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Solid Pseudopapillary Neoplasm of Pancreas; A Case Series and Review Literature

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ABSTRACT

BACKGROUND

Information regarding solid pseudopapillary neoplasm (SPN) of the pancreas is limited in Iran. We aimed to review the clinicocytopathological features and follow-up of patients with SPN of pancreas who were diagnosed in a single center in Iran.

METHODS

Seven patients with SPN of the pancreas were diagnosed during January 2010 to March 2015 at the Digestive Disease Research Institute of Tehran University of Medical Sciences. The patients were reviewed prospectively.

RESULTS

Six out of the 7 patients were female and the mean age of all the patients was 29.4 years ranging from 15 to 61 years. The most common clinical presentation was nonspecific abdominal pain (N=6). The tumors were located mostly in head and neck of the pancreas. SPN was diagnosed in all patients by fine needle aspiration through endosonography (EUS-FNA). All patients underwent surgery. Histological findings of surgical tissues were consistent with EUS-FNA. The postoperative follow-up period of about 14 months was uneventful.

CONCLUSION

SPN of the pancreas is a rare pancreatic tumor which affects primarily young women. EUS-guided FNA could play an important role in preoperative diagnosis of SPN of the pancreas.

KEYWORDS
Solid pseudopapillary neoplasm, Pancreas, Immunohistochemistry

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INTRODUCTION

Solid pseudopapillary neoplasm (SPN) is a rare pancreatic tumors, characterized by low malignant potential and strong female predilection. SPN was first described in 1959. This tumor had several names including Frantz's tumor, solid and papillary tumor, solid-cystic tumor, papil-

lary cystic tumor, and solid and papillary epithelial neoplasm until 1996 when World Health Organization defined it as solid pseudopapillary tumor of the pancreas. It previously accounted for 0.2-2.7% of all exocrine tumors of the pancreas.[1-3] However, due to the recent advantages in medical imaging, the incidence of SPN has increased to 5-6% of all diagnosed pancreatic tumors. SPN is diagnosed much more common in children than in adults consisting of 26% of pancreatic tumors.[4] SPN shows a strong female predilection, 90% of them arising in adolescent and young adult women.[5] Few cases have been reported in men and children.[6-8] The overall mortality rate of SPN is about 2% and recurrence occurred in almost 10-15% of patients after resection.[9]

The etiopathogenesis of SPN has not been fully understood. The predominant occurrence of SPN in young women at the beginning of the reproductive period along with the presence of progesterone receptors, indicate the role of female hormones in the growth of this tumor.[10] This idea has been supported by the fact that genital ridges are closed to the pancreatic anlage during embryogenesis.[10-12] Chromosomal abnormalities are the other mechanism that may have an etiological role in the development of this neoplasm. Some studies suggested that mutation in B-catenin, could play a major role in the tumorogenesis of SPN.[13] According to immunohistochemical and electron microscopic studies, it has been suggested that these tumors originate from undifferentiated pluripotent emberyonal cells.[14]

Herein, we describe the clinical, radiological and cytopathological features of solid pseudopapillary tumor of the pancreas (SPNP) diagnosed by endoscopic ultrasound-guided (EUS-guided) fine-needle aspiration (FNA) and review of relevant literature.

MATERIALS AND METHODS

Patients with final diagnosis of pseudo papillary tumor who referred for EUS to Shariati Hospital, affiliated to Tehran University of Medical Sciences from November 2010 to March 2015 were enrolled. The demographic, clinical and pathological features of all patients were recorded in the Digestive Disease Research Institute. The database included age, sex, associated symptoms, laboratory data, tumor size and location, arterial and perineural invasion, distant metastasis, lymphadenopathy, operative data, and postoperative complications.

The first diagnosis in all patients was made by EUS-FNA cytology samples and finally by surgical tissue. EUS was performed using conscious sedation and linear array Pentax echoendoscopes. The endosonographer inserted a 22 gauge needle into the target lesion and aspirated samples by three passes, almost without applying suction. Aspiration of lesions located in the head of the pancreas or uncinate process was done through the transduodenal approach and lesions in the body and tail of the pancreas through the transgastric route. All samples were enough for cytologic evaluation and there was no need to repeat FNA in any patient. Details of fine-needle aspiration and surgical pathology results were recorded.

Diagnosis of SPNP was confirmed using immunohistochemical (IHC) staining. IHC was done on FNA cell block samples using Dako REAL™ En Vision™ Detection System, Peroxidase/DAB$^+$, Rabbit/Mouse. After surgical operation, all specimens were sent for pathological analysis as well. The hematoxylin and eosin (H and E) stained sections of all FNA and surgical samples were reviewed by an expert pathologist to confirm the diagnosis. The IHC markers (primary antibodies) used in the analysis, included vimentin (clone; v9), pan cytokeratin (CK) (clone; AE1 and AE3), β-catenin (clone; Ncl-β-catenin), CD10 (clone; 56c6), progesterone receptor (PR) (clone; PR88), Synaptophysin (clone; 27G12), and chromogranin A (clone; LK2H10). The patients were followed up through out-patient visits or by telephone interviews. The last follow-up was on March 2015. All of the patients underwent a variety of radiological examinations for preoperative diagnosis including transabdominal ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI).

