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Case Presentation
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Solid Pseudo-Papillary Tumor of Pancreas - A Rare Case Report

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Abstract

Solid Pseudopapillary Tumor (SPPT) of the pancreas is a rare tumor accounting for 1% to 3% of exocrine pancreatic neoplasm. It typically affects mostly young women, often in their 20's. Present case is of 28 years old female patient with complaint of abdominal pain. Her radiological investigation showed large retroperitoneal mass, measuring 10 cm × 9 cm × 8 cm with multiple small central? Necrotic foci origin of this mass could not be ascertained. FNA done from retroperitoneal mass under USG-guidance showed few atypical cells in clusters and scattered singly. These cells showed moderate anisonucleosis, indistinct nucleoli and abundant cytoplasm. Few intracellular and extracellular hyaline globules (PAS positive) present. Some cells showed coarsely vacuolated cytoplasm. On this basis, differentials considered were SPPT, adrenocortical carcinoma, renal cell carcinoma and rhabdoid tumor. Pancreatic mass along with pancreatic tail and spleen was excised. According to cytological, radiological, gross, histological and immunological findings, final diagnosis of solid pseudopapillary neoplasm of the pancreas was made. This case is of interest due to its rarity, presence of hyaline globules and cytoplasmic vacuoles in microscopy, new molecular markers and good prognosis of patients.

Keywords: Hyaline globules; Cytoplasmic vacuoles; Good prognosis; Pancreas

Case Presentation

A 28 years old female patient presented in surgery department with complaint of abdominal pain. Her abdominal CT was advised and showed large heterogeneous hyperdense retroperitoneal mass measuring 10 cm × 9 cm × 8 cm with multiple small central necrotic foci. Origin of this mass could not be ascertained (Figure 1). FNA done from retroperitoneal mass under USG- guidance showed mainly hemorrhage along with few atypical cells in clusters, pseudorosettoid pattern, scattered singly and arranged around capillaries and thick blood vessels. These cells showed moderate anisonucleosis, indistinct nucleoli and abundant cytoplasm. Few intracellular and extracellular hyaline globules (PAS positive) were present.

Some cells showed coarsely vacuolated cytoplasm (PAS negative) (Figure 2). Our case didn't show prominent nucleoli, nuclear grooving and cercariform cells. Mitosis was infrequent. According to cytological findings, differentials considered were SPPT, adrenocortical carcinoma, renal cell carcinoma and rhabdoid tumor (Table 1). Subsequent MRI study showed pancreas as the origin of this solid cystic mass (Figure 1). Biochemical markers were done (Amylase- 69U/L, and Lipase- 98U/L). Distal pancreatectomy along with mass and spleen was excised. Gross showed a well-defined pancreatic mass measuring 10 cm × 9 cm × 8 cm with pancreatic tail measuring 4 cm at one site. Cut surface of which was variegated, fleshy and showed greyish-white solid, cystic and few hemorrhagic areas. Sections showed capsulated tumor mass showing tumor cells arranged in mainly micro- and macro acinar pattern and focal pseudopapillary pattern. Cells showed mild anisocytosis, round to oval nuclei, finely stippled chromatin, nuclear grooves, indistinct nucleoli and eosinophilic cytoplasm. Intracellular and extracellular hyaline globules were present (PAS positive) (Figure 3). Mitosis was insignificant. IHC showed beta catenin and cyclinD1 positive, CD10 focal cytoplasmic positive, PR focal nuclear positive, DOG1 focal cytoplasmic and membranous positive and CK7, CD56, CD117, chromogranin negative and Ki-67- Very low (Figure 4). Multiple sections examined from spleen along with hilar vessels were free from metastasis. On the basis of cytological, gross, histological and IHC findings, final diagnosis of Solid pseudopapillary tumor of the pancreas was made.

