Original Article

Solid pseudopapillary epithelial neoplasm of pancreas

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Abstract

Solid pseudopapillary epithelial neoplasm of pancreas (SPEN) is a rare pancreatic tumor with an unclear pathogenesis and good prognosis after resection. We report our experience with three cases of SPEN of the pancreas. All patients were females with an age range of 15 – 42yrs. Preoperatively FNAC was done in one of the patients and two patients underwent surgery without preoperative diagnosis because of high suspicion of SPEN based on clinical and radiological findings. By immunohistochemistry, all cases stained strongly for vimentin, CD 10 and variably with pankeratin. Patients have been on a regular follow up showing no evidence of recurrence or metastatic disease. In conclusion, SPEN of the pancreas should be considered in the differential diagnosis of any solid and partly cystic pancreatic or upper abdominal mass, particularly in young females. Solid pseudopapillary epithelial neoplasms of pancreas are a rare but treatable pancreatic tumor. Complete surgical excision is the treatment of choice and can be achieved through an open or minimal access technique.

Keywords: Solid pseudopapillary neoplasm, SPEN, Immunohistochemistry

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INTRODUCTION

A solid-pseudopapillary epithelial neoplasm of pancreas (SPEN) is a rare and "enigmatic" pancreatic neoplasm which was first observed in 1927 in a 19-year old woman following which it was first described by Frantz in 1959. Hence, the tumor was initially recognised as Guber - Frantz's tumor and over the time many other terminologies were used such as, papillary cystic tumor, solid cystic pancreatic neoplasm, papillary epithelial neoplasm of pancreas of childhood and adenocarcinoma of the pancreas[1]. In 1996, the term SPEN was included in the WHO classification and has been reclassified in the current WHO classification as low-grade malignant neoplasm of the exocrine pancreas. Solid pseudopapillary epithelial neoplasm (SPEN) of the pancreas is a rare neoplasm with an overall incidence of 0.2 – 2.7% and over 700 cases being reported worldwide with very few cases from India. The number of reported cases have increased over the last decade, probably due to the familiarity of the entity.[2] Herein, we present the histopathological and immunohistochemical characteristics of three cases of SPEN, and discuss them together with a review of the literature.

CASE 1

A 15-year-old female referral patient presented in our Gastroentrology Outpatient Department with history of intermittent abdominal pain of one month duration. The pain was dull aching and not associated with nausea, weight loss, or any other systemic complaints. CT scan done had revealed a predominantly solid mass involving the head of pancreas with a probable diagnosis of an exophytic pancreatic cystic neoplasm. USG guided FNAC of the pancreatic mass was performed. Cytology smears were highly cellular and showed few large papillary fragments with thin fibrovascular cores lined by

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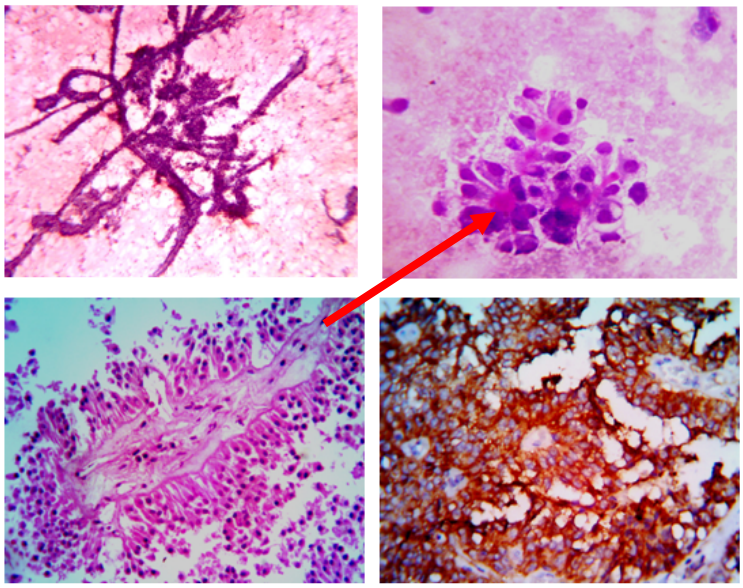
small bland uniform tumor cells, along with many scattered cells and few cystic macrophages. The cells showed round to oval nucleus with finely granular chromatin, with some cells showing prominent nuclear grooves. Pseudorossette formation with central thick proteinaceous material was noted. There was no evidence of, significant pleomorphism or increased mitotic figures. Thus, a diagnosis of SPEN was suggested. A week later the patient underwent whipples procedure. Gross examination revealed a cystic irregular mass measuring 6x6cms. Cut surface was partly solid and partly cystic. The surgical resected margins appeared uninvolved by the tumor. On histopathological examination, the tumor was partially encapsulated. Cells were predominately arranged in nodules and islands separated by thin fibrovasular septae and in pseudopapillary pattern. Cells were monotonous, with round to oval nucleus, granular chromatin and moderate amount of eosinophilic cytoplasm. Focal increase in foamy macrophages and lymphoid aggregates was observed. The resected margins and lymph nodes were free of tumor. Immunohistochemistry performed showed strong positivity for vimentin and NSE, with 70% cells positive for CD 10. The tumor cells were negative for chromogranin and cytokeratin.

