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SOLID PSEUDOPAPILLARY NEOPLASM OF THE PANCREAS - RAISING AWARENESS OF A RARE TUMOR

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Abstract
Solid pseudopapillary neoplasm (SPN) is a rare clinical entity. One third of the patients are asymptomatic and the diagnostic is based on imaging studies (abdominal ultrasound, computed tomography, magnetic resonance imaging) and histological examination of biopsies obtained most frequently by endoscopic ultrasound-guided fine-needle aspiration. In this article we made a short review of the literature and present the imaging and histological aspects found in our patients with SNP.
Keywords: *solid pseudopapillary neoplasm, pancreatic tumors.*

Rezumat
Neoplasmul pseudopapilar solid este o entitate clinică rară. O treime dintre pacienți sunt asimptomatici, iar diagnosticul se bazează pe studii imagistice (ecografie abdominală, tomografie computerizată, imagistică prin rezonanță magnetică) și examenul histologic al biopsiilor obținute cel mai frecvent prin aspirație endoscopică cu ac fin ghidată ecografic. În acest articol am făcut o scurtă trecere în revistă a literaturii și am prezentat aspectele imagistice și histologice întâlnite la pacienții noștri cu neoplasm pseudopapilar solid.
Cuvinte cheie: *neoplasm pseudopapilar solid, tumori pancreatice.*



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Introduction

Solid pseudopapillary neoplasm (SPN) is a rare entity firstly described by Virginia Franz in 1959, representing about 2-3 % of pancreatic tumors[1]. Over time, it has had a variety of names, including papillary epithelial neoplasm, solid and cystic acinar cell tumor, papillary cystic carcinoma, Hamoudi tumor or Franz tumor, before receiving its current term, designated by the World Health Organization[2]. SPN is reportedly known to affect young females, with a study performed on 553 cases in Chinese literature showing a mean age of 27.2 years and a female to male ratio of 8.37:1[3].

Although the tumor can occur anywhere in the pancreas, most of them are located in the body or tail[1]. The prognosis of this neoplasm is very good, with a 5-year survival rate of 96.9%, the overall malignant potential being rather low[1,3].

Clinical features

Up to one third of the patients are *asymptomatic*, with the tumor being incidentally discovered during a routine physical examination[3]. The most common clinical features are *abdominal pain* or *palpable mass*, each found in about 30% of patients[1,3]. Other symptoms that may be present are nonspecific and include nausea, vomiting, anorexia, fever, weight loss or jaundice and are most likely caused by tumor compression to the pancreas[1,3].

Diagnosis

Tumor markers (including CEA, CA 19-9, AFP, CA125), pancreatic enzymes and blood glucose levels are not usually elevated and stay within *normal* ranges[4,5].

Transabdominal *ultrasound* usually displays a well-encapsulated mass with an homogenous or heterogenous structure, containing solid echogenic and hypoechoic components. Intratumoral calcifications may be present and the tumor might cause displacement of the nearby anatomical structures[6].

Computer tomography imaging demonstrates an encapsulated mass with well-defined borders and heterogenous attenuation, which includes central areas of calcification, haemorrhage, necrosis and cystic degeneration[6,7]. It has been observed that the calcification rate is higher in male patients, as well as the percentage of solid tumors[4]. No differences between males and females were found as far as the capsule, bleeding or enhancement of the lesions are concerned[4].

Pre-contrast administration, the lesion has a solid/soft-tissue attenuation and may exhibit several hyperdense foci due to the

