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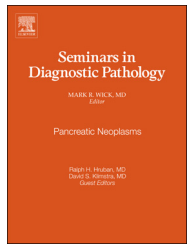

Diagnosis and molecular aspects of solid-pseudopapillary neoplasms of the pancreas

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ABSTRACT

Solid-pseudopapillary neoplasm of the pancreas (SPN) is an uncommon low-grade malignant neoplasm occurring mostly in young women. In addition to its distinctive pathological appearance of pseudopapillae with poorly cohesive neoplastic cells, rare variants exist raising the differential diagnosis especially with neuroendocrine neoplasms. The overall prognosis for patients with SPNs is excellent after surgical resection. Nevertheless, 10% of cases may have malignant behavior characterized by tumor recurrence and/or metastasis. Despite numerous studies, the histogenesis of this neoplasm remains unclear. Distinctive molecular alterations such as the presence of *CTNNB1* mutations are observed in nearly all cases, while mutations classically observed in ductal adenocarcinoma, such as *KRAS*, *TP53*, and *SMAD4*, are not observed in SPNs, reinforcing its distinct nature compared to all other pancreatic neoplasms. Recent transcriptional studies have shown that activation of the Wnt/beta-catenin pathway in these tumors is associated with the upregulation of genes belonging to Notch, Hedgehog, and androgen receptor signaling pathways.

Solid-pseudopapillary neoplasm of the pancreas (SPN) is a rare tumor, first described in 1959 by Frantz[1] before entering in the WHO classification in 1996.[2] SPN can be distinguished from other pancreatic neoplasms by its epidemiological, clinical, and histological features.[3] SPN is characterized by a predilection in young women and a usually good prognosis. Although SPN is considered to be a tumor of low malignant potential, a subgroup of patients with SPNs occasionally present with liver metastasis or invasion of vascular vessels and/or adjacent organs, develop recurrence, and some even die of their disease. Because it is an uncommon tumor type, little is known about its pathogenesis and the direction of differentiation of the neoplastic cells. However different studies have recently led to progress in the understanding of the carcinogenesis and histogenesis of this rare tumor. This review presents the distinguishing histological features of SPNs and the molecular genetic alterations of SPN, with emphasis on clinical applications.

Characteristic pathological features of solid-pseudopapillary neoplasms of the pancreas

SPNs account for 1–2% of all pancreatic neoplasms. More than 90% of patients are young women in their 20s but, occasionally, the tumor occurs in older women, men or children.[4,5] Common presenting symptoms are either abdominal pain or discomfort (63%) or the tumors are detected incidentally

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(38%). The increase in use of abdominal imaging explains notably the 7-fold increase in number of cases detected since 2000.[6] Macroscopically, SPNs can be located in any part of the pancreas and they are typically large at diagnosis (mean = 7.5 cm in diameter).[3,7] Because the extent of cystic degeneration is highly variable among cases, a wide spectrum of macroscopic appearances can be seen. SPNs vary from entirely cystic (Fig. 1A) to pure solid (Fig. 1B) forms. This heterogeneous macroscopic aspect explains why SPN has been designated under various names in the past (papillary and cystic tumor, solid and cystic tumor, solid and papillary tumor, etc.).[8–10] Small tumors tend to be more solid, whereas large ones have more hemorrhage, necrosis, and cystic degeneration, sometime simulating the appearance of a pseudocyst. Although most cases are grossly well-circumscribed, there is no real fibrous capsule, and microscopically the neoplastic cells may infiltrate the surrounding pancreatic parenchyma, entrapping acinar cells and islets.[11] Invasion of adjacent organs, such as the spleen or the duodenal wall, is rare.

