Solid and cystic papillary neoplasm of pancreas: 
A clinico-pathological and immunohistochemical study: 
A tertiary care center experience

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Abstract

Background: Solid pseudopapillary tumor of the pancreas (SPT) is a rare tumor of low malignant potential, mostly described in young women. Materials and Methods: In this retrospective study from January 2000 - December 2010, there were 50 pancreatic tumors. In this period, four SPTs were encountered, which were analyzed with respect to clinical, imaging, histopathological, and immunohistochemical findings. Results: There was a female preponderance with mean age of 22.2 years. Two of the tumors were located in head of the pancreas and two in the body and tail region. On imaging, majority were large cystic tumors. Histopathologically, they exhibited extensive necrosis and presence of pseudo papillae in viable areas. Immunohistochemically, they were positive for alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, vimentin, CD10, and CD99. Progesterone receptor and p53 exhibited mild positivity in all of the four cases, whereas neuron specific enolase (NSE), synaptophysin, and chromogranin showed focal positivity in one case. Conclusion: Despite its non-specific clinical, imaging, and even immunohistochemical features, characteristic gross and microscopic findings provide reliable diagnosis of SPTs. 

Key words: Immunohistochemistry, pancreas, solid pseudopapillary tumor of the pancreas

Introduction

Solid pseudopapillary tumor of the pancreas (SPT) is a rare tumor, mostly encountered in young women, first described by Frantz way back in 1959.[1,2] Its various synonyms include papillary cystic neoplasm, papillary epithelial neoplasm, papillary and cystic tumor, papillary and cystic epithelial carcinoma, papillary and solid neoplasm, solid and cystic acinar cell tumor, and Gruber - Frantz’s tumor.[3] This tumor is of low malignant potential.[2,4] It offers diagnostic and therapeutic challenges because of its rarity and uncommon clinical manifestations.[4] In this study, we present the clinico-pathological and immunohistochemical analyzes of four cases of SPT with review of relevant literature.

Materials and Methods

In this retrospective study from January 2000 - December 2010, a total of 50 pancreatic tumors diagnosed histopathologically were retrieved from the archives of department of pathology. Out of these, 36 were ductal adenocarcinoma, three were islet cell tumor, six were adenoma, and five were cystic pancreatic tumors. Clinical data were obtained from the medical records. SPT accounted for four of the cases. Hematoxylin and eosin-stained slides were reviewed in each case of SPT. Immunohistochemistry was performed on formalin-fixed, paraffin-embedded sections using the super sensitive polymer horse radish peroxidase method along with appropriate controls. After application of pre-diluted antibodies, immunoreactivity was visualized using 3, 3’ di-amino benzidine tetrachloride as chromogen. The immunohistochemical stains used were alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, neuron-specific enolase (NSE), synaptophysin, chromogranin, vimentin, progesterone receptor, p53, CD10, and CD99. All these markers were from BioGenex (San Ramon, CA).

This study mainly involves the histopathology review of the paraffin blocks submitted to the department of pathology. The patients and their relatives have given consent to utilize the information for publication purpose as noted from the standard case sheet record obtained from the medical records department. As the study had no intervention other than standard care, we have not obtained permission from the institutional review board.

Results

Out of the four SPTs, three were females and one was male. Age range was 18-27 years with a mean age of 22.2 years. Two of the SPTs were located in the head of the pancreas, whereas the other two were in the body and tail region. Three patients were symptomatic with abdominal pain being the commonest presentation. In one case, the tumor was detected incidentally with...
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previous history of trauma. One patient had complaints of vomiting and jaundice in addition to abdominal pain. Pre-operative imaging like ultrasound and computed tomography (CT) revealed large tumors with both cystic and solid area in three cases, and in one case, the tumor was predominantly cystic. [Figures 1, 2] The surgery done for two tumors located in the body and tail region was distal pancreatectomy and splenectomy. For the tumors located in the head of the pancreas, Whipple’s pancreaticoduodenectomy was done. Grossly, all the tumors were large with mean diameter of 9.2 cms. All of these tumors revealed presence of hemorrhagic and necrotic areas on the cut surface. [Figure 3] [Table 1] Microscopically, they were well-circumscribed with presence of fibrous capsule. [Figure 4] They exhibited extensive areas of necrosis. The tumor cells in the viable area were predominantly arranged in the form of pseudo-papillae and solid islands. Mitotic activity was infrequent in all except one where mitotic figures were present 1-2/10 high power field. The tumor was seen infiltrating the capsule and adjacent pancreas in two of the

