Ultrasound-guided fine-needle aspiration cytology of solid pseudopapillary tumor of the pancreas: a tertiary care centre experience

Ram Nawal Rao^{1*}, Preeti Agarwal¹, Deepti Mishra¹, Praveer Rai², Shaila Mitra³ and Megha Bansal¹

*Correspondence: rnrao@sgpgi.ac.in

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¹Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, UP, India.

²Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, UP, India.

³Department of Pathology, BRD Medical College, Gorakhpur, UP, India.

Abstract

Background: Solid pseudopapillary tumours (SPT) of pancreas is an unusual neoplasm with uncertain malignant potential. It is seen predominantly in adolescent girls and young women. We present the clinical, ultrasound-guided fine needle aspiration (US-FNA) cytologic features, differential diagnosis and immunohistochemical findings in SPT.

Methods: A retrospective 4-year (2007–2010) fine needle aspiration samples of 8 solid pseudopapillary tumours of pancreas were reviewed.

Results: The entire cases were cured with exploratory laparotomy. This study includes 8 cases (1 male, 7 female) of solid pseudopapillary tumours of pancreas. All these cases showed characteristic cytomorphological features displaying hypercellular smears with presence of several papillary fragments lined by multilayered anisomorphic atypical cells having fine chromatin with delicate nuclear groove, myxoid stroma and foamy macrophages in a haemorrhagic background.

Conclusions: Correct preoperative cytological diagnosis of solid pseudopapillary tumours of pancreas may be accurately possible by US-FNA technique and also aids in treatment of the surgically curable cancer in the patients.

Keywords: Fine-needle aspiration cytology, ultrasound, cystic, solid pseudopapillary tumour and pancreas

Introduction

Solid-pseudopapillary tumour of the pancreas (SPT) is a rare uncertain malignant potential tumour which has distinctive cytopathologic features. It is also known as "Frantz tumor" which was first described by Dr. Frantz in 1959 [1]. SPT occurs more frequently in the body and tail of the pancreas of adolescent girls and young women. This tumour can be large and can undergo degenerative cystic changes that are evidenced on clinical and radiographic studies [2]. SPT typically is limited to the pancreas at the time of preliminary diagnosis, and a complete surgical excision is treatment of choice. Metastases are rare after excision, and even patients with metastasis at initial diagnosis often survive for years or decades [3,4]. On the contrary pancreatic adenocarcinoma is an aggressive neoplasm. So targeted therapy and chemotherapy have been found to

be beneficial in the patients which were highlighted in some studies [5]. Interestingly, IFN- β was significantly more effective than IFN- α in inducing cell growth inhibition in pancreatic cancer because it induces a more potent and early cell cycle arrest and apoptosis activation compared with IFN- α [6].

SPT from other pancreatic cystic neoplasms of similar radiologic and cytologic appearance Endoscopic FNA as well as US-FNA can have an important role and provide an accurate preoperative cytodiagnosis, particularly when the USG findings of the mass are inconclusive. US-FNA can differentiate but with different biologic behavior and treatment, such as pancreatic endocrine tumours, acinar cell carcinoma, and papillary mucinous carcinoma [7-13]. SPT behaves like a low-grade malignancy and has an excellent prognosis and hence its differentiation from its other counterparts is important [14]. This study highlights

mainly the cytomorphologic features, differential diagnosis and immunohistochemistry of the cases of SPT diagnosed by US-FNA.

Materials and methods

This retrospective study in which US guided FNA of pancreatic cases between years 2007-2010 were reviewed. Total number of 150 US guided FNA of pancreas were performed at our institute. Eight out of them were diagnosed as SPT on US-guided FNA smears and surgical resection. The clinical details, radiology, cytopathology and histopathology data was retrieved for re-evaluation from the records. US-FNA was performed using 22 gauge needles via a transhepatic (6 cases) or a transgastric (2 cases) approach. The aspirated material was quickly smeared into glass slides, air dried, wet fixed in 95% ethyl alcohol for subsequent Papanicolaou staining and remaining for cellblock (if any). Adequacy of aspirated material was checked under light microscope during the procedures. Immunohistochemical stains for CD10, vimentin, cytokeratins, chromogranin, synaptophysin, neuron-specific enolase and progesterone were performed on 4 cases consisting of surgical resection (two cases) and cellblock samples (two cases). All smears, cell block and tissue sections were reviewed with emphasis on the evaluation of cytomorphologic features and immunohistochemical results. Histopathological tissue sections of all resected specimens were reviewed and findings correlated with those obtained by US-FNA.