CASE 2

A 16 year old female patient presented to our gynaecology department with complaints of menorrhagia. For the same, USG abdomen was done which revealed an incidental finding of pancreatic mass. CT abdomen and pelvis reported on a solid cystic pancreatic neoplasm arising from the body of pancreas with possibility of a serous cystic neoplasm, NET or SPEN. Thus the patient was posted for an operative procedure and underwent central pancreatectomy. Grossly the tumor was cystic and measured 6x5.5x2.5cms. Cut surface showed friable grayish white material and hemrrhage. Histopathological examination observed hyalinised fibromuscular cores lined by several layers of bland epithelial cells with eosinophilic cytoplasm with round nucleus, stippled chromatin and prominent nuclear grooves. Surrounding areas showed fibrosis. Margins were free of tumor infiltration. The tumor cells showed diffuse positivity for CD10 while chromogranin and pan cytokeratin were negative.

CASE 3

Here we have a 37years female patient presenting with complaints of vague abdominal pain since 1 week and tenderness in the epigastric region. CT abdomen suggested a mucinous cystic neoplasm arising from the body of pancreas. Also with a clinical suspicion of pseudocyst of pancreas or mesenteric cyst, within a week the patient underwent median pancreatectomy and cyst excision. Grossly we received a cystic structure measuring 10 x 8 x 4cm. External surface was congested. Cut surface showed areas with papillary projections. Microscopically the tumor cells were arranged in solid nests and also in pseudopapillary pattern. Cells showed mildly anisocytic round to oval nucleus, some showing nuclear grooving and moderate eosinophilic cytoplasm. Stroma showed areas of hyalinization and congested blood vessels. No significant mitotic figures seen. No areas of necrosis present. Immohistochemistry performed, revealed tumor cells to be positive for vimentin and CD10 and unusually positive for pan cytokeratin.



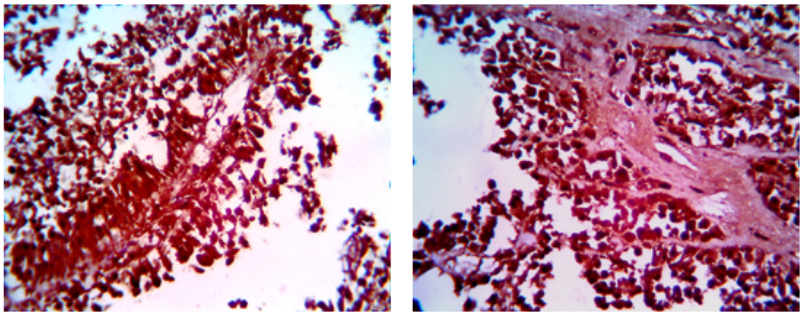


Figure 1: Cytology smears shows long papillary fragments intersecting each other. HE x10
Figure 2: Cytology smears showing pseudorossette formation of tumors cells around central proteinacous material. MGG; x 40
Figure 3: Tissue sections showing papillary structures lined by several layers of tumor cells with central fibrovascular core.HE 10x
Figure 4: Immunohistocheistry - Tumor cells positive for CD10. x10
Figure 5: Immunohistochemistry - Tumor cells showing diffuse positivity for vimentin. x10
Figure 6: Immunohistochemistry - Tumors cells positive for cytokeratin. X10