![Figure 1: Contrast enhancing CT axial image showing heterogeneously enhancing mass in the head and uncinate process of pancreas with necrosis within](image1)

![Figure 2: Contrast enhancing CT axial image, showing well-defined heterogeneously enhancing mass with cystic areas within in the tail of pancreas](image2)

![Figure 3: Large pancreatic tumor with cystic and necrotic areas](image3)

![Figure 4: SPT demarcated from the adjacent pancreas by fibrous capsule (H and E, x10)](image4)

| Case no | Age/sex | Location | Symptoms | CT findings | Surgical treatment |
|---------|---------|----------|----------|-------------|-------------------|
| 1       | 18/F    | Head     | Pain abdomen, vomiting, jaundice | 8×4 Cystic and solid | Whipple’s pancreaticoduodenectomy |
| 2       | 20/F    | Body and tail | Incidental finding | 9.5×7.5 Cystic and solid | Distal pancreatectomy and splenectomy |
| 3       | 27/M    | Body and tail | Mass abdomen | 11×11 Cystic | Distal pancreatectomy and splenectomy |
| 4       | 24/F    | Head and uncinate process | Pain abdomen | 11×8.4 Cystic and solid | Extended Whipple’s pancreaticoduodenectomy |

CT=Computed tomography
cases. However, neither vascular nor perineural infiltration was noted in any of them. There was also no evidence of lymphnodal metastasis. Immunohistochemically, alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, CD10, and CD99 were positive in all the tumors. CD99 showed intra-cytoplasmic dot-like positivity in three cases and intense membrane positivity in one case. [Figure 5] Mild and focal positivity for progesterone receptor and p53 was observed. One of the cases showed focal positivity for NSE, synaptophysin, and chromogranin. All of our patients had uneventful post-operative period.

**Discussion**

Solid pseudopapillary tumor is rare, but in recent times, several cases have been documented in the literature. It accounts for approximately 1-2% of all exocrine pancreatic tumors. Most commonly, it is seen in adolescent girls and young women with mean age of 20-25 years. It is rare in men, accounting for 7% of the cases.

In our study of four SPT, there were three females and one male. Majority were in their second decade with mean age of 22.2 years (range 18-27 years). Usually, these patients present with non-specific clinical features like abdominal discomfort and pain. Sometimes, abdominal trauma is the only preceding event. Most often, these neoplasms are found incidentally on routine physical examination. Large SPTs may cause symptoms like abdominal pain, nausea, and/or vomiting, possibly due to compression of adjacent viscera by the tumor. Jaundice is rare even for tumors originating from the head of the pancreas. These tumors are not associated with functional endocrine syndrome.

In our cases, abdominal pain was the commonest complaint followed by mass in the abdomen. One case was incidentally detected after trivial fall with blunt injury to abdomen. Though jaundice is described as rare, one of our patients had jaundice at presentation.

Imaging studies like ultrasonography (US) and computed tomography (CT) often reveal classic imaging characteristics of SPT like large size, mixed solid and cystic nature, encapsulation, and hemorrhage.

On imaging, all the tumors were large, majority had both solid and cystic areas. These tumors have no preferential localization within the pancreas.

Zeytunlu et al. in their study of four cases of SPTs have described them in young women presenting with non-specific symptoms, located in the body and tail of pancreas as large tumors. We also had similar findings with a younger age group, and half of our cases were located in the body and tail region.

The pre-operative diagnosis of SPT is possible by means of fine needle aspiration cytology, which reveals loose aggregates of small, monotonous cells with scant cytoplasm surrounding thin-walled capillaries. There is also characteristic presence of pseudo-papillae, intra-cytoplasmic globules, stripped nuclei, and non-necrotic background, which helps in the cytological diagnosis of SPT. However, in our cases, pre-operative FNAC was not done.

Grossly, it is usually a well-circumscribed, often encapsulated tumor ranging in size from 3-18 cm in diameter. Its cut surface has a variegated appearance with solid, cystic, and papillary areas with necrosis and hemorrhages. All the tumors in our study were large and exhibited areas of hemorrhage and necrosis on cut surface.

Microscopically, these tumors are well-circumscribed and usually encapsulated. Extensive necrosis and degenerative changes are common. The tumor cells are arranged mostly in pseudopapillary and with occasional monomorphic pattern. The nuclei are uniform and round with an even chromatin pattern and small nucleoli. Often, nuclear grooves are seen. Hyaline globules are also noted in many cases. They have low mitotic activity, and usually do not have perineural and vascular invasion.