Results

A total of 8 patients with cytological diagnosis of solid pseudopapillary tumours of pancreas were identified. Patients' age ranged from 15 to 47 years. Average tumour size was 5.5x4.5 to 16.0x15.0 cm and majorities were located in the pancreatic body and head. Sonologically the tumours were solid in 3 patients (37.5%), mixed solid and cystic in 4 patients (50.0%), and cystic in 1 patients (12.5%). A preoperative diagnosis of solid pseudopapillary tumour was made in 8 patients on the basis of US-FNA cytology. Surgical resection was performed in all cases of SPT.

Patients clinical, USG findings and Cytohistologic findings are summarized in [Table 1](#). The smears showed variable degree of cellularity and characteristically branching papillary fragments in 7 out of 8 cases which composed of vascular stalks with a perivascular amorphous myxoid substance festooned by bland-appearing tumor cells ([Figure 1](#)). These tumor cells have variable amounts of scant to moderate cytoplasm with focally projections in some; uniform oval to round nuclei with nuclear grooves, fine chromatin, 1-2 small nucleoli and variable amount of cytoplasm in all cases ([Figure 2](#)). The cytology smears also showed areas of necrosis (1 case), mitosis (1 case), cytoplasmic hyaline globules, nuclear groove (7 cases) and cluster of atypical cells with pseudorosette forming structure in 2 cases ([Figure 3](#)). In case 5, smear showed prominent large nucleoli in some cells. Some atypical cells have binucleation

Figure 1. Cytology smears showed tumor cells composed of predominantly branching papillary fronds with central capillaries cores and myxoid stromal fragments in case #1 (MGG, $\times 200$).

Figure 2. Smears showed tumor cells arranged in pseudopapillary pattern lined by multilayered mildly anisomorphic atypical cells displaying round to oval nuclei with nuclear grooves, fine chromatin and moderate to abundant amount of cytoplasm with characteristic myxoid stroma in case #1 (MGG, $\times 400$).

and multinucleation with abundant plasmacytoid cytoplasm (2 cases). Background showed areas of haemorrhage (all cases), foam cells (5 cases) and cholesterol crystals in 2 cases ([Figure 4](#)). 1 of 8 cases US-FNA in cystic mass of the pancreas yielded haemorrhagic fluid and smear shows predominantly myxoid material and occasional singly scattered small to round atypical cells with nuclear groove, fine chromatin and foamy histiocytes. Cytomorphologic findings with histopathologic diagnosis were described in [Table 2](#). Contrast enhancing computed tomography (CECT) were done in all the cases and showed

Table 1. Clinical, USG findings and cytohistopathologic diagnosis of SPT (n=8).

Case No	Age/Sex	Tumor Location	Clinical findings	Tumor Size(mm)	USG Findings	Surgery	Cytohistopathologic Diagnosis
#1	47/F	Head & Body	Pain and lump abdomen, vomitingx10yrs	110X80	Cystic Hypoechoic	Central Pancreatectomy	SPT
#2	21/F	Uncinate process	Pain in abdomen x1yrs	52X38	Solid, calcified	Pylorus preserving Pancreaticoduodenectomy	SPT
#3	27/F	Head	Pain in abdomen, Jaundicex6yrs	75X53	Solid, cystic echogenic	Central Pancreatectomy	SPT
#4	36/F	Head	Pain in abdomen x11 Yrs	60X50	Solid, Echogenic	Pylorus preserving Pancreaticoduodenectomy	SPT
#5	32/F	Head	Pain and lump in Abdomenx3yrs	85X70	Solid and cystic	Central Pancreatectomy	SPT
#6	25/M	Body & Tail Mass	Pain in abdomen Radiating to backx 4months	50X45	Solid Hypoechoic	Pancreaticoduodenectomy	SPT
#7	15/F	Head	Epigastric pain, Fever & Vomiting x3yrs	120X95	Solid and cystic heterogeneous Hypoechoic	Central Pancreatectomy, Splenectomy	SPT
#8	25/F	Tail	lump and pain in epigastrium, Vomitingx4months	160X150	Solid and cystic Hypoechoic and calcification	Pancreaticoduodenectomy	SPT

SPT: Solid pseudopapillary tumor of the pancreas

Table 2. Cytomorphologic findings with histopathological correlation (n=8).

