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Solid Pseudopapillary Neoplasm of the Pancreas: Clinicopathologic Features, Review of the Literature

Pankreasın Solid Psödopapiller Neoplazmı: Klinikopatolojik Özellikler, Literatürün Gözden Geçirilmesi

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Abstract

Objective: Solid pseudopapillary neoplasm (SPN) of the pancreas is a rarely seen epithelial tumor with low malignant potential. The aim of our study was to describe the morphology, differential diagnosis and prognosis of pancreatic SPNs and to present a detailed review of the literature.

Methods: A retrospective analysis of all patients diagnosed and treated with SPN in our hospital between 2011 and 2021 was performed. A database of these patients including age, gender, tumor location and size, histopathological and immunohistochemical features and treatment modalities was developed.

Results: The study population consisted of 8 (80%) female and 2 (20%) male patients with an overall mean age of 45.7 years (range: 10 -85 years). A 10-year-old boy was also diagnosed with neuromuscular disease. Tumor diameters ranged from 10 to 95 mm (mean: 48.5 mm). The tumor was localized in the tail of the pancreas in 3 (30%) and both in the body and tail of the pancreas in the remaining 7 (70%) patients. Patients underwent distal pancreatectomy in combination with splenectomy (n=6), total mass excision (n=2) or pancreaticoduodenectomy (n=1). Among the poor prognostic factors, only 1 patient had liver metastasis and another patient had perineural invasion. No patient had lymphovascular invasion and lymph node metastasis.

Conclusion: SPN is a rare neoplasm, typically in young women. It has a slow course and can be treated with surgical resection. Patients have a good prognosis but show recurrence and metastasis.

Keywords: Solid pseudopapillary neoplasm, pancreas, histopathology, immunohistochemistry

Öz

Amaç: Pankreasın solid psödopapiller neoplazmı (SPN) nadir görülen ve düşük malign potansiyele sahip epitelyal bir tümördür. Çalışmamızın amacı pankreas SPN'lerinin morfolojisi, ayırıcı tanısı ve prognozunu tanımlamak ve ayrıntılı bir literatür derlemesi sunmaktır.

Yöntem: Hastanemizde 2011-2021 yılları arasında SPN endikasyonu ile tanı konulan ve tedavi edilen tüm hastaların retrospektif bir analizi yapıldı. Bu hastaların yaş, cinsiyet, tümör yerleşimi ve boyutu, histopatolojik ve immünohistokimyasal özellikleri ve tedavi yöntemlerini içeren bir veri tabanı geliştirildi.

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Öz

Bulgular: Çalışma popülasyonu 8 (%80) kadın ve 2 (%20) erkek hastadan oluşmakta olup yaş ortalaması 45,7'dir (aralık: 10-85). Ayrıca 10 yaşında bir erkek çocuğa nöromusküler hastalık tanısı verilmiştir. Tümör çapları 10 ila 95 mm arasında değişmekteydi (ortalama: 48,5 mm). Tümör 3 (%30) hastada pankreas kuyruğunda, kalan 7 (%70) hastada ise hem pankreas gövdesinde hem de kuyruğunda lokalize idi. Hastalara splenektomi (n=6), total kitle eksizyonu (n=2) veya pankreatikoduodenektomi (n=1) ile birlikte distal pankreatektomi uygulandı. Kötü prognostik faktörler arasında sadece 1 hastada karaciğer metastazı ve diğer bir hastada perinöral invazyon vardı. Hiçbir hastada lenfovasküler invazyon ve lenf nodu metastazı yoktu.

Sonuç: SPN, tipik olarak genç kadınlarda görülen nadir bir neoplazmdır. Yavaş seyirlidir ve cerrahi rezeksiyon ile tedavi edilebilir. Hastaların prognozu iyidir ancak rekürrens ve metastaz gösterir.

Anahtar Kelimeler: Solid psödopapiller neoplazm, pankreas, histopatoloji, immünohistokimya

Introduction

Pancreatic solid pseudopapillary neoplasms (SPNs) were first described as pancreatic papillary cystic tumors by Frantz [1] in 1959. In 2010, World Health Organization (WHO) named these tumors SPNs[2]. In the 5th edition of the 2019 WHO classification of digestive system tumors, SPNs were included in the group of low-grade malignant tumors consisting of less cohesive epithelial cells that do not show specific epithelial differentiation of the pancreas, but display solid and pseudopapillary structure[3]. SPNs are rare tumors constituting 1-3% of pancreatic neoplasms. They present in young females as a well-circumscribed encapsulated solid cystic mass in the tail and body of the pancreas[4,5]. SPN has also been reported in children, elderly patients, and male patients[6]. It was frequently found in the head of the pancreas in pediatric patients[7]. SPNs are typically detected through computed tomography scans or abdominal ultrasound in patients experiencing persistent, unexplained upper abdominal pain of long duration[3]. The levels of carcinoembryonic antigen and amylase in the cyst fluid are decreased[8]. Histologic and/or cytologic evaluation continues to be the most accurate approach for ensuring a definitive diagnosis[9].