DISCUSSION

The broad spectrum of cystic and solid and cystic neoplasms of the pancreas comprises an arbitrary minimum of 14 different tumor types. [3] For practical purposes, the most commonly encountered cystic neoplasms of the pancreas may be classified into five categories: serous cystic neoplasms, mucinous cystic neoplasms, intraductal papillary mucinous neoplasm (IPMN), cystic neuroendocrine neoplasms and solid pseudopapillary neoplasm of the pancreas (SPEN). Among these uncommon pancreatic tumors, SPEN represents an exceedingly rare entity. SPEN usually affects young women at a mean age of 22 years. One quarter of cases have been reported in children, men and elderly patients. One of our patients presented at a relatively higher age (37 yrs) compared to most reported cases. Most patients including our patients present with nonspecific symptoms including abdominal discomfort, mild abdominal pain, palpable abdominal mass, nausea, loss of weight, vomiting etc. SPEN being a slow growing neoplasm, reaches large sizes before being detected, as the patient sometimes remain asymptomatic.[4] The most common localization of SPEN is the tail and body of pancreas (64%) with head tumors accounting for a lesser percentage. One of our cases presented with a pancreatic head mass. They rarely present as multifocal tumors with in the pancreas and more exceedingly rare in extrapancreatic sites, such as the mesocolon, retroperitoneum, omentum, liver and duodenum, possibly representing synchronous tumor spread. None of our cases presented with any extrapancreatic tumor lesions.[5] The pathogenesis of SPEN remains unclear and has been postulated to arise from primitive pancreatic cells. It has been suggested that SPEN might be an hormone-dependent tumor as studies reveal that it commonly expressed PR receptor and becomes apparent at the time of pregnancy.[6] A preoperative cytological diagnosis of SPTs shows highly cellular smears with several layers of tumors cells lining slender branching fibrovascular stalks. Pseudorosette formations are also described. The individual tumor cells appear monomorphic with round to oval eccentric nuclei, bland nuclear chromatin, tiny nucleoli and longitudinal grooves with eosinophilic cytoplasm. In our case, tumor cells showed similar cytomorphology.[7] Grossly, solid-pseudopapillary neoplasms appear to be well circumscribed or partially encapsulated with a fibrous capsule. Cut surface reveals, both cystic and solid components. The solid areas are usually red-tan, friable, and hemorrhagic, with rare calcification. Sometimes, near complete cystic change may occur, simulating a pseudocyst. Invasion of adjacent organs or the portal vein is rare.[8] Serous and mucinous cystic neoplasms, pancreatoblastoma, acinar cell tumor and NET can have similar solid cystic components competing with the diagnosis of SPEN. Histologically, these tumors with variegated appearance show a mixture of solid, cystic, an d pseudopapillary patterns. Solid areas show discohesive polygonal cells separated into nests by abundant capillary-sized vessels. In areas away from the vessels, cell drop away, leaving a ragged cuff of neoplastic cells clinging to the blood vessels resulting in the characteristic pseudopapillae. There is also no true lumen formation.[9] The finding of true luminal spaces with lack of pseudopapillary pattern is helpful to suggest one of these rather than solid-pseudopapillary neoplasm. Sometimes, the degenerative changes of solid-pseudopapillary neoplasms can result in a gross and microscopic pattern almost indistinguishable from a pseudocyst.The nuclei are round to oval, uniform, and have frequent longitudinal nuclear grooves and are sometimes oriented away from the vessels, resulting in a zone of cytoplasm surrounding the capillaries. Moderate amount of eosinophilic cytoplasm is seen, sometimes being clear or vacuolated. PAS-positive hyaline globules

and stromal hyalinization are other characteristic features.[10] The interface of SPEN with surrounding tissue often demonstrates entrapped pancreatic acini within the tumor. Also red cells are found admixed with nests of neoplastic cells, forming 'blood lakes' at the periphery of the neoplasm giving the appearance of vascular invasion. These findings are not to be considered as malignant features.[11]

Malignant transformation occurs in 15% of adults and 13% of children. These Aggressive variants show prominent nuclear pleomorphism and atypia, extensive necrosis and increased mitotic rate (up to 30 mitoses per 50 high-power fields [HPFs]. Angioinvasion, perineural invasion and deep invasion of pancreatic tissue characterize malignancy and bad prognosis. One of our cases showed tumor infiltrating the peripancreatic adipose tissue.[12] Most solid-pseudopapillary neoplasms stain for vimentin, CD10 (96%), neuron-specific enolase, CD56, progesterone receptors(79%) and α-1-antitrypsin, with none being specific for a diagnosis of SPEN. These tumors express variable expression of synaptophysin and cytokeratins and are consistently negative for chromogranin, ductal markers (glycoproteins), and acinar markers (trypsin and chymotrypsin). Immunolabeling for β-catenin and cyclin D1 have been reported to be significantly specific. Although they are classified under epithelial tumors of the pancreas, many usually do not express epithelial markers such as cytokeratin and epithelial membrane antigen thus differentiating SPEN from other epithelial tumors.[13] The pattern of staining is not typical for any normal epithelial cells of the pancreas. Positivity for CD56 and synaptophysin might suggest an endocrine phenotype, the most specific endocrine marker (chromogranin) is always negative.[14]

Table 1: Immonohistochemistry panel for diagnosis of pancreatic neoplasms

	DAD	ACC	NET	SPEN
PAN CK	+	+/-	+/-	+/-
S100	+	-	-	-
β- CATENIN	M*	M/N**	M	NandM
E- CADHERIN	+	+	+	-
CHROMOGRANIN	-	-	+	-
CD 10	-	-	+	+

*Membranous ; **Nuclear

Metastases are found 10-15% of cases usually limited to the liver and peritoneum, lymph node metastases being exceptional. By electron microscopy solid-pseudopapillary neoplasms show epithelial differentiation including an incomplete basal lamina, rudimentary lumina, and poorly defined intercellular junctions.[15]

CONCLUSION

Solid-pseudopapillary neoplasm is an extremely rare, indolent tumor with low grade malignant potential. Surgical resection usually results in complete recovery in the majority of patients. Malignant transformation and metastasis although uncommon have been documented. Irrespective of the malignant potential of the tumor it is uncommon for patients to die from direct effects of the tumor. Certainly, our case series illustrates many of the salient features of this tumor, such as higher frequency in females, indolent clinical course and potential curability after complete surgical removal.

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