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Solid and cystic papillary neoplasms of the pancreas: Report of four cases

Pankreasın solid-kistik papiller tümörleri: 4 olgu

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Background/aims: *In this report we present four cases with solid and cystic papillary neoplasms (SCPN) of the pancreas, and discuss the histopathological and immunohistochemical findings with a review of the literature.* ***Methods:*** *The four cases reported here consisted of three women (ages 20-48, mean: 32) and one man (age: 58). The clinical diagnoses were confirmed with ultrasound (US) and computerized tomography (CT). The surgical management of the tumors included enucleation (1 patient), distal pancreatectomy with splenectomy (1) and distal pancreatectomy (2).* ***Results:*** *The tumors were large (mean diameter of the resected tumor was 15 cm), had cystic degenerations between solid areas, and were distributed in the body and the tail of the pancreas. The cystic spaces contained hemorrhagic, necrotic and thrombotic material. The immunohistochemical studies revealed that the four tumors were all positive for a1 antitrypsin and neuron specific enolase, and were all negative for chromogranin. Vimentin and synaptophysin were positive in three different cases. The follow-up of the patients has been uneventful for 2, 1, 7 and 12 years, respectively.* ***Conclusions:*** *SCPN of the pancreas is an uncommon clinicopathologic entity with a relatively low grade malignant potential. The majority of the cases are young women. Fifty percent of the cases are asymptomatic, and the patients with symptoms generally suffer from an abdominal mass or abdominal pain. In spite of the characteristic macroscopic and microscopic aspects, the immunophenotypical view is nonspecific. Prognosis is excellent after complete surgical resection and recurrence is rarely seen. Metastatic spread is not expected and the tumor usually has a manner of local invasion. Acinar cell carcinoma, pancreatoblastoma and pancreatic endocrine tumor must be considered in the differential diagnosis.*

Key words: Solid cystic papillary neoplasms, pancreatic tumors, Frantz's tumor

Amaç: *Bu yazıda pankreasın solid ve kistik papiller neoplazisi saptanan dört olgu, histopatolojik ve immunohistokimyasal bulguları tartışılarak, literatür incelemesi eşliğinde sunulmaktadır.* ***Yöntem:*** *Bu yazıda sunulan dört olgu, üç kadın (yaşlar: 20-48, ortalama 32) ve bir erkekten (yaş: 58) oluşmaktadır. Klinik tanı ultrason (US) ve bilgisayarlı tomografi (BT) ile doğrulanmıştır. Cerrahi girişim olarak iki hastaya enükleasyon, bir hastaya distal pankreatektomi ile birlikte splenektomi ve bir hastaya ise total pankreatektomi uygulanmıştır.* ***Bulgular:*** *Pankreas gövde ve kuyruk bölümlerine yerleşmiş olan tümörler büyük çaplara ulaşmıştı, (ortalama rezeke edilen tümör çapı: 15 cm) ve solid alanlar arasında kistik dejenerasyonlar izlendi. Kistik boşluklarda hemorajik nekroz ve trombotik yapılar saptandı. Yapılan immunohistokimyasal çalışmalar sonucunda dört tümörde de a1 antitripsin ve nöron spesifik enolaz pozitif, kromogranin ise negatif olarak bulundu. Vimentin ve sinaptofizin üç farklı olguda pozitif bulundu. Hastaların sırasıyla 2, 1, 7 ve 12 yıllık takiplerinde sorun yaşanmadı.* ***Sonuç:*** *Pankreasın solid ve kistik papiller neoplazisi düşük dereceli malignite potansiyeli taşıyan ve nadir görülen bir klinik antitedir. Hastaların büyük çoğunluğu genç kadınlardır. %50 hasta asemptomatiktir ve semptomu olan hastalar en çok karında kitle ya da karın ağrısı yakınması ile hastaneye başvururlar. Karakteristik makroskopik ve mikroskopik görünüme sahip olmakla beraber, bu tümörlerin spesifik bir immunofenotipi yoktur. Bu tümörler daha çok lokal invazyon yapma eğilimindedirler ve metastatik yayılım beklenmez. Tam bir cerrahi rezeksiyon sonrası prognoz mükemmeldir ve rekürrens çok nadir görülür. Asiner hücreli karsinom, pankreatoblastom ve pankreatik endokrin tümör ayırıcı tanıda düşünülmelidir.*