On histopathological examination, the tumor consists of solid and pseudopapillary structures[4]. Tumor cells usually have a uniform appearance, contain intracytoplasmic hyaline globules (periodic acid-schiff-positive and diastase resistant, positive for alpha-1-antitrypsin), and have moderately eosinophilic cytoplasm with perinuclear vacuoles. The stroma usually contains varying degrees of hyalinization or hemorrhage, foamy macrophages, calcification, and signs of degeneration such as cholesterol clefts.

SPNs are immunohistochemically (IHC), nuclear positive for β-catenin. There is a loss of membranous expression of E-cadherin. However, CD56, synaptophysin, antichymotrypsin, and alpha 1 antitrypsin, vimentin, SOX11, progesterone and androgen receptors are positively stained[10]. Transcription factor E3 (TFE3), which supports several genes that take part in cell growth and proliferation has been proven to be a very sensitive indicator in 75-96% of cases with SPN. lymphoid enhancer-binding factor 1 (LEF1) is a component of the LEF1/T-cell factor (TCF) complex and has higher diagnostic sensitivity and specificity for SPN[11]. Mitosis is generally rare in SPNs. The Ki67 proliferation index is very low[12].

Point mutation in exon 3 of the *β-catenin* gene *(CTNNB1)* is found in 90% of SPNs. *APC* gene mutation has rarely been detected[13]. The goal of the current study is to describe the IHC, clinico-epidemiologic, and morphologic discoveries and characteristics of SPNs identified during our clinical practice.

Materials and Methods

A total of 10 cases diagnosed with SPN between 2011 and 2021 at the medical pathology department of our hospital were involved in the study. Our study was approved by the University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital Non-interventional Research Ethics Committee (decision no: 2024/03-07, date: 03.04.2024). Informed consent is waived by the ethics committee of our hospital. Patient data were obtained from the pathology database of our hospital. Age, gender, tumor location and size, histopathological and immunohistochemical features, and clinical course of the cases with SPN were evaluated.

Statistical Analysis

Statistical analysis was performed using the IBM Statistical Package for the Social Sciences version 28.0 software (IBM Corp., Armonk, NY, USA).The distribution of variables is measured by Kolmogorov-Smirnov and Shapiro-Wilk tests.

Results

Our study population consisted of 2 male and 8 female patients with a total average age of 45.7 years (range 10-85 years), and a female to male ratio of 4:1. The youngest patient, a 10-year-old boy, also had Becker muscular dystrophy. Most commonly, tumors were seen in the body and tail (70%), and the tail only (30%) of the pancreas (Figure 1). Tumor indicators varied from 10 to 95 mm (mean: 48.5 mm). Distal pancreatectomy combined with splenectomy was performed on the patients (n=6); total mass excision on the patients (n=2); Whipple resection on the patient (n=1); and tru-cut liver biopsy on the patient (n=1). Interestingly, the location of the SPN was learned from the radiological findings of the patient who was diagnosed based on a histopathological examination of a tru-cut needle biopsy material obtained from one of the multiple metastatic lesions of the liver. One of the patients had liver metastasis, and the other had perineural invasion. Lymph node metastasis and lymphovascular invasion were not detected in any patient. Demographic information in addition to clinicopathologic characteristics of the patients is presented in Table 1. The patient with liver metastasis received the diagnosis of malignant SPN, and died within 3 weeks.

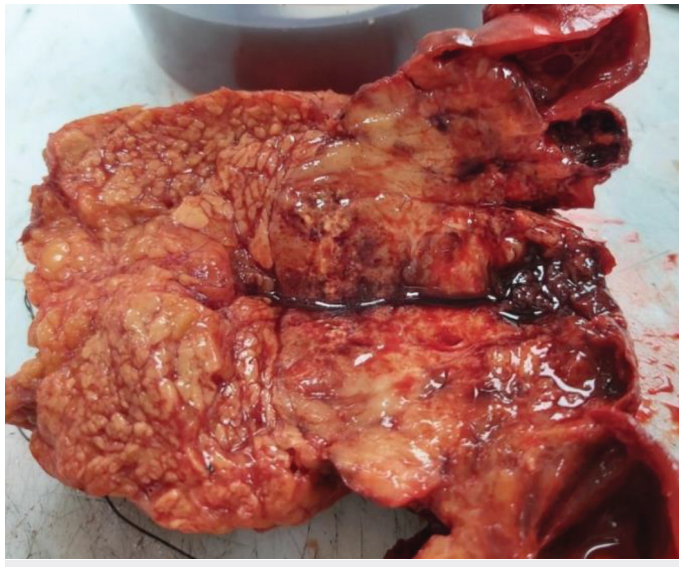

Figure 1. Gross appearance of pancreatic solid pseudopapillary neoplasm

Immunohistochemical staining performed after histopathological evaluation revealed cytoplasmic and nuclear beta-catenin, synaptophysin (Figure 2A-C), pan cytokeratin, and vimentin positivity in all patients.