The study was approved by the Ethics committee and Institutional Review Board of the Digestive Disease Research Institute of Tehran University of Medical Sciences, Tehran, Iran.

Table 1: Clinical and pathological features of patients

Case No.	Age (year)	Sex	Symptoms	Tumor location	Tumor size (mm)	Post-operative complication	IHC findings
1	24	F	Abdominal discomfort, bloating, nausea, vomiting and early satiety	Head	19×16	Uneventful	Strongly positive for Vimentin Positive for Synaptophysin, PR snd CD10 Weakly positive for Chromogranin
2	19	F	Abdominal pain	Neck	47×34	Uneventful	Positive for Vimentin, CD10, and PR
3	21	F	Epigastric pain, nausea, vomiting, early satiety and itching	Head	60×31	Abdominal pain	Positive for Vimentin, CD10, NSE and PR Weakly positive for Pan CK
4	61	M	Asymptomatic	Body	40×30	Uneventful	Positive for NSE, Chromogranin, Synaptophysin Weakly positive for Pan CK and PR
5	20	F	Bloating, abdominal pain	Neck	12×10	Uneventful	Positive reaction to Vimentin Weakly positive for CD10
6	15	F	Abdominal pain	Body and tail	60×58	Uneventful	Strongly positive for B-catenin and Vimentin Weakly positive for Synaptophysin, CD10 and PR
7	40	F	Asthenia, abdominal pain, nausea and vomiting	Tail	60×57	Uneventful	Positive for Vimentin, and PR , Weakly positive for CD10

NSE: Neuron specific enolase, PR: Progesterone receptor, Pan CK: Pan cytokeratin

Data were analyzed using SPSS software, version 20 (IBM, New York, USA).

RESULTS

Seven patients underwent surgical treatment for SPN of the pancreas during the study period. Preoperative diagnosis was made by EUS in all patients. Of these patients, 6(85.7%) were female. The mean±SD age of diagnosis was 29.4±17.2 ranging from 15 to 61 years. Six out of 7 patients presented with nonspecific abdominal pain. In one patient, the tumor was incidentally identified by CT. The level of serum amylase and tumor markers was within the normal range in all patients except in one. The tumor cells were mostly positive for vimentin, PR and CD10, each in 6 cases. Synaptophysin was positive in 3 patients, followed by NSE and cytokeratin, each in 2 patients. β-catenin was only positive in 1 patient. Patient characteristics are summarized in table 1.

Surgical treatment

All patients underwent surgical treatment. The most common location of the tumor was the head and neck of the pancreas, each in 2 (28.5%) patients, followed by the body, tail and both the body and tail, each in one patient. The mean diameter of the tumor was 42.5 mm (range: 12-60 mm). Two patients had perineural invasion; however, none of the patients showed distant metastasis. Four patients with lesion in the head or neck underwent pancreaticoduodenectomy. The other three patients with lesions in the body and/or in the tail underwent distal pancreatectomy. There were no perioperative surgical deaths or perioperative complications.

EUS findings

A mixed solid and cystic appearance was identified in three patients, and others had predominantly solid appearance. The margin of the masses was well defined in all the patients. There was no evidence of vascular, or lymph node involvement.

DISCUSSION

The most common presenting symptoms of SPNs are abdominal pain followed by increased abdominal girth, poor appetite and nausea resulting from tumor compression on the adjacent organs

and a palpable mass.[15] Although almost 30% of patients are completely asymptomatic and discovered incidentally during routine clinical examination or diagnostic imaging procedures, some patients (8%) present with acute abdomen as a result of abdominal blunt trauma or spontaneous rupture of the capsule.[16] Clinical presentations of our patients included abdominal pain, nausea and vomiting, weight loss, bloating and feeling of fullness.

It has a strong female preponderance with female-male ratio of 5:1.9[17] and up to 10:1.[3] Male patients presented much later compared with women (mean age: 31 years).[18,19]

The diagnosis of SPN has increased during the recent years due to advances in diagnostic imaging techniques. However, clinical and radiological findings are insufficient for reaching a definite diagnosis and tissue sampling should always be considered. EUS-FNA needle aspiration and cytology is the best technique for preoperative diagnosis of SPN and less invasiveness than surgical procedures. EUS-FNA is increasingly using for identifying the tumor over the recent years, however it still constitutes fewer than 5% of performed imaging. SPN lesions have been shown as well-circumscribed, hypoecho, heterogenous solid and cystic masses by EUS. EUS-FNA is significantly more effective than CT in differentiating neoplastic from non-neoplastic, along the identifying malignant pancreatic cysts.[20] Furthermore, immunohistochemical staining and mutation analysis of beta catenin gene are helpful in distinguishing SPN from other pancreatic tumors.[21]