Discussion

SPPT of the pancreas is a rare tumor and accounts for 1% to 3% of exocrine pancreatic neoplasm

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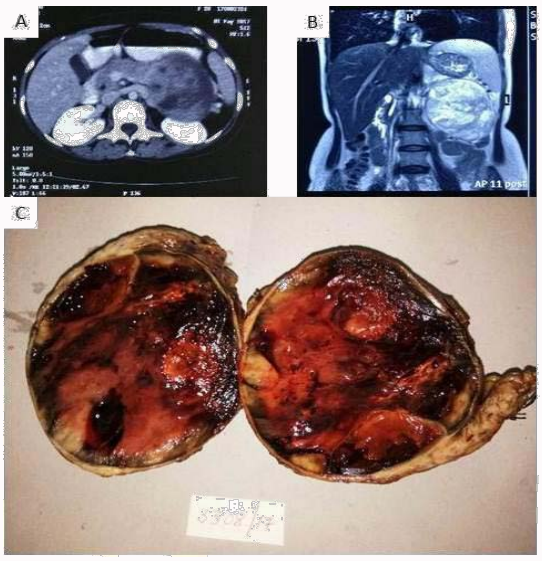

Figure 1: CT & MRI: Axial image on contrast CT & T2 coronal image on MRI shows well defined lesion with heterogenous enhancement seen originating from body and tail of pancreas with mass effect on kidney posteriorly and stomach anteriorly.
Gross: Well circumscribed capsulated mass (10 cm × 9 cm × 8 cm) along with tail of pancreas. Cut surface is fleshy with solid, cystic and hemorrhagic areas.

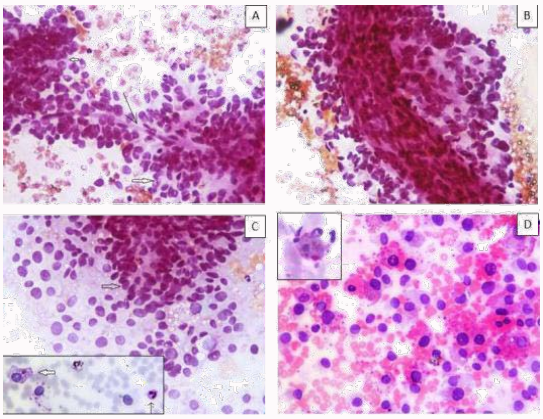

Figure 2: A) Perivascular arrangement of tumor cells with pseudo rosette formation (solid arrow) around capillary (arrow), (PAP × 400).
B) Arrangement around thick blood vessel, (PAP × 400).
C) Tumor cells scattered singly with naked nuclei as well as pseudo rosette formation (solid arrow) (PAP × 400). [Inset: PAS negative intracytoplasmic vacuoles (solid arrow) with internal positive control (arrow)].
D) Extracellular and intracellular hyaline globules (H&E × 400) [Inset: PAS-D positive].

of non-endocrine pancreatic neoplasms [1]. It typically affects mostly young women, often in their 20's [2]. Unlike other pancreatic tumor it is not associated with any clinical syndrome. SPPT is also named as 'papillary cystic neoplasm' and 'Frantz's tumor'. SPPT is the most recent name advocated by the WHO [2]. Previously it has been called by various other names as 'solid and cystic', 'solid and papillary', 'cystic and papillary' and 'papillary-cystic' [3]. This plethora of names is due to unknown origin of tumor as it lacks clear evidence of ductal, acinar or endocrine differentiation. Recent studies have shown no correlation between malignant potential with age and sex [1].

The patients with SPPT usually present as abdominal pain, nausea, vomiting and palpable abdominal mass. Rarely, patients may present with intestinal occlusion, jaundice, pancreatitis or traumatic rupture with haemoperitoneum [1]. In present case patient present with abdominal pain and mass was detected during general examination. SPPT can be found anywhere in the pancreas.

Reported that the most common location of the tumor is the tail of the pancreas (35.9%), then the head (34%), the body (14.8%) and lastly the neck (1.01%) [4].

Radiologically, SPTs have a wide range of appearance from solid to cystic, but a well encapsulated mass, with solid and cystic component has been identified as a typical imaging finding of SPPT [5]. Nakeeb AE et al. proved no difference in benign and malignant component in pattern of calcification and solid and cystic proportion of tumor and pancreatic duct dilatation [1]. Pancreatic masses may mimic large non-pancreatic lesions on CT imaging which is a known diagnostic pitfall as in this case [6]. Characteristic cytology is presence of scattered intact papillary structures with delicate fibrovascular cores as well as single and small loose clusters. Fibrovascular cores may contain metachromatic material. Cells have delicate, finely granular cytoplasm with frequently grooved nuclei and finely stippled chromatin. Background may contain myxoid material [7]. Mitosis is rare. Few studies shows the presence of hyaline globules that may be seen extracellularly and intracellularly [7,8] and few of the studies does not describe their presence [9,10].