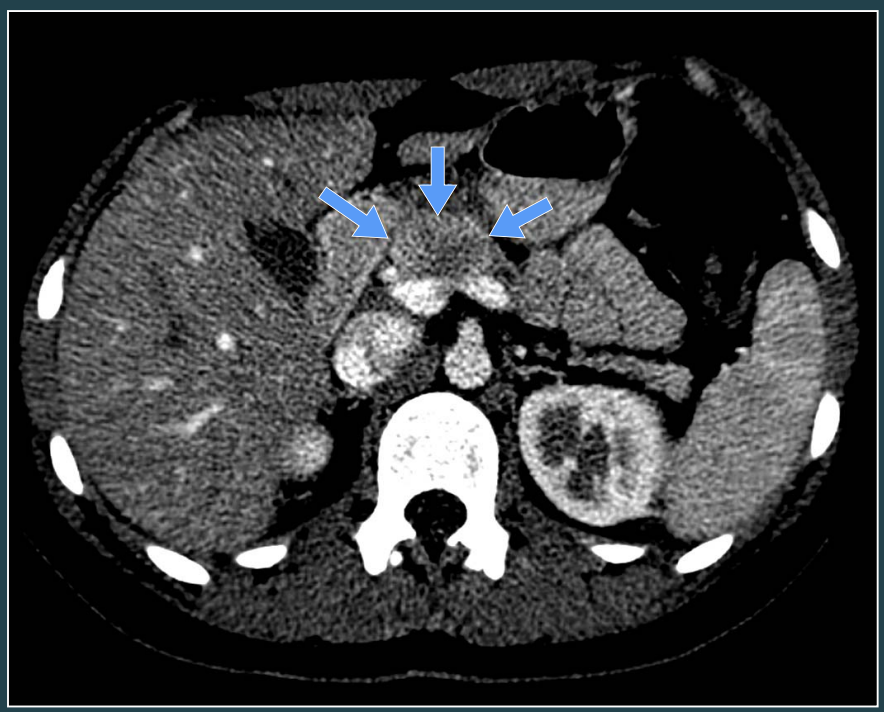


Figure 1. *Axial post-contrast CT image demonstrating a 3.5 cm well-defined pancreatic mass (blue arrows) with peripheral enhancement and a hypoattenuating center in a 19-year-old woman, which was proved to be a SPN*

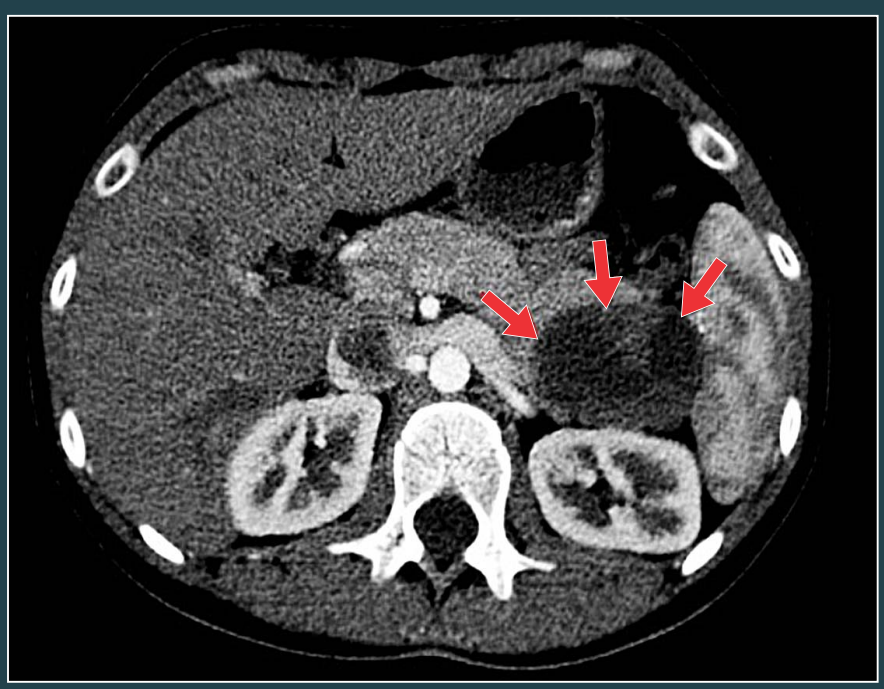


Figure 2. *Axial CT arterial phase image showing a 5 cm encapsulated lesion located in the pancreatic tail (red arrows), demonstrating moderate peripheral enhancement with central hypodense areas, with a slight mass effect on the spleen and left kidney. The patient is a 24-year-old female that presented with abdominal pain and fatigue.*



calcifications[7]. The solid parts of the tumor display slight to moderate enhancement, while the cystic regions remain unenhanced[7] (Figure 1).

Peripheral enhancement is often noticeable in both arterial and venous phases of the CT scan, with a density that is very close to that of the normal surrounding pancreatic parenchyma[6] (Figure 2). This characteristic is of great importance when it comes to differentiating SPN from adenocarcinoma, which presents as a hypoattenuated mass in the venous phase, and from neuroendocrine tumors of the pancreas, which show enhancement during the arterial phase[7].

Pancreatic duct dilatation is a rare finding that might occur when the lesion is located in the pancreatic head[4]. However, this imaging feature, along with vessel invasion or capsular disruption with invasion of the adjacent pancreatic parenchyma or peripancreatic fat, either with or without metastases, are signs of aggressive behavior of the tumor and can aid the radiologist in differentiating between a benign SPN and solid pseudopapillary carcinoma, which requires a more aggressive surgical approach[6,8,9]. Tumor size greater than 6 cm is also correlated with a more aggresive nature (vascular involvement and capsular invasion)[9].

Magnetic resonance imaging is also an important diagnostic tool, since it allows a better characterization of certain tissues and offers a better identification of intratumoral blood compounds or necrosis[6]. The general MRI aspect of SPN is of a well-defined, encapsulated lesion presenting heterogenous high/low signal intensity on T1-weighted images and hetereogenous high signal intensity on T2.-weighted images (Figure 3). Following gadolinium administration, the tumor exhibits either peripheral heterogenous enhancement in the arterial phase in most cases, or complete homogenous enhancement (Figure 4). In the portal venous phase, the lesion shows progressive, incomplete fill-in[10].