Anahtar kelimeler: Solid kistik papiller neoplazi, pankreatik tümör, Frantz tümörü

INTRODUCTION

The dubious nature of the solid and cystic papillary neoplasms (SCPN) began with the first report by Frantz in 1959, when he described the entity as "papillary tumor of the pancreas - benign or malignant?" (1). The tumor is rarely seen where all the cystic tumors of the pancreas are considered as ac-

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counting for approximately 0.5% of all primary pancreatic neoplasms (2). It is very difficult to establish the real incidence of SCPN of the pancreas because of the variety of synonyms ascribed to it, as well as misdiagnosed cases as acinar cell carcinoma, nonfunctioning islet cell tumor, pancreatoblastoma, cystadenoma and even adenocarcinoma (3, 4). Various synonyms include papillary cystic neoplasm, papillary epithelial neoplasm, papillary and cystic tumor, papillary and cystic epithelial neoplasm, papillary and solid neoplasm, papillary cystic carcinoma, solid and cystic tumor, solid and cystic acinar cell tumor and Frantz's tumor (5). The term SCPN should be preferred because it best expresses the histopathological features of the tumor.

Solid and cystic papillary neoplasms of the pancreas are frequently diagnosed during investigation of gastrointestinal complaints such as abdominal pain or abdominal masses, in case of large tumors, or they are found incidentally in smaller tumors (6, 7). Abdominal ultrasonograpy (US) and computed tomography (CT) appear to be the most effective diagnostic tools revealing a well demarcated solid and cystic lesion with accurate localization 8,9. Fine needle aspiration cytology may facilitate the preoperative diagnosis (10); however, there may be some difficulty in typing the cells because of the cytological similarity to islet cell tumor (11).

We herein report our experience in four consecutive patients with SCPN of the pancreas during the last 12 years.

MATERIALS AND METHODS

The hospital files of four cases who were treated for SCPN at the Hepatopancreatobiliary Unit of the Department of Surgery, Ege University Faculty of Medicine between 1990-2002 were reviewed.

All the specimens from resected tumors were fixed in 10% neutral buffered formalin and embedded in paraffin. The specimens were stained for hematoxylin and eosin, periodic acid-Schiff (PAS), Alcian blue, and Grimelius argyrophil, and immunostained for alpha-1 antitrypsin (a1 AT, polyclonal antibody; Dako; dilution 1:2500), neuron specific enolase (NSE, polyclonal antibody; Dako; dilution 1:0), chromogranin and synaptophysin (both monoclonal antibodies; Camon; dilution 1:0 [Wiesbaden, Germany]), vimentin (monoclonal antibody; Dako; dilution 1:50), S-100 (monoclonal antibody; Dako; dilution 1:1000), and cytokeratin 19 (CK19, monoclonal antibody; Paesel; dilution 1:5).

RESULTS

Clinical features: There were four patients (3 female, 1 male) aged 48, 58, 28 and 20 years old, respectively. They had no comorbidity problems. The clinical data are summarized in (Table 1). The tumor of case 1 was found during an investigation of her nonspecific complaints. Abdominal US revealed a mass at the tail of the pancreas which was confirmed by abdominal CT (Figure 1). Splenectomy was performed with distal pancreatectomy because of the adherence to the spleen. The tu-

