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Solid-Pseudopapillary Neoplasm, Pancreas: A Pathologist's Perspective

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Introduction

Solid-pseudopapillary neoplasm of the pancreas is an uncommon tumor, which lately has attracted a lot of attention. Typically it is seen more often in young women. Not only does it have nonspecific clinical and radiologic manifestations, but has an equally enigmatic nature. It was earlier considered benign, however now it is currently considered a low-grade malignant epithelial neoplasm with low metastatic rate as well as high overall survival rate. It accounts for approximately 1% to 2% of all exocrine pancreatic tumors. Its synonyms are Solid-cystic tumor, papillary-cystic tumor, solid and papillary epithelial neoplasm, low-grade papillary neoplasm, Hamoudi tumor, and Frantz tumor. The most accepted terminology is SPT/SPN, as coined by WHO. It more frequently affects adolescent girls and young women (mean 35 years) are. It is rare in men and shows no apparent ethnic preference. Despite the strong gender difference, the tumor has no known genetic, hormonal or any endocrine disturbances [1,2].

Till date, the available information on SPN are mostly available from individual case reports and small series. As of now, more than 750 cases have been reported in the English literature, that too mostly within the last 20 years, reflecting thereby the increased awareness of this uncommon neoplasm [1,3,4].

The phenotype of these tumors is poorly understood, and these neoplastic cells are not clearly related to any of the well characterized cells of the pancreas and has been postulated to arise from primitive pancreatic cells, which could be acinar cells, ductal epithelial, endocrine cells or even pluripotent cells [5,6]. Female genital buds have also been implicated. Cell lines from despite this, clonality of this tumor has been lately confirmed [1,5-8].

Usually, these neoplasms are incidental in patients presenting with nonspecific complaints of abdominal discomfort and pain, occasionally after abdominal trauma. Even where these tumours arise from the head of the pancreas, there is no associated functional endocrine syndrome. All the known tumour markers are normal. Computed Tomography (CT) shows a well demarcated, mass, variably solid and cystic, but without any internal septations. Calcifications may be noted at the margins. These lesions are usually hypovascular or mildly hypervascular [4,9-11].

Pathology

Since this tumor has an excellent prognosis as compared to neuroendocrine and acinar cell carcinoma, the close morphologic differential diagnoses, it is crucial to diagnose SPTP correctly. Endoscopic/ultrasound-guided/Computed Tomography (CT)-guided FNA, using a panel of immunohistochemical staining on cell block preparations can be of tremendous help in establishing right preoperative diagnosis. The smears are usually cellular showing cell clusters in delicate papillary fronds with branching capillaries or sometimes only as nonspecific cell clusters. The tumor cells are bland and uniform with moderate cytoplasm. The nuclei are round to oval with finely granular chromatin. Cytoplasmic eosinophilic hyaline globules, large clear cytoplasmic vacuoles, nuclear grooving, and myxoid stroma have been variably described [12-16].

SPN shows no predilection for any specific location, although tail has been report frequent site [3,4,17]. The tumors size may vary from 0.5 cm to 34.5 cm. Larger lesions characteristically have a solid and cystic appearance, whereas smaller lesions are usually more solid but less sharply circumscribed as compared to larger lesions. Larger lesions usually have a fibrous pseudo capsule and a variegated cut surface, showing friable and cystic degeneration and hemorrhage, on the other hand smaller lesions are less delineated. In presence of extensive cystic degeneration, it may simulate a pseudo cyst [3,17,18].

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SPN shows vascular zones of polygonal epithelial cells alternating with cystic spaces. The characteristic pseudopapillary appearance is due to degenerative changes resulting in tumor cell discohesion. As the lesion is highly vascular the capillary-sized vessels surrounded by a cuff of neoplastic cells having scanty cytoplasm, resemble papillae [17,18].

The cells have abundant eosinophilic cytoplasm with uniform, round to oval, nuclei lacking the endocrine salt-and-pepper type of chromatin. Nuclear grooves can be invariably seen. These cells show low mitotic activity. Clear cell variants with vacuolated cytoplasm have also been described, which is attributed to the distended mitochondria and endoplasmic reticulum [19]. Focal aggregation of intracytoplasmic and extracytoplasmic hyaline globules have been usually described, which are periodic acid-Schiff positive and diastase resistant [17,18]. Foamy macrophages, hemorrhage, and cholesterol clefts, myxoid change and microcalcifications, are other features noted ,attributed to degenerative changes. Malignant transformation and focal sarcomatoid component is very rare with occasional case reports, which may show diffuse growth with more cellular atypia, tumor necrosis, and high mitotic activity. Local infiltration into adjacent structures, perineural invasion as well as vascular invasion may sometimes be seen, despite indolent behavior [4,11].

Recent Advances

Solid-pseudopapillary neoplasm has been tested for numerous immunohistochemical markers and has been equally enigmatic. In recent reports, most SPNs demonstrated nuclear localization of β-catenin and loss of membrane expression of E-cadherin with disruption of the activated Wnt pathway [20-24]. Another consequence of this disruption is cyclin D1 over expression [21]. In addition, results for CD10 are positive in a significant number of cases and neuroendocrine markers have been seen to be variably expressed in SPN [22,25]. With the exception of the consistently negative results for chromogranin A, variable expression of other neuroendocrine markers, that is, synaptophysin, neuron-specific enolase, and CD56, was demonstrated. This staining profile thus complicates the differentiation of SPN from pancreatic neuroendocrine tumor, which is the most important entity in its differential diagnosis. CytoKeratins (CK), i.e. pancytokeratin, CK8 and CK18 are also variably expressed [25]. However, CK7 and CK19 are mostly negative [20,25]. Solid-pseudopapillary neoplasm also stains for vimentin, progesterone receptor, and estrogen receptor β (but not estrogen receptor α), there by supporting genital ridge theory of its origin [7]. DOG1 has been demonstrated in some reports and has been found to be a novel marker for centroacinar cells and for solid-pseudopapillary neoplasms, which on the other hand is suggestive of a centroacinar origin of these neoplasms [26] Stains for α_1-antitrypsin are positive, highlighting the periodic acid-Schiff-positive hyaline globules, and are negative for pancreatic enzymes [25,27]. Other sporadic reported stains include DPC4, CD117, p21, p27, and to a lesser extent, p16 [21,28]. Expression of Ki-67 is usually low, although it was reported to be high in clinically aggressive cases only [29]. Other markers, such as carcinoembryonic antigen and CA 19.9, are not expressed [27].

This lesion having generated so much interest recently, definitely needs a detailed evaluation with complete IHC support to give the patient the desired benefits.

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