Discussion

SPN of the pancreas is a rare neoplasm with low malignant potential. It commonly impacts young women in their 20s or 30s. Much research has suggested that between the ages of 24 and 39 years is the mean age of diagnosis (age range: 7-83 years)[14]. In a multicenter study by Sun et al.[15] with 118 cases, 80% of the patients were female and the mean age was 30.8 years. Consistent with the literature data, 80% of the patients in our study were female with an overall mean age of 45.7 years, which is slightly higher than the average age of SPN patients reported in the literature.

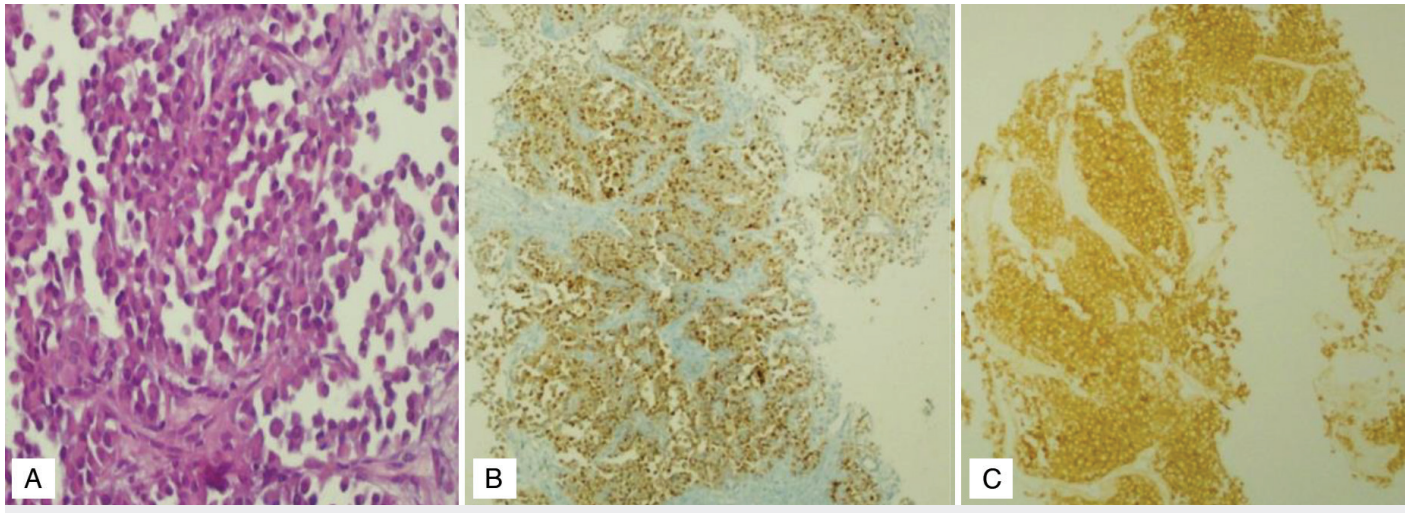

Figure 2. Histopathologic and immunohistochemical features of solid pseudopapillary neoplasm. A. Uniform tumor cells showing pseudopapillary structure (hematoxylin and eosinx100); B. Nuclear and cytoplasmic beta-catenin positivity (DABx40); C. Synaptophysin positivity (DABx40)

Table 1. Demographic and clinicopathologic characteristics of patients with pancreatic solid pseudopapillary neoplasm

n	Age (year)	Gender M/F	Intrapancreatic location of the tumor	Tumor diameter (mm)	Surgical procedures	Perineural invasion	Lymphovascular invasion	Lymph node involvement	Survived/exited
1	38	F	Body and tail	10	Distal pancreatectomy	No	No	No	Survived
2	49	F	Body and tail	30	Distal pancreatectomy	No	No	No	Survived
3	63	F	Body and tail	50	Distal pancreatectomy	No	No	No	Survived
4	10	M	Body and tail	30	Whipple resection	No	No	No	Survived
5	35	F	Body and tail	72	Mass excision	Yes	No	No	Survived
6	71	F	Tail	30	Distal pancreatectomy	No	No	No	Survived
7	47	F	Body and tail	70	Distal pancreatectomy	No	No	No	Survived
8	45	F	Tail	50	Distal pancreatectomy	No	No	No	Survived
9	14	F	Tail	95	Mass excision	No	No	No	Survived
10	85	M	Tail	20	Tru-cut needle biopsy of the liver	-	-	-	Exited

SPNs need to be differentiated from endocrine tumors, which may be morphologically very similar but have a worse prognosis. Although endocrine tumors often lack the diffuse degenerative features, pseudopapillary growth, and nuclear notching of SPNs, IHC is invaluable for solving the challenging issue of differential diagnosis[11,12].