Case No	Papillary Fronds	Central Capillaries	Myxoid Stroma and descrete Cells	Nuclear Grooves	Amount of Cytoplasm	Necrosis	Mitosis	Background	Cytologic Diagnosis	Histologic Diagnosis
#1	+	+	Present	+	Scant	-	-	Haemorrhagic, Foam cells & cholesterol crystals	SPT	SPT
#2	+	+	Present	+	Moderate	-	-	Haemorrhagic	SPT	SPT
#3	+	+	Minimal	+	Abundant	-	-	Haemorrhagic	SPT	SPT
#4	+	+	Present	+	Moderate	-	-	Haemorrhagic, Foam cells & mucin blobs	SPT	SPT
#5	+	+	Present	+	Abundant	-	-	Haemorrhagic, Foam cells	SPT	SPT
#6	+	+	Abundant	-	Scant	-	-	Haemorrhagic	SPT	SPT
#7	+	+	present	+	Abundant	+	Rare	Haemorrhagic, Foam cells	SPT	SPT
#8	-	+	+	+	Moderate to abundant	-	-	Haemorrhagic, Foam cells & cholesterol crystals	SPT	SPT

SPT: Solid pseudopapillary tumor

a large heterogeneous circumscribed solid and solid-cystic mass in head, body and tail regions of the pancreas (**Figure 5**).

Histopathological examination were done in all eight cases and showed similar microscopic findings. Outer surface of gross specimen showed well circumscribed mass having variegated solid to cystic cut surface with areas of haemorrhage and necrosis (**Figure 6**). Tumour cells arranged in papillary fronds,

sheets and cords around delicate fibrovascular septae (**Figure 7**). These cells were small to medium size displays uniform round to oval nuclei with groove, fine chromatin and mild to moderate cytoplasm. Marked degenerative changes were also seen in all the cases. Immunohistochemistry was performed only in four cases and results showed strong positivity for CD10 (**Figure 8**) and vimentin, cytokeratin and focal positivity for synaptophysin,

Figure 3. Smear showed cluster of atypical cells with pseudorosette forming structure and prominent nuclear grooves in case #2 (arrow, MGG, $\times 400$).

Figure 4. Smear showed singly lying atypical cells with eccentric nuclei, fine chromatin, small 1-2 conspicuous nucleoli, bi/multinucleation, foam cells (up arrow), cholesterol crystal (down arrow) and abundant plasmacytoid cytoplasm misleading to those of pancreatic endocrine tumors in case #8 (MGG, $\times 200$).

Figure 5. Contrast enhancing computed tomography (CECT) showed a large heterogeneous circumscribed solid-cystic mass (arrow) in body and tail regions of the pancreas in case #8.

Figure 6. Pancreatic tail mass measuring 16x14x10cms in size and showing encapsulated-firm variegated solid cystic (arrow) friable grayish white to grayish brown areas with papillary excrescences, hemorrhage and necrosis in case #8.

neuron-specific enolase (NSE) and progesterone receptors. These immunohistochemical stain results were consistent with previously described immunohistochemistry of the solid pseudopapillary tumour of the pancreas.

Discussion

Solid pseudopapillary tumour of the pancreas (SPT) is very rare tumour with low malignant potential having a distinctive clinicopathological profile [15,16]. SPT is most commonly seen in young women with a mean age of 27 years (range, 2-81 years). It is rare in men pediatric population [17-20]. Similarly our study showed female dominance with average

age of 27.25 years. Clinical symptoms of the patients usually present on and off abdominal pain in epigastrium and palpable abdominal mass with compression of adjacent organs when the mass is large. In one case of the patient also showed symptoms of vomiting, jaundice and anorexia. Thus, a cystic mass in the pancreas of a young woman raises a clinical suspicion for SPT. Out of eight cases, five of them showed cystic component on ultrasound. In most patients, the tumour follows an indolent clinical course, and complete resection often is curative. However, approximately 10% to 15% of SPT are malignant and show local infiltration, recurrence, or distant metastasis [21,22]. SPT with malignant behaviour seems more prevalent in the pediatric population, it has been

Figure 7. Histopathology section showed tumour arranged in papillary fronds, sheets and cords around delicate fibrovascular septae. Tumour cells were small to medium size displays uniform round to oval nuclei with grooves, fine chromatin and mild to moderate cytoplasm with marked degenerative changes in case #8 (H&E, x400).