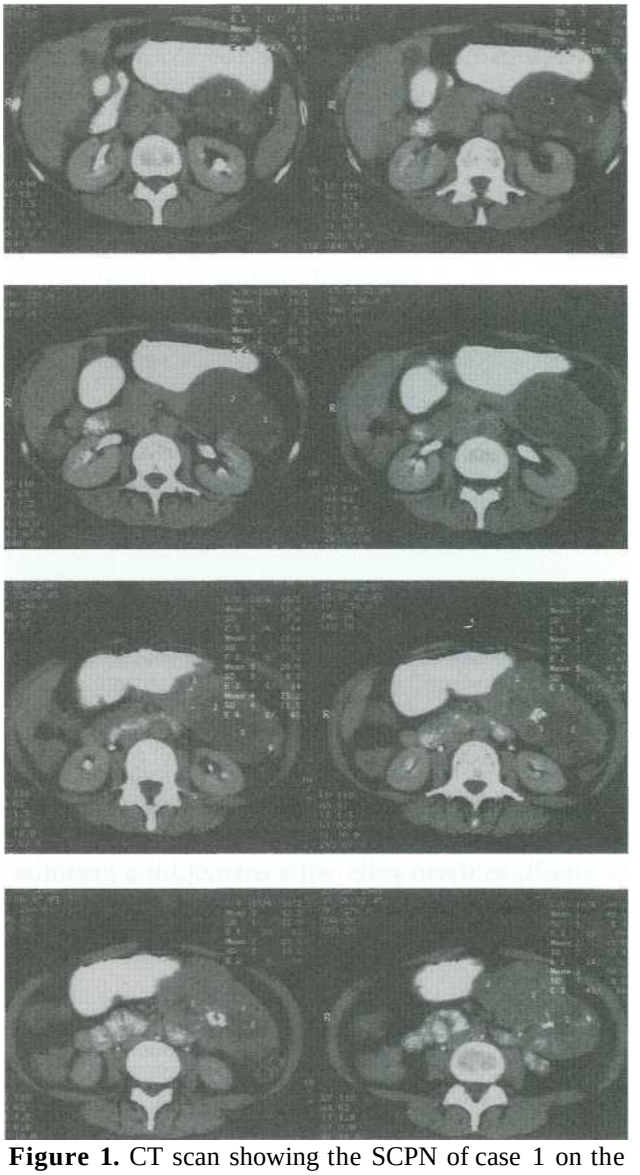

Figure 1. CT scan showing the SCPN of case 1 on the tail of the pancreas

Table 1. Patient's demographic data, type of operation and duration of follow-up

Case #	Age/sex	Symptoms	Location / size	Operation	Follow-up
1	48/f	Nausea, fatigue	Tail 9.5x7x4 cm	Distal pancreatectomy+ splenectomy	PO 2 years / recurrence (-)
2	58/m	Abdominal mass	Body and tail 5x4x4 cm	Distal pancreatectomy	PO 1 year / recurrence (-)
3	287f	Abdominal mass and pain	Body 20x16x5 cm	Distal pancreatectomy	PO 7 years / recurrence (-)
4	20/f	Abdominal pain	Tail 4x4x4 cm	Enucleation	PO 12 years / recurrence (-)

mors of the other three patients were also disclosed by abdominal CT. Distal pancreatectomy and enucleation were the surgical procedures performed on these patients.

The follow-up between 1 and 12 years was uneventful in all cases. All patients are alive with no recurrence or distant metastasis.

Pathologic features: The gross examination of all tumors revealed a thick fibrous capsule surrounding the tumor. On the cut surface, the tumor had multicystic degenerations between solid areas containing hemorrhagic, necrotic and thrombotic material (Figure 2).

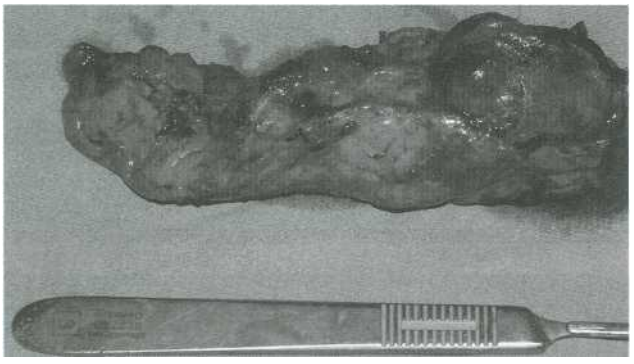

Figure 2. Resected specimen of case 1 with the macroscopic appearance of SCPN

The microscopic features of the tumors were similar in all cases (Figure 3 a-e). The tumor consisted of small, uniform cells with eosinophilic granular cytoplasm. Characteristic papillary protrusions formed by tumor cells around the fibrovascular stalks were present. Solid areas surrounding the cystic spaces disclosed necrotic and thrombotic material with foamy macrophages, cholesterol crystals and calcification. Capsular invasion was noted in cases 1 and 2.

The results of the immunohistochemical staining are summarized in (Table 2). Alpha-1 antitrypsin (a1AT) and NSE were positive, whereas chromogranin and CK 19 were negative in all cases. Vimentin and synaptophysin were positive in three cases and S-100 protein was focally positive in two cases.