A combined IHC panel of LEF1, TFE3, and beta-catenin demonstrated a sensitivity of 100% and a accuracy of 91.9% in differentiating SPNs from neuroendocrine tumors (Pan-NETs) and pancreatic ductal adenocarcinomas . Therefore, the importance of SOX11 and other transcription factors is critical as diagnostic parameters for SPNs and in distinguishing them from pancreatic ductal adenocarcinomas and Pan-NETs[11,12,16].

Poor prognostic factors involve tumor diameter larger than 5 cm, necrosis, male sex, vascular and perineural invasion, invasion of adjacent structures, and cellular atypia[17]. Chen et al.[18] found that overall survival was significantly associated with tumor size, Ki-67 index, and lymph node metastasis in a series of 63 cases of pancreatic SPN. Liu et al.[19] published a large cohort study of 454 cases of postoperative pancreatic SPN from a single center. In their retrospective study, perineural invasion was reported in 2.2%, lymphovascular invasion in 0.7%, lymph node metastasis in 2%, and distant metastasis in 3.1%. Additionally, 4.1% developed postoperative local recurrence and metastasis, although the patients showed very favorable long-term survival. Perineural invasion was observed in the tumor, with a diameter of 72 mm, in our 35-year-old female patient. Although SPNs have a comparatively lower malignancy potential, metastases develop in up to 15% of these cases. The most prevalent regions of metastases are mesentery, liver, regional lymph nodes, peritoneum, and omentum. One of our cases had liver metastasis, which was evaluated as malignant SPN[20-22]. In a patient with SPN who developed liver metastasis, an uncommon estimated glomerular filtration rate mutation at L861Q in the kinase domain of exon 21 was detected, which was thought to take part in the metastatic progression of SPNs. Genetic examination could not be performed in one patient with liver metastasis.

Two of our patients were pediatric. One of them had Becker muscular dystrophy. No association between this disease and SPN has been found in the literature. Waters et al.[23] compared pediatric and adult SPNs and found similarities in demographics, tumor characteristics, and treatment modalities. However, survival was shown to be better in children. In a series of 16 pediatric SPNs, Samuel et al.[24] found a benign course in eight of nine children classified as malignant SPNs. In one child, the tumor recurred 4 years after the initial resection. The child showed a disease-free survival of 77 months after chemotherapy and radiotherapy.

It has been reported that a multimodality treatment approach is required in recurrent cases.

SPN is primarily localized to the pancreas in over 95% of cases and can be treated with radical resection. The rate of local recurrence is below 10%, typically occurring within 4 years post-surgery[25,26]. In our study, nine patients did not develop recurrence after excision of the mass nor did they receive any additional treatment. These patients are still being monitored as healthy individuals. Only one elderly male patient with multiple metastatic nodules in the liver passed away.

Study Limitations

The retrospective nature of the study and the small patient population can be stated as the limitations of the study. More case series should be included in the literature to evaluate the recurrence and disease progression status of patients with solid pseudopapillary neoplasia after treatment.

Conclusion

In conclusion, SPNs are rarely seen tumors that can be diagnosed based on the results of radiological, histopathological, and immunohistochemical studies. SPNs should be considered in the differential diagnosis of solid cystic neoplasms in the pancreas. Surgically resecting the tumor early leads to a good prognosis and complete resolution, prevents the development of local metastasis and invasion in patients with aggressive tumors. More research is needed both to comprehend the pathogenesis to recognize risk factors and biomarkers for recurrence.

Ethics

Ethics Committee Approval: Our study was approved by the University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital Non-interventional Research Ethics Committee (decision no: 2024/03-07, date: 03.04.2024).

Informed Consent: Informed consent is waived by the ethics committee of our hospital. Patient data were obtained from the pathology database of our hospital.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.S.K., G.D., B.G.Ö., M.D., B.Ç., Concept: D.S.K., G.D., Design: D.S.K., Data Collection or Processing: D.S.K., G.D., B.G.Ö., M.D., B.Ç., Analysis or Interpretation: D.S.K., G.D., Literature Search: D.S.K., Writing: D.S.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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