Endoscopic ultrasound-guided fine-needle aspiration is most commonly used for obtaining a cytological diagnosis. The appearance of the smears is usually described as highly cellular, with branching capillaries surrounded by small neoplastic cells with monomorphic nuclei. Important *cytologic* features include the presence of myxoid clear material around the papillae and the presence of cercariform cells, foamy histiocytes and multinucleated giant cells.

Pathological examination is an important step towards the formulation of a definitive diagnosis.

Macroscopically, the tumor is round, well demarcated and relatively large, while the cut surface is quite variable in appearance, usually showing a combination of cystic, solid, necrotic and hemorrhagic areas (Figure

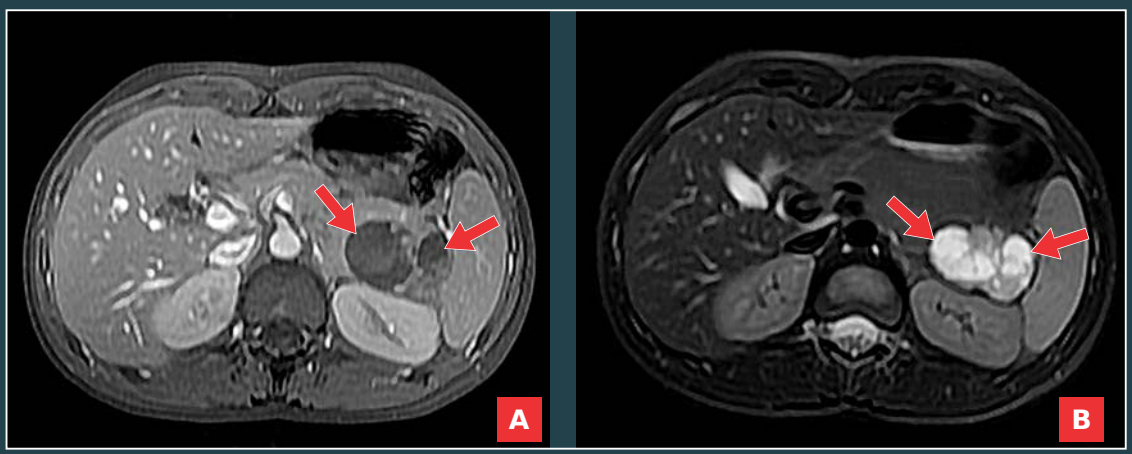


Figure 3. *MRI studies of the same patient from Figure 2. Axial post-contrast T1-weighted image showing a well-defined mass with heterogenous enhancement and a mixture of hypo- and hyperintense regions (3a). The lesion shows heterogenous high signal intensity on T2.-weighted images (3b).*

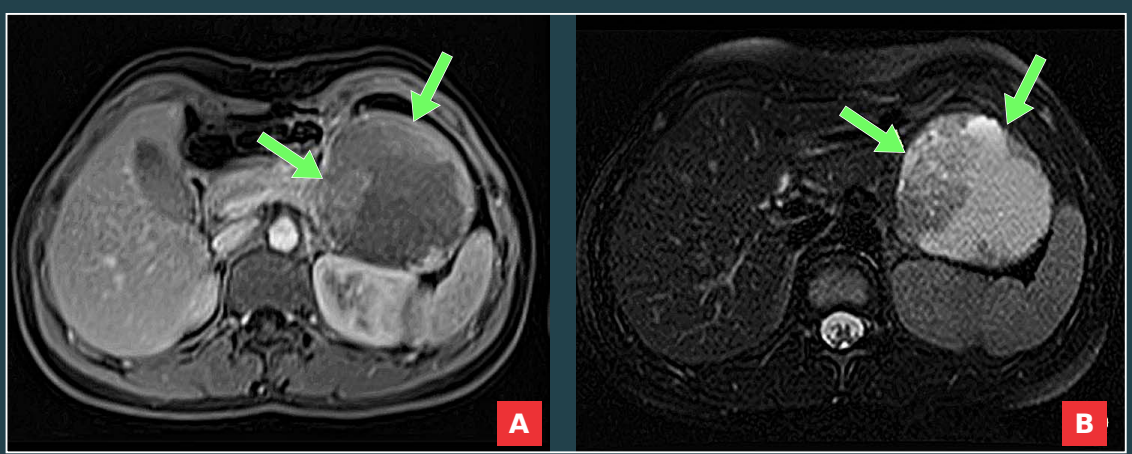


Figure 4. *20-year-old patient with a large encapsulated mass in the pancreatic tail that compresses adjacent anatomical structures. The lesion shows peripheral enhancement post-gadolinium administration (4a) and is heterogenous and hyperintense on T2-weighted images (4b).*