DISCUSSION

Solid and cystic papillary neoplasms of the pancreas can occur anywhere in the pancreas and frequently show exophytic growth (4, 8). The localization and presence of local invasion affect the surgical management. The tumors in the head of the pancreas usually necessitate pancreaticoduodenectomy, while tumors in the body or tail can be treated with distal pancreatectomy or even enucleation.

In differential diagnosis, endocrine tumor, pancreatoblastoma and acinar cell carcinoma should be considered (12). Endocrine tumor occurs at a slightly older age than SCPN of the pancreas and is with no gender predilection (13). Pancreatoblastoma is a childhood malignant pancreatic neoplasm with poor prognosis and has a male predominance. Its confusion with SCPN relies most commonly on the cystic necrosis with or without he-

Table 2. Pathologic features of our four SCPN cases

Cases #	a_rAT	NSE	chromogranin	vimentin	synaptophysin	S-100	CK19
1	+	+		+		+(focal)	
2	+	+			+		-
3	+	+		+	+		
4	+	+		+	+	+(focal)	

a1-AT: a1-antitrypsin, NSE: neuron specific enolase, CK19: cytokeratin 19

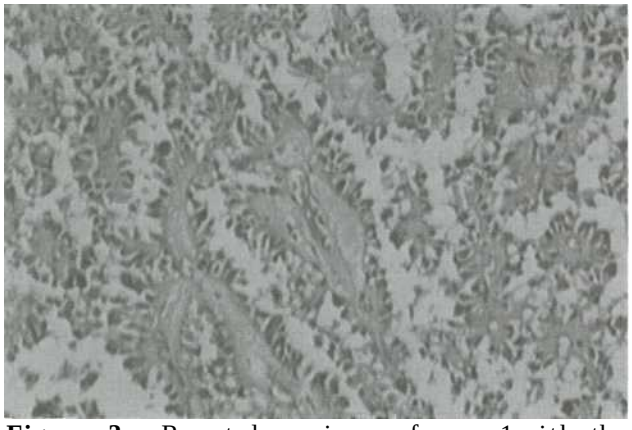

Figure 3a. Resected specimen of case 1with the macroscopic appearance of SCPN

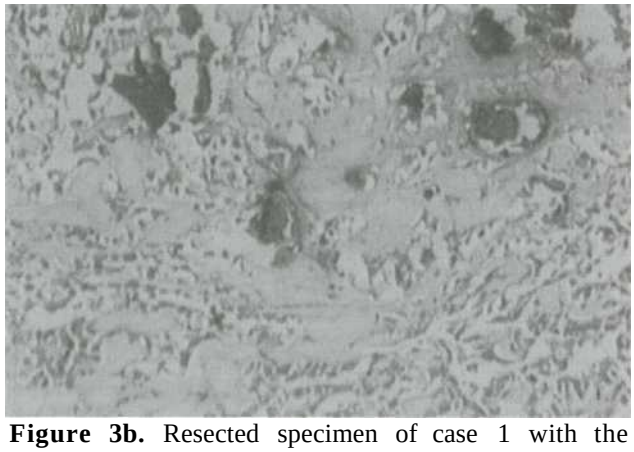

Figure 3b. Resected specimen of case 1 with the macroscopic appearance of SCPN

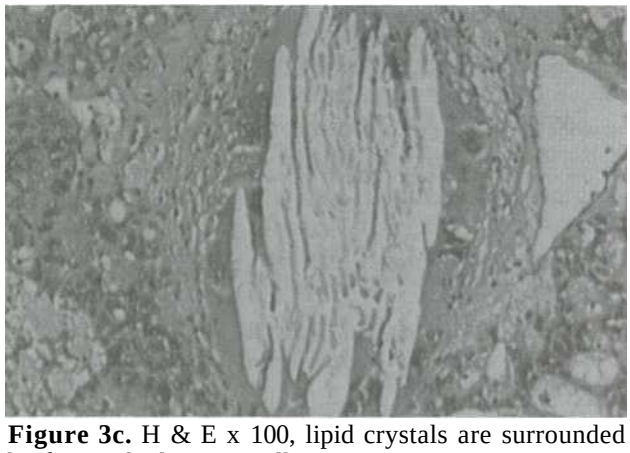

Figure 3c. H & E x 100, lipid crystals are surrounded by foreign body giant cells

