literature

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Following ethical approval from the Istanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee (approval number 2021/0350), the study was initiated. All patients were female, with a mean age of 42.2 (33-50) years. Four patients presented with abdominal pain, while one patient was asymptomatic and incidentally diagnosed during abdominal imaging for another pathology (Table 1). Four patients underwent magnetic resonance imaging,

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Table 1: Patients characteristics, symptoms and operation features.

	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5
Age/Gender	33/ Female	47/Female	50/Female	34/Female	42/Female
Additional health conditions	None	Hypertension	None	13 weeks pregnancy at initial diagnosis	None
Symptoms	Right upper quadrant and epigastric pain	Abdominal pain and vomiting	Incidental	Left upper quadrant pain	Abdominal pain
FNAB	No malignant features. Uniform cell proliferation with eccentric cytoplasm	Suspicious for adenocarcinoma	N/A	Acellular smear	N/A
Tumor Location	Body of pancreas	Body of pancreas	Neck of pancreas	Tail of pancreas	Tail of pancreas
Operation	Distal pancreatectomy with splenectomy	Distal pancreatectomy with splenectomy	Distal pancreatectomy with splenectomy	Distal pancreatectomy	Distal pancreatectomy
Lypmh node status	0/3	0/9	0/8	0/0	0/0
Follow-up (years)	9.25	8	2.17	1.75	0.5

Table 2: Imaging findings of the patients.

	Patient #1 (MRI)	Patient #2 (CT)	Patient #3 (MRI)	Patient #4 (MRI)	Patient #5 (MRI)
Heterogeneity	(+)	(+)	(+)	(+)	(+)
Solid component	(+)	(+)	(+)	(+)	(+)
Cystic component	(+)	(-)	(-)	(+)	(+)
Hemorrhage	(+)	(-)	(-)	(-)	(-)
Calcification	(-)	(-)	(+)	(-)	(-)
Diffusion restriction	(+)	N/A	(-)	(+)	(+)

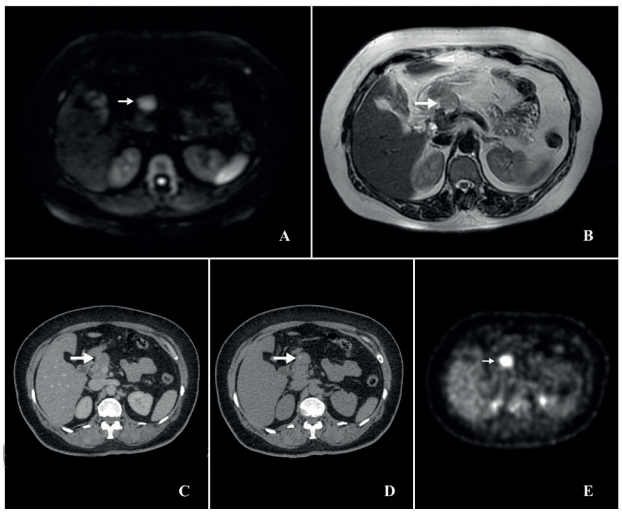

Figure 1: Tumor at the body of the pancreas (Patient #3) High signal intensity in the lesion on diffusion-weighted image (A). Nodular lesion with moderate signal intensity on T2-weighted image (B). Nodular hypovascular lesion on non-contrast-enhanced computed tomography (C). Millimetric calcification within the lesion on non-contrast-enhanced computed tomography (D). PET-CT image with FDG uptake (SUVmax:8.5) (E).

and one patient underwent contrast-enhanced computed tomography, revealing typical or atypical SPN features (Table 2). All tumors appeared as heterogeneous lesions (Figures 1,2,3). Four tumors exhibited both solid and cystic components, while one had only solid features. The mean tumor size was 5.2 cm (2.5-8.0). Three patients underwent fine needle aspiration biopsy during the preoperative period. One biopsy showed suspicion of malignancy, one exhibited benign features, and the other was acellular. Preoperative tumor markers (CEA, CA 19-9, CA 125, CA 15-3, and AFP) were within normal limits for all patients. Other laboratory studies (biochemistry panel, complete blood count) were unremarkable. Tumor locations included two in the body of the pancreas, two in the tail, and one in the neck. All patients (100%) underwent distal pancreatectomy; three of them required additional splenectomy, two due to macroscopic adhesions suggesting invasion and one due to splenic artery injury. No metastatic lymph nodes were detected. Histopathological features of the tumors are summarized in Table 3. Microscopic evaluation revealed pseudopapillary patterns forming solid areas of poorly cohesive cells surrounding blood vessels, along with hyalinization and degeneration

Table 3: Histopathological features of tumors.