Figure 8. Tumor cells are strongly positive for CD10 on immunohistochemical staining in case #8 (IHC CD10, x400).

found in older men and also has indolent behavior [23,24]. The benign-appearing SPT might contrast with the cellular anaplasia present in the metastatic deposits [25]. Thus, there are no histologic features that can predict aggressive clinical behavior. Proposed pathologic features related to aggressive behavior or metastatic potential include diffuse growth pattern, venous invasion, nuclear pleomorphism, mitotic rate, necrosis, and areas of dedifferentiation [26].

Imaging studies of SPT show a well-circumscribed, hetero-

geneous, solid and cystic mass with sometimes calcification and have often central cystic degeneration. Similarly, tumoral calcification can be seen in the often cystic and nonfunctional large pancreatic endocrine tumor, serous cystadenoma, and mucinous cystadenocarcinoma and less commonly in ductal adenocarcinoma [27]. Two of our cases showed calcification. Thus, image diagnosis is not specific [28]. EUS permits a better evaluation of SPT, but the findings also are not specific. The majority of preoperative diagnoses of SPT have been made by percutaneous approach via EUS or US-FNA techniques. These US-FNA cytomorphic features are highly characteristic and distinct from those of other cystic or solid tumors of the pancreas [29].

US-guided FNA diagnosis of SPT is simple, accurate and cost effective technique. In most of our SPT cases, US-FNA cytology smears showed numerous isolated branching papillaroid fronds with capillaries having multilayered mildly anisomorphic round to oval atypical cells displaying nuclear groove, fine chromatin, scant to moderate cytoplasm along with myxoid stroma, foamy histiocytes, occasional bi/multinucleated cells, cellular debris, psammoma bodies and eosinophilic cytoplasmic hyaline globules on a hemorrhagic background. These hyaline globule are periodic acid-Schiff-positive with diastase-resistant inclusions and similar findings are also described in some previous cases [30-36]. Thus we recommend that when these cytological features are present in the smears, cell block and in combination with immunohistochemical profile, the diagnosis of SPT can be made straight forward. However, pancreatic endocrine tumors, papillary mucinous carcinoma, acinar cell carcinoma and, occasionally, intraductal papillary mucinous tumour and serous cystadenoma must be excluded. In one of our case the US-FNA in cystic mass of the pancreas yielded haemorrhagic fluid and smear shows myxoid material and few singly scattered small to large atypical cells with round to oval eccentric nuclei with nuclear groove in some, fine chromatin and moderate to abundant cytoplasm along with few foamy histiocytes on the background.

Immunohistochemically, most SPT are immunoreactive for vimentin (vim), α 1-antitrypsin, α 1-antichymotrypsin [37], occasionally positive for neuron specific enolase and synaptophysin [38] and nonreactive for S-100, CA 19.9 and chromogranin A. In our cases, SPT showed strong expression of vimentin, CD10 along with focal for neuron-specific enolase, synaptophysin, progesterone receptors and variable cytokeratin. Lack of expression of epithelial membrane antigen and chromogranin is inconsistent with any of the normal pancreatic cell types and reinforces the epithelial, mesenchymal, and endocrine cell phenotype that suggests a pluripotential embryonic stem cell origin for SPT [39,40]. Immunohistochemical detection of progesterone receptors has been found in the neoplastic epithelium of SPT in women but not in men [41].

The main differential diagnoses of SPT includes pancreatic neuroendocrine tumour, acinar cell carcinoma, papillary

mucinous carcinoma and intraductal papillary mucinous tumour (IPMT) (Table 3). Pancreatic endocrine tumours mainly occur in older patients and may be associated with a variety of clinical syndromes. Pancreatic neuroendocrine tumours might show similar cytomorphologic features, and, in the absence of papillary structures with perivascular myxoid substance, the distinction between the two is difficult. The presence of rosettes, without papillary structures, occasional multinucleated giant cells, and spackled nuclear chromatin or "salt and pepper" chromatin indicates in favor of a pancreatic endocrine tumour [42,43]. Cystic neuroendocrine tumours of the pancreas usually are functional but occasionally might be nonfunctional and are more likely to be confused with SPT on imaging studies [44]. These tumors express neuroendocrine markers such as chromogranin, neuron-specific enolase, and synaptophysin which are usually nonreactive in cases of SPT.