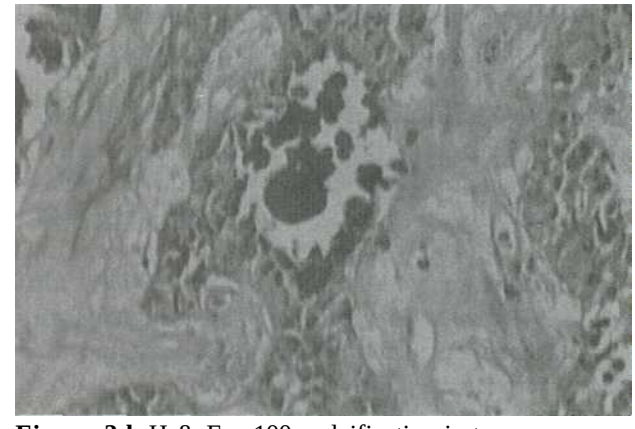

Figure 3d. H & E x 100, calcification in tumor

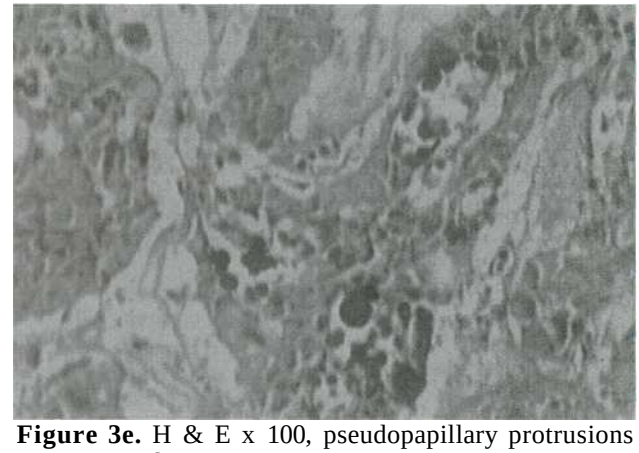

Figure 3e. H & E x 100, pseudopapillary protrusions are seen in the tumor

morrhagic content (14). Although SCPN of the pancreas show acinar cell differentiation due to the well developed Golgi complexes, rough endoplasmic reticulum and zymogen granules in the tumor cells (6, 15), acinar cell tumors are always malignant and affect patients of both sexes, in their sixth or seventh decades (16).

Macroscopically the tumors usually have large masses, sharply demarcated from the pancreatic tissue (3). A fibrous capsule encloses the mass. The cut surface usually reveals nodular solid areas surrounding cystic spaces with hemorrhagic, necrotic and thrombotic contents. Calcifications are also reported in some cases and may occasionally be seen on plain X-ray films (5 ,8, 17, 18). The microscopy of the tumor shows a mixture of papillary and solid patterns (3). The papillary structures are the fibrovascular stalks surrounded by tumor cells (8, 9). The cystic areas correspond to the abundant necrotic material, blood, cholesterol crystals and foam cells (16).

The biologic behavior of SCPN is considered as low-grade malignancy with favorable prognosis after aggressive surgical resection (4). The tumor has been generally regarded as a tumor of young adult females; however, as reported cases accumulate, increase in the age, the rate of the male patients and the malignant potential are observed at higher rates (4, 5). In our experience the eldest female patient (case #1) was 48 and the male patient (case #2) was 58 years old. These relatively elder patients were the ones in whom the tumor had microscopic invasion to the capsule.

The immunohistochemistry of the tumor cells usually shows diversity in most cases. The tumor cells may show mixed or unexpected immune activities. In our patients the epithelial marker a1 -AT was positive in all cases; however, another epithelial marker, S-100 protein, was only focally positive in two cases. As to the neuroendocrine markers, NSE was positive in all patients, whereas synaptophysin was positive in three patients and chromogranin was negative in all cases. The mesenchymal marker vimentin was positive in three cases. These results are consistent with many of the previous reports (19, 20, 21), and support the concept that the origin of SCPN of the pancreas may be the totipotential primordial cells found in the development of the embryonic pancreas (6).

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