Jahangir et al. described cercariform cells in their study that look like cells with cytoplasmic tails and have been detached from the fibrovascular cores during aspiration or smearing [11]. Present study didn't show these forms.

Recent study has shown importance of vacuolated cytoplasm in differentiating SPPT from Pancreatic Neuroendocrine Neoplasm (PET) that could be a close mimicker as aspirates from both tumors show moderate to high cellularity, low N:C ratio, nucleoli along with plasmacytoid appearance [10]. Mehta N et al. described the presence of pseudorosette pattern in their study which is again a point to differentiate it from PET [9].

Intraductal papillary carcinoma show columnar cells with variable nuclear anaplasia, irregular chromatin, and prominent nucleoli and should also be rule out. Thick glistening and viscid mucus material, almost always present in intraductal papillary mucinous tumor, is an important feature that distinguishes this neoplasm from SPPT. In case of ductal adenocarcinoma smears show cells arranged in three dimensional clusters, microglandular pattern and occasional true papillary fragments with obvious features of malignancy [11].

Pancreatoblastoma, a tumor of childhood lacks the pseudopapillary pattern and fibrovascular stalks with myxoid stroma and is consistently negative for vimentin and positive for pancreatic enzymes, that distinction it from SPPT. Due to presence of varied morphology and hyaline globules, differential diagnosis considered were SPPT, adrenocortical carcinoma, renal cell carcinoma and rhabdoid tumor as the origin of tumor could not be made by CT.

Grossly, it is usually large (mean 9 cm) and encapsulated, with variable solid and cystic areas, as well as hemorrhagic and necrotic foci. It has been studied that the cavities in SPPTs are not 'true' cysts as they lack epithelial lining but rather represent a necrotic/degenerative process [3].

On histopathology, tumor contain pseudopapillae with hyalinized fibrovascular cores lined by several layers of bland fragile epithelial

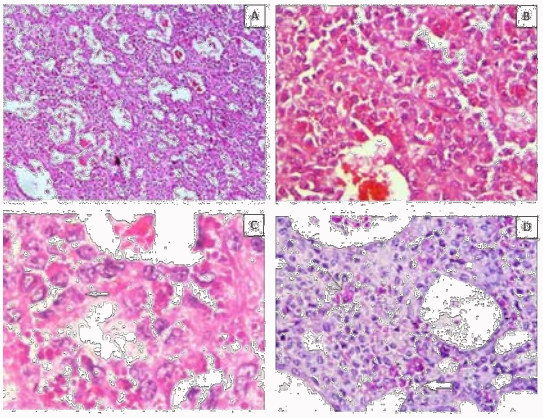

Figure 3: A) Tumor cells arranged in predominantly micro- and macro-acinar pattern. (H&E × 100).
B) Tumor cells show mild anisocytosis, round to oval nuclei, finely stippled chromatin, indistinct nucleoli and eosinophilic cytoplasm (H&E × 400).
C) Few tumor cells show grooving (solid arrow) (H&E × 1000).
D) PAS-D positive intracellular (arrow) and extracellular (solid arrow) hyaline globules (PAS-D × 400).

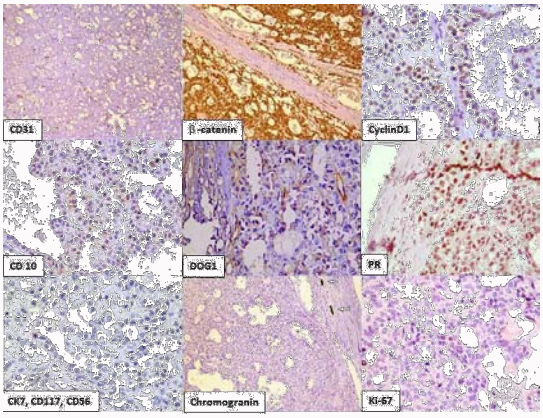

Figure 4: IHC: CD31 highlightling vascularity with lack of papillary configuration, β- catenin- Nuclear and cytoplasmic positivity, Cyclin D1- Nuclear positivity, CD10- Focal cytoplasmic positive, DOG1 - Focal cytoplasmic and membranous positive, PR - Focal nuclear positive, CK7, CD117 , CD56-Negative, Chromogranin- Negative with internal positive control, Ki-67- Very low.