	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5
Tumor Size (mm)	50x30x30	80x80x70	26x25x20	80x70x50	25x20x10
Local invasion	Not present	Not present	Invasion to peripancreatic adipose tissue	Focal invasion to pancreatic parenchyma	Focal invasion to pancreatic parenchyma
Vascular invasion	(-)	(+)	(-)	(-)	(-)
Lymphatic invasion	(-)	(+)	(-)	(-)	(-)
Perineural invasion	(+)	(-)	(-)	(-)	(-)
Cell atypia	(-)	(-)	(-)	(-)	(-)
Tumor necrosis	(-)	(-)	(-)	(-)	(-)
Mitotic activity	(-)	(-)	(-)	(-)	(-)

Table 4: Immunohistochemical features of the tumors.

	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5
Beta-Catenin	(+)	(+)	(+)	(+)	(+)
Vimentin	(+)	Disseminated Strong (+)	(+)	N/A	N/A
Synaptophysin	(-)	Focal slight (+)	(-)	N/A	(+)
Chromogranin	(-)	(-)	(-)	N/A	(-)
Progesterone	Disseminated Strong (+)	N/A	(+)	N/A	N/A
Ki-67	<%1	N/A	N/A	N/A	<%1
CD10	Focal strong (+)	Disseminated Strong (+)	(+)	(-)	N/A
CD56	N/A	Disseminated Strong (+)	(+)	N/A	N/A

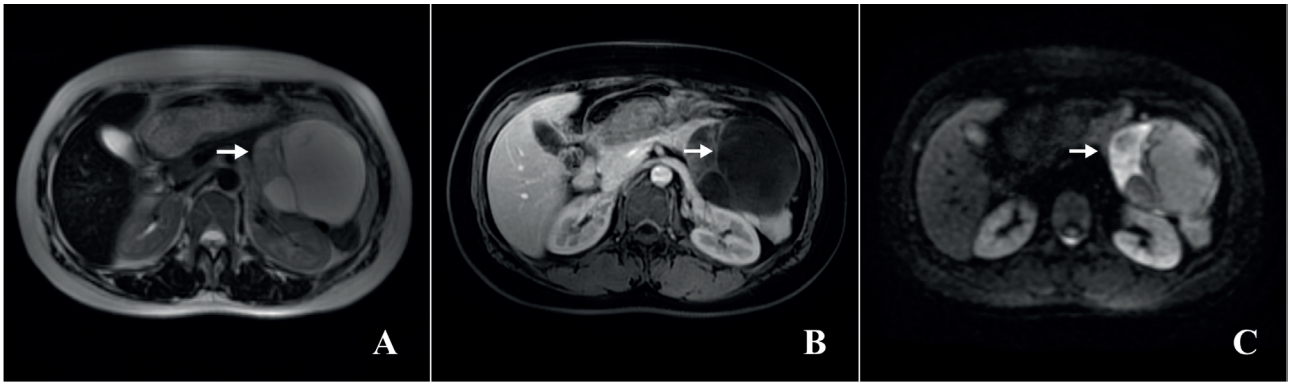

Figure 2: Tumor at the tail of the pancreas (Patient #4) A heterogeneous cystic lesion on T2-weighted images (A). Contrast enhancement of the solid components of the lesion (B). High signal intensity of solid components on diffusion-weighted image (C).

features such as hemorrhage and macrophages (Figure 4). Three patients exhibited microscopic focal invasion into peripancreatic adipose tissue or pancreatic parenchyma. One patient had lymphovascular invasion, while another had only perineural invasion. No cell atypia, mitotic activity, or tumor necrosis were observed. Immunohistochemistry showed all patients exhibited positive expression of Beta-catenin, with three patients displaying positive cytoplasmic Vimentin expression and three patients showing positive staining for CD10 (Table 4). Median follow-up time was 4.33 years (ranging from 0.5 to 9.25 years). None of the patients experienced metastatic disease or recurrence during surveillance. None of the patients received additional adjuvant chemotherapy or radiotherapy.