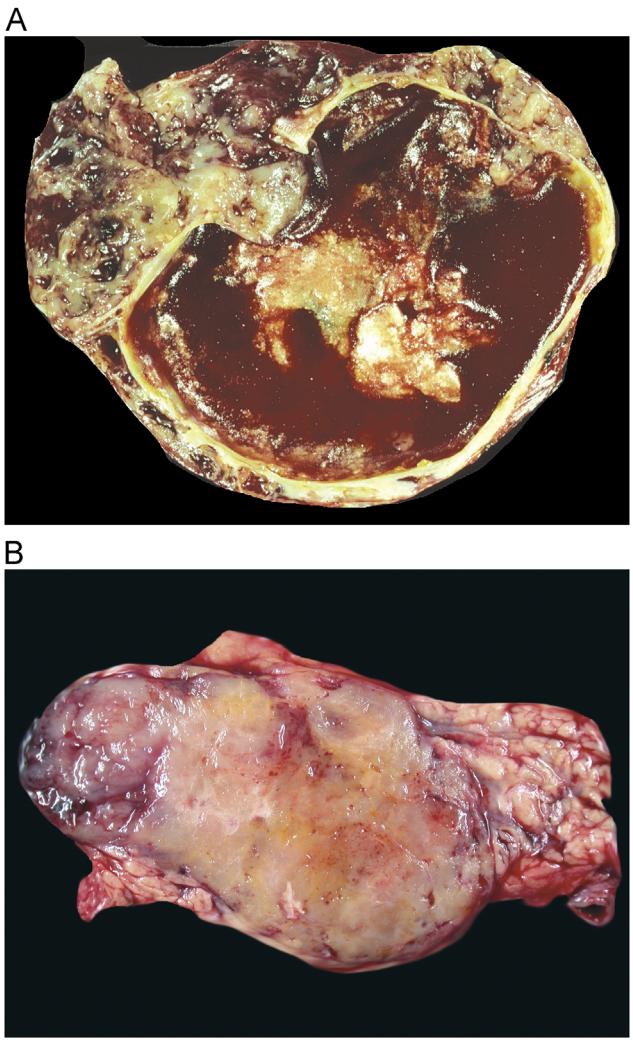

Fig. 1 – (A and B) Cross-sections of 2 SPNs showing the range of macroscopic patterns. In the first case (A) the tumor exhibits extensive necrotic–hemorrhagic changes and appears almost completely cystic. In contrast, the second case has a pure solid macroscopical pattern.

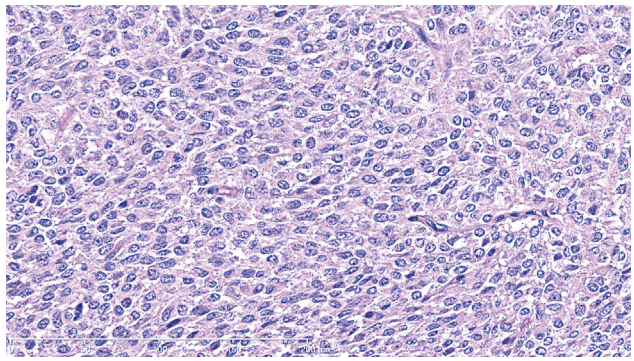

Fig. 2 – SPN showing microscopically a solid growth pattern.

SPNs microscopically have solid, cystic, and pseudopapillary components. The solid areas are formed by cords of monomorphic cells separated by small vessels, which exhibit a variable degree of perivascular collagen deposition (Fig. 2). The most characteristic feature of SPN is presence of pseudopapillary areas with fibrovascular stalks or rosette-like structures secondary to poor cohesion of the neoplastic cells (Figs. 3 and 4).[4] The neoplastic cells are small and regular with clear or eosinophilic cytoplasm sometimes containing aggregates of small hyaline periodic acid Schiff (PAS)-positive globules (Fig. 5).[12] Nuclei are uniform, ovoid with finely dispersed chromatin, and inconspicuous nucleoli; longitudinal nuclear grooves are characteristic. Mitoses are usually rare. Foamy histiocytes, scattered cholesterol granulomas, and calcifications are common in areas of tumoral necrosis and hemorrhage

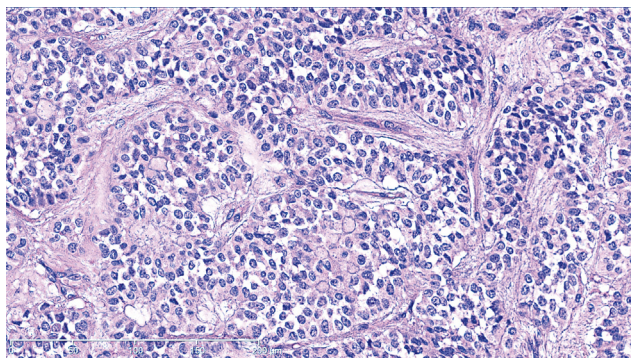

Fig. 3 – SPN with typically pseudopapillary structures with hyalinized fibrovascular cores.

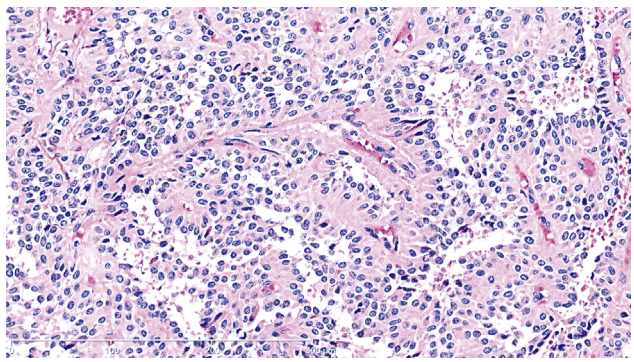

Fig. 4 – SPN exhibiting pseudopapillary structures with loss of cell cohesion.