cells with clear to eosinophilic cytoplasm with variable mucinous changes within the core and intracytoplasmic PAS + diastase resistant hyaline globules. Pseudopapillary pattern is due to solid nests minus cells degenerating away from the small vessels, resembling rosettes in cross section. Ren et al. showed solid areas are composed of sheets and cords of discohesive tumor cells with extensive microcystic space formation and apparent hyaline degeneration in the stroma, features that is similar to present case [12]. Nuclei are round/oval with finely stippled chromatin, nuclear grooves, indistinct nucleoli and few mitoses. Tumor cells infiltrate without any stromal reaction. The cystic areas often contain blood, necrotic debris, clusters of foamy macrophages, giant cells along with stromal degeneration in the form of myxoid change and calcification. These changes are mainly seen in large tumors and represents inflammatory response due to necrotic change.

A clear cell variant of SPPT has been described where the tumor cells have clear cytoplasm. This has been attributed to distended mitochondria and endoplasmic reticulum. This creates a diagnostic challenge in distinguishing it from other clear cell tumors of the pancreas such as metastatic renal cell carcinoma, ectopic adrenocortical nodules, clear-cell variant of pancreatic endocrine neoplasm, and ductal adenocarcinoma. IHC is helpful in making a definitive diagnosis in such cases [13].

SPPT was classified according to the WHO as either SPPT with an uncertain potential for malignancy or Solid Pseudopapillary Carcinoma (SPC). Study have shown that unequivocal perineural invasion, angioinvasion, deep invasion into the surrounding tissue or distant metastasis indicate malignant behavior, and such lesions should be classified as SPC [2], whereas other studies have shown non-specific malignant behavior and malignant potential could not be completely excluded even in the absence of pathological feature [14] Papavramidis et al. concluded that 20 % of SPPT shows malignant behavior [4]. Almost all tumors have mutations in exon 3 of the beta-catenin gene, which causes abnormal immunostaining patterns for beta-catenin (nuclear and cytoplasmic, compared to membranous staining in normal pancreas) and overexpression of cyclinD1. Present case was positive for beta-catenin (Cytoplasmic and nuclear positivity) and Cyclin D1 (nuclear positivity). Previous studies showed APC/β-catenin pathway and cyclin-D1 alterations uniformly present in almost >90% of this tumor [15] Recent studies have also shown nuclear localization of E-cadherin with absence of membranous and cytoplasmic localization, which may account for the dyscohesive nature and cystic formation of the tumor [16].

Tumor cells are also immunoreactive for non-specific markers like CD 10, CD56, CD99, progesterone receptor, alpha-1-antitrypsin and vimentin [1]. Synaptophysin and NSE are commonly positive, however, chromogranin, the most specific endocrine marker is typically negative, hence differentiation from neuroendocrine tumor could be made. As SPPT occur more commonly in female and express progesterone receptor, suggesting the role of female hormone in the evolution of these tumors. A recent hypothesis mentions that SPPT arise from pancreatic pluripotent stem cells [12]. Present case showed focal cytoplasmic positivity for CD10 and negative for CD99.

Recently, c-kit (CD117) expression was detected in most cases of SPPTs. The molecular mechanism of KIT over expression in these tumors remains unknown. Immunohistochemical staining of KIT has been demonstrated in many types of tumors that do not or only very rarely harbor KIT mutations. The absence of KIT mutations in these neoplasms suggests that there is other mechanism than activating mutations to over express KIT protein. One possible mechanism is gene dose effect as a result of increased copies of KIT gene could be result of c-kit overexpression [17]. Also recent literature had shown the expression of DOG1 in SPPT [18]. As DOG1 is expressed in centroacinar cells and also in SPPT, centroacinar cells could be the cell of origin of this tumor. However, CD117 was negative and DOG1was focally positive in present case.

SPPT has a low malignant potential and excellent prognosis, with a high cure rate after resection. Even in the presence of disseminated disease, the clinical course is usually favorable [19] with very low reccurence rate of 8.3% [1]. Nakeeb et al. also described slightly increased levels of tumor markers (CEA and CA19-9) in patients SPN showing malignant change [1].

Conclusion

This case is of interest due to its rarity, presence of hyaline globules as well as cytoplasmic vacuoles in cytology, new molecular

markers and good prognosis of patients.

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