Complete surgical resection is the mainstay of treatment in all patients with SPN even in the presence of local invasion or distant metastasis. The most common surgical procedures performed for pancreatic SPN are distal pancreatectomy and pancreaticoduodenectomy (Whipple surgery). Local invasion and distant metastasis were reported in 5% and 6% of SPN patients, respectively.[22] The most frequent sites affected by metastases include the liver (28%), wall of vena cava (27%) and the spleen (17%). Duodenum, omentum, colon, and lung are the other preference location of metastases.[23] Invasion to regional lymph nodes has been rarely reported which is consistent with our series.[24,25] The efficacy of non-surgical approaches including chemotherapy and radiotherapy has not been proven.[26,27] The prognosis of SPN is favorable, even in the presence of metastases or invasion to other organs.[28-30] Considering the fact that the 5-year survival rate of SPN is 94-97%, it is very important to differentiate it from other pancreatic lesions. However, if metastatic lesions are impossible to be removed, long-term survival is undeterminable. There are several reports of liver transplantation in patients with unresectable hepatic metastases.[31]

According to the largest report of patients with SPN, pancreatic tail and the head of pancreas are the most common localizations of the tumor followed by pancreatic body, body and tail, head and body, neck and the uncinate process of the pancreas.[5] However, in this series, only one of our patients had tumor in the tail region and most of the tumors were located in the pancreatic head and neck. In our series, perineural invasion was found in two patients. Vimentin was positive in 4 (57%) of the patients. Our small sample size did not allow us to compare different tumor characteristics with the sex of the patients. Lymph node metastases were not found in none of the patients in this series which is consistent with other reports. The mean follow-up period of our patients was 14 months (7-30 months) which is short for giving a comprehensive opinion on recurrence rate. In previous studies, SPN have a mean diameter of 6.08 Cm (range 0.5 to 34.5 Cm). Metastasis or local recurrence rate of SPNP in patients treated by radical surgical excision is 9%- 15%.[22,32] There was no evidence of local or distant metastases in our patients. As we presented in our series, there was no association between SPNP and laboratory test results including serum tumor markers.[33,34]

The data regarding prognostic factors for malignant transformation of SPN are controversial. Factors that can be useful in predicting the malignant potential of the tumor are perineural and vascular invasion, lymph node involvement and deep invasion of surrounding tissues.[15] The morphological appearance is not a good predictor of clinical behavior of these

Table 2: Comparison of clinical characteristics and outcome of SPN patients between present study and worldwide studies

Study	Number of cases	Age, mean (range) year	Sex ratio (F/M)	Tumor size, mean (range) Cm	Follow-up, mean (range) month	No.distant meatastases	Survival, %
Salvia et al.[33]	31	34 (7-56)	27/4	5.4 (2-20)	58 (12-229)	0	100
Tipton et al.[26]	14	30 (15-57)	13/1	7 (4-16)	88 (3-240)	2	100
Goh et al.[24]	16	30 (14-53)	15/1	9.5 (5-24)	67 (3-186)	0	100
Yang et al.[41]	26	32 (15-64)	22/4	6.25 (2-15)	33 (3-69)	2	96.2
Guo et al.[42]	24	31 (11-61)	23/1	7.5 (2-26)	68 (4-109)	2	95.8
Zhang et al.[43]	9	30 (14-68)	8/1	5.4 (2-10.5)	30 (NA)	2	88.8
Vassos et al.[44]	4	24.5 (15-42)	4/0	5.5 (1-16)	40 (24-57)	0	100
Present study	7	29.7 (15-61)	6/1	4.03 (1.2-6)	14 (7-30)	0	100

tumors; SPN with subtle histological malignant appearance can show local invasion to adjacent structures.[30]

Several studies indicated that male sex, large tumor size (>5 Cm), and tumor necrosis could predict malignant transformation.[35] However, most of the studies do not report any association between age and tumor location with malignant potential of SPN.[36]

The clinical features and outcome of our patients were compared with recent reports from other countries in table 2. There are similar characteristics among these reports especially regarding age and female predominance.

In our study, IHC analysis showed strong positivity for vimentin, CD10, and PR. These findings are consistent with previous studies that reported positivity for vimentin in 100% and 70% of cases, respectively.[37,38] Tumor cells of SPN showed strong positivity for CD10 in two previous studies,[39, 40] In the present series, PR was positive in 6 out of 7 patients. Machado et al,[25] reported PR positivity in 80% of cases and the percentage of PR positivity was 64.5% in a study by Uppin et al.[37] Taken together, the frequent expression of PR and strong female predilection of SPN indicate the importance of hormone dependency in the pathogenesis of this tumor.

CONCLUSION

SPN is a rare tumor mostly seen in young women. SPN of the pancreas have an excellent prognosis. EUS-guided FNA with preparing cell block from the aspiration and using IHC with relevant markers are a very helpful techniques for preoperative diagnosis of SPN.

CONFLICT OF INTEREST

The authors declare no conflict of interest related tothis work.

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