

**Q 1. It is suggested providing a detailed introduction to the clinicopathologic and immunohistochemical features of serous cystic adenoma of the Solid pseudopapillary neoplasm (SPN) of the pancreas.**

Answer: Microscopically, SPNs are typically characterized by solid sheets of neoplastic cells, which are often interspersed with regions where the tumor cells are organized around the fibrovascular cores<sup>[17]</sup>. A distinctive feature of these tumors is the presence of Periodic Acid-Schiff (PAS)-positive hyaline globules<sup>[18]</sup>. Other histological characteristics include the presence of pseudo-papillary architecture, microcystic changes, clear cells, nuclear grooves, eosinophilic cytoplasm, myxoid stroma, and hyaline globules. Additional features such as atypical cells, tumor giant cells, mitotic activity, calcification, cholesterol clefts, fibrosis, hemorrhage, infarction, and tumor necrosis might also be noted during histological evaluation<sup>[18]</sup>.

To complement the histological findings and to differentiate SPNs from histological mimics, immunohistochemical (IHC) staining is crucial. A panel of commonly used IHC markers includes CD10, CD56, beta-catenin, Cyclin D1, CD99, cytokeratins, Chromogranin A, synaptophysin, and progesterone receptor (PR) <sup>[17]</sup>.

**Q 2. The molecular pathological characteristics of solid pseudopapillary tumor of the pancreas are currently the key to diagnosis. Provide some molecular test results for this case, I think it's a question worth examining.**

Answer: All patients with SPN possess activating somatic mutations in the  $\beta$ -catenin gene (CTNNB1, located on chromosome 3p)<sup>[19]</sup>. Increased expression of certain proteins involved in Wnt signaling, such as DKK4, along with other proteins like NONO and FUS, that interact directly with  $\beta$ -catenin, are upregulated in solid pseudopapillary tumor<sup>[20]</sup>. Moreover, nine metabolic proteins such as SLC25A13, GPI, PGK1, HK1, ENO2, PDHB, ALDH7A1, PKM2, and DLD are overexpressed<sup>[21]</sup>. But in our case, due to the limited resources available, the diagnosis was largely made based on the typical clinical

presentation, imaging results, and histopathological features, which are often sufficient to confirm the diagnosis in such situations.

**Q 3. This case highlights the significant possibility of solid pseudopapillary Neoplasm of Pancreas (SPN) occurring in adolescent girls, which is often overlooked in clinical practice. It underscores the importance of vigilance and thorough assessment in adolescent patients, ensuring that conditions like SPN are not missed and that appropriate care is provided promptly. Early intervention can significantly alter the course of the disease, leading to more favorable results and ultimately improving the quality of life for young patients. It is suggested providing a more detailed description of the treatment methods and their effects.**

Answer: The mainstay of treatment of SPNs remains the surgical removal of the tumor<sup>[6]</sup>. Depending on the location, procedures such as distal pancreatectomy with or without splenectomy, pylorus-preserving pancreatoduodenectomy, Whipple procedure, or enucleation may be carried out<sup>[22]</sup>. Small tumors located away from the main pancreatic duct are enucleated, those located on the head or uncinate process of the pancreas are treated with pancreatoduodenectomy, while central pancreatectomy is carried out for the tumors of the neck or body of the pancreas, without vessel involvement<sup>[23]</sup>. The surgical resection must be performed carefully, as the spillage of the tumor contents can lead to the implantation of the tumor cells into the peritoneum<sup>[13,24]</sup>.

Studies show that the patients who had limited resection with microscopically positive margins showed outcomes similar to those who underwent extensive surgery with R0 resection<sup>[25]</sup>. Thus, longevity can be attained with minimally invasive procedures<sup>[26]</sup>, even in patients with advanced or metastatic disease<sup>[27]</sup>.

Moreover, Chemotherapy (primarily 5-fluorouracil and gemcitabine) and Radiotherapy have been reported to be effective treatment modalities in a limited number of patients<sup>[28]</sup>. Other modalities such as Radiofrequency Ablation (RFA)<sup>[29]</sup>, Transcatheter arterial chemoembolization (TACE) with Pharmorubicin and iodized oil<sup>[30]</sup>, and selective internal radiotherapy<sup>[31]</sup> have also been found to be suitable for inducing long-term remissions of

the strongly vascularized liver metastases. In a study done by Dovigo A, et al, liver transplantation was done and found to have survival free of recurrence at 1 year later<sup>[32]</sup>.