DISCUSSION

SPNs, also known as Frantz tumors, are uncommon pancreatic lesions first described by Virginia Frantz in 1959 as a new type of papillary tumor (10). Although SPNs are more common in young women, cases in pediatric and adolescent populations have also been reported (2,3,5,11,12). In our series, all patients were female, and their ages ranged from 33 to 50, which is consistent with the literature. One patient (patient #4), a 34-year-old experiencing left upper quadrant pain, was radiologically diagnosed during the 13th week of pregnancy. After consulting a multidisciplinary board, she underwent surgery after giving birth. During a 14-month period of close surveillance, no radiological progression or clinical complications were observed. While there are few cases of SPNs during pregnancy in the literature, no proven link between elevated hormone levels and SPNs has been established (13,14). As in our case, close clinical and radiological monitoring can enable safe surgery in

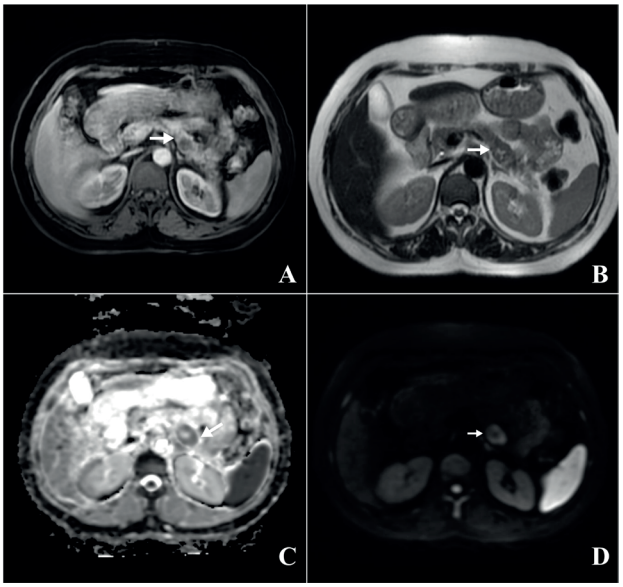

Figure 3: Tumor at the tail of the pancreas (Patient #5) Peripheral thick enhancement of the lesion on contrast-enhanced image (A). A cystic appearance in the central part of the lesion on the T2-weighted image (B). Restricted diffusion of lesion on diffusion weighted imaging (C). Apparent diffusion coefficient (ADC) mapping with restricted diffusion (D).

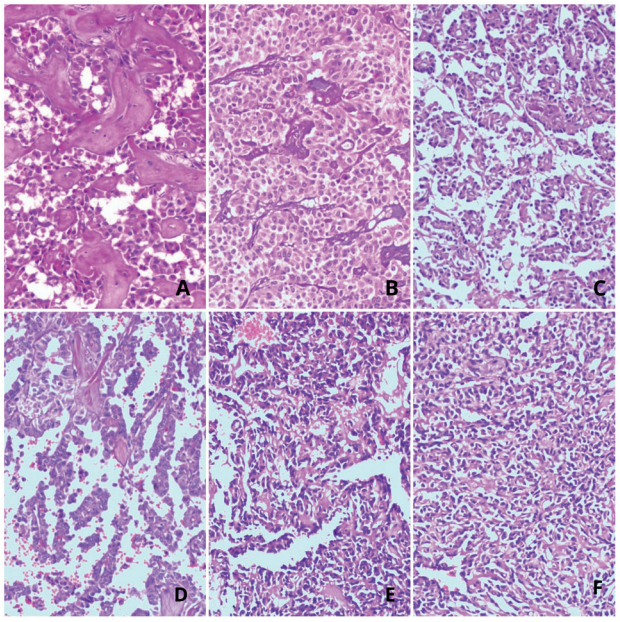

Figure 4. Histologic features of tumors at microscopy. The solid tumors component is composed of poorly cohesive monomorphic cells that cling to hyalinized fibrovascular cords (A,B). SPN exhibiting pseudopapillary structures with loss of cell cohesion (C). Pseudopapillary structures and hemorrhage sites (D). Solid, cystic and papillary structures (E). The tumor cells are uniform with round and small nuclei lining a delicate capillary-sized vessel (F) (Hematoxylin-eosin, original magnification x200).