In our cases, extensive areas of necrosis were observed in addition to the characteristic microscopic features like presence of pseudo-papillae. The individual cells were oval to polygonal with scant to moderate amount of eosinophilic cytoplasm. The nuclei were vesicular with clumped chromatin. All these cases had insignificant mitotic activity except one. Capsular infiltration was observed in two of the cases. None of these cases showed either vascular or perineural invasion, and metastasis also was not seen in any of them.

The clinical differential diagnosis includes many non-neoplastic and neoplastic cystic lesions like inflammatory pseudo cyst, mucinous cystic tumors, microcystic adenoma, and mucinous cystadenocarcinoma. The characteristic morphologic features of SPT like areas of degeneration (cholesterol clefts, foamy macrophages), cyst formation, and the absence of lumen formation helps in the correct diagnosis. Histopathologically, pancreatic endocrine tumor remains a close differential diagnosis. But,
Solid and cystic papillary neoplasm of pancreas. have mentioned that the chromatin pattern of SPT is also more diffuse compared to the salt and pepper type seen in neuroendocrine tumors. Moreover, immunohistochemical analyses of pancreatic endocrine tumors show strong diffuse staining with neuroendocrine markers such as synaptophysin. SPTs typically show only focal staining with synaptophysin. Also, SPTs mostly stain for CD10,[15,16] and CD99 positivity in all cases in addition to markers like alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, vimentin, and progesterone. Though one of our cases showed CD99 positivity in all cases in addition to markers like alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, vimentin, and progesterone. Similarly, pancreatoblastomas express pancreatic enzymes, which distinguish them from SPTs.[14]

The histogenesis of SPT remains uncertain without any evidence for ductal, acinar, or frank endocrine differentiation.[15] Literature reviewed shows that SPTs shows variable immunohistochemical expression for various epithelial, mesenchymal, and endocrine markers. There is usually immunoreactivity for vimentin, alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, NSE, and progesterone.[1,15]

Li et al., in a recent article, have observed intra-cytoplasmic dot-like immunoreactivity of CD99 in SPTs in contrast to membranous staining in all pancreatic endocrine tumors and most of acinar cell carcinomas, along with negative immunostaining in ductal carcinomas. They have concluded that CD99 combined with E-cadherin/β-catenin and CD10 can be used as a relatively specific expression profile of SPTs.[16,17] In our study of SPTs, we noted CD10 and CD99 positivity in all cases in addition to markers like alpha-1-anti-trypsin, alpha-1-anti-chymotrypsin, vimentin, and progesterone. Though one of our cases showed CD99 membrane positivity, taking into account its gross and microscopic features, it was included in SPT. We have not done E-cadherin/β-catenin in this study. P53 expression was also mild in our cases.

Histological criteria of malignancy include capsule thickness of more than 2 mm, high nuclear grade, prominent necrobiotic nests, capsular invasion, vascular invasion, and metastasis.[13,18] But, out of these criteria, tumor showing perineural and vascular invasion or deep invasion into surrounding tissue are classified as solid-pseudopapillary carcinoma. Only few metastasizing solid-pseudopapillary neoplasms have been reported. Common metastatic sites include regional lymph nodes, liver, peritoneum, and greater omentum.[14,19,20]

After complete surgical removal, more than 95% of the patients are cured.[10,15,21,22] For tumors with aggressive histological features, adjuvant chemotherapy (gemcitabine and cisplatin-based neoadjuvant chemotherapy) is advocated in addition to surgery.[23] Seo et al. have described complete surgical resection as the treatment of choice. In their series of eight patients, seven underwent surgical procedures like distal pancreatectomy with/splenectomy, and one patient was subjected to Whipple operation.[21] In our study, distal pancreatectomy with splenectomy was done in two patients where tumor was located in the body and tail region of pancreas and Whipple operation in another two patients, who had tumor in the head of pancreas. All the patients had an uneventful post-operative period. None of the patients received adjuvant chemotherapy.

Yang et al. have reconfirmed the utility of surgical procedure in their literature review of Chinese case. They are of the opinion that surgical debulking should be done even with the presence of metastasis.[4,22] SPTs are rare and should be considered in the differential diagnosis of the cystic pancreatic tumors, especially in young females. Its characteristic gross and microscopic findings help in reliable diagnosis, despite its non-specific clinical, imageological, and even immunohistochemical features. Further study with better follow-up is desired to characterize these uncommon tumors.

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