Pancreatoblastoma is a tumour of childhood that lacks the pseudopapillary pattern and fibrovascular stalks with myxoid stroma and consistently is negative for vimentin and positive for pancreatic enzymes, features that allow its distinction from SPT. Acinar cell carcinomas with an endocrine component having immunostains and ultrastructural features of both tumours have been described [42]. Serous cystadenoma showed a well-demarcated solid or cystic mass by EUS and might exhibit prominent papillary differentiation on FNA.

Papillary mucinous carcinoma presents a single, large, often unilocular cystic mass in patients [45]. In compare with SPT, the cells in papillary mucinous carcinoma are columnar with variable nuclear anaplasia, irregular chromatin, and

prominent nucleoli [46]. The abundant mucinous background of papillary mucinous carcinoma must not be confused with the myxoid stroma and globoid structures seen in SPT. Thick glistening and viscid mucus material almost always present in intraductal papillary mucinous tumour is an important feature that distinguishes this neoplasm from SPT [47].

Ricardo H et al., focused on the cytomorphologic features and differential diagnosis of 6 new cases of SPT diagnosed EUS-guided FNA and briefly addressed the recent advances in his understanding of the histogenesis, immunohistochemical analysis, and genetic events of this tumor [48]. Salla et al., reported the clinical, imaging, cytomorphologic features and differential diagnosis of a 17-year-old woman having SPT diagnosed by EUS-guided FNA with a review of the literature in which patient has complaints of an unexplained episodic pain for 2 months and a short history of hypertension. The cytomorphology of the tumor is highly characteristic, with features that are distinctive from those of other cystic and solid tumors of the pancreas [49]. Mehta et al., also described the cytomorphology of solid pseudopapillary tumor of the pancreas and its differential diagnosis in six cases diagnosed preoperatively on US- FNA [50].

An accurate FNA diagnosis will alter the eagerness of patient and surgeon to a complete resection of the tumour, since recurrence has not been reported after complete local resection. In addition, while surgery might not be different, the diagnosis is important if considering preoperative (neo-adjuvant) chemotherapy, radiotherapy, or both for acknowledged carcinoma.

Table 3. Differential diagnosis of solid pseudopapillary tumor of pancreas (SPT).

Features	SPT	Pancreatic Endocrine	Acinar Cell Carcinoma	Papillary Mucinous Carcinoma	IPMT
Clinical features	M/F ratio, 1:10; young, women; rare in children	M/F ratio, equal; rare in children; may be functional	M/F ratio, 2:1; adults; rare in children and adolescents	Adult women; after fifth decade	Adult men; after sixth decade
US-FNA findings	Papillary fronds; central capillaries, cell clusters of variable size	Scattered small cell clusters; Rosette/acini formation	Loosely clustered of atypical acinar cells with prominent nucleoli	Papillary fragments; atypical cell clusters of variable size	Sparse cellularity; tight clusters, sheets; infrequent papillary clusters
Myxoid stroma	Present	Absent	Absent	Mucin instead of myxoid stroma	Thick, viscid mucus
Branching fronds	Present	Present	Can be Present	Can be Present	Can be Present
Nuclear groove	Present	Absent	Absent	Absent	Absent
Necrosis	Rare	May be present	Commonly present	can be present	Present in rare cases
Immunohistochemical study					
CD10	+	+	–	–	–
Vimentin	+	+	–	–	–
Chromogranin	–	+	–	–	–
Synaptophysin	+	+	–	–	–
NSE	+	+	–	–	–
Cytokeratin	+	+	+	+	+
Progesterone receptor	+	–	–	–	–

SPT: Solid pseudopapillary tumor

Conclusions

We consider as that US-FNA can present as best cellular yield with an overall diagnostic accuracy and sensitivity for the correct and early cytological diagnosis of SPT. Clinical correlation, imaging findings and cytomorphologic features from US-FNA reach the exact diagnosis of SPT.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	RNR	PA	DM	PR	SM	MB
Research concept and design	✓	✓	--	--	--	--
Collection and/or assembly of data	✓	✓	✓	--	✓	✓
Data analysis and interpretation	✓	✓	✓	--	✓	✓
Writing the article	✓	✓	✓	✓	--	--
Critical revision of the article	✓	✓	--	✓	--	--
Final approval of article	✓	--	--	✓	--	--
Statistical analysis	--	--	--	--	--	--

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