the postpartum period without compromising patient survival. SPNs tend to be diagnosed at larger sizes during presentation, with reported tumors reaching sizes of up to 25 cm (15). Consequently, clinical presentation of SPNs varies, with symptoms often related to tumor size and location, including abdominal pain, early satiety, nausea, and vomiting (15,16). In our study, a 47-year-old patient (patient #2) presented with persistent vomiting due to external compression of the tumor on the stomach, while another patient (patient #4) with a smaller tumor size (26 mm) was incidentally diagnosed during abdominal imaging. Overutilization of abdominal imaging modalities has contributed to the increased diagnosis of incidental lesions in recent clinical practice. A systematic review in 2014 reported that 40% of SPN cases were incidental, with 90% of these incidental cases diagnosed in recent years (2). Given the non-specific clinical symptoms of this disease, preoperative diagnosis of SPNs is typically based on radiological findings. On magnetic resonance imaging, a typical appearance is a well-defined lesion, with around 80% of cases exhibiting a pure solid structure. These tumors demonstrate low to heterogeneous signal intensity on T1-weighted images and heterogeneous to high signal intensity on T2-weighted images (17). Larger tumors often contain both solid and cystic components and exhibit pseudopapillary structures with hemorrhage (18,19). Unlike pancreatic islet tumors, SPNs do not demonstrate peripheral hypervascularity and may exhibit peripheral or focal calcifications (20,21). SPNs also tend to exhibit high FDG PET/CT uptake, with studies suggesting a potential link between higher FDG uptake and features like cellularity, vascular invasion, perineural invasion, and parenchymal invasion (21). In our series, one patient (patient#3) underwent FDG PET/CT, revealing an SUVmax of 8.5 and histopathological evidence of parenchymal invasion. Despite radiological suspicions, the use of fine-needle aspiration or percutaneous core biopsy for preoperative diagnosis remains controversial. A literature review by Papavramidis et al. reported 52 preoperative biopsies confirming SPNs out of 718 patients (15). Among our patients, biopsies did not successfully diagnose the disease preoperatively. SPNs are essentially malignant epithelial tumors with uncertain cellular differentiation, often exhibiting low-grade dysplasia. Microscopically, poorly cohesive, uniform cells with nuclear grooves can be observed, accompanied by hyalinized or myxoid vascular stalks along with papillary fronds (10). Although SPNs were described decades ago, their genetic profile and molecular behavior have only been elucidated over the past two decades. SPNs commonly harbor beta-catenin gene mutations, distinguishing them from pancreatic adenocarcinomas that typically exhibit KRAS or DPC4 mutations (16,22,23). While SPNs also express progesterone receptor, vimentin, and CD10, these markers are less specific. In a study by Ohara et al., investigating immunohistochemical profiles for differential diagnosis of SPN and neuroendocrine tumors, beta-catenin labeling was reported as the most specific biomarker for SPNs (24). In our series, all patients exhibited positive beta-catenin expression on immunohistochemistry. Additionally, positive staining was observed for vimentin, synaptophysin, progesterone receptor, CD10, and CD56. SPNs are considered borderline malignant neoplasms. According to WHO classification and current literature, features such as vascular or perineural invasion, lymph node involvement, invasion into peripancreatic tissue, and growth beyond the tumor capsule have been linked to more aggressive and metastatic disease (2,16,25,26).

Nonetheless, SPNs generally have an excellent prognosis compared to other pancreatic malignant tumors, with favorable survival outcomes even in cases with lymph node metastasis or positive surgical margins (16). In our patients, the longest follow-up period was 9 years without disease recurrence (patient #1). In a systematic review of 2,744 patients, Law et al. reported a 95% 3-year disease-free survival rate after initial resection (2). Given the favorable prognostic features, aggressive surgical resection of SPNs is the primary approach for managing the disease, including both metastatic and locally invasive cases. While SPNs tend to localize to the body or tail of the pancreas, cases located in the head or uncinate process have also been reported (27,28). Surgery type varies based on location, size, and invasion status of adjacent structures, with the aim of achieving complete excision with negative microscopic margins. R1/R2 resections and inoculations are potential risk factors for recurrence and postoperative complications, such as pancreatic fistula (29,30). The primary limitation of this series is its retrospective design, leading to data availability issues, particularly regarding the immunohistochemistry panel. In conclusion, SPNs are uncommon pancreatic neoplasms that predominantly affect young women. Excellent survival outcomes can be achieved through complete resection, even in cases involving locally invasive tumors.

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Ethics: Ethical approval from the Istanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee (approval number 2021/0350) and all patient informed consent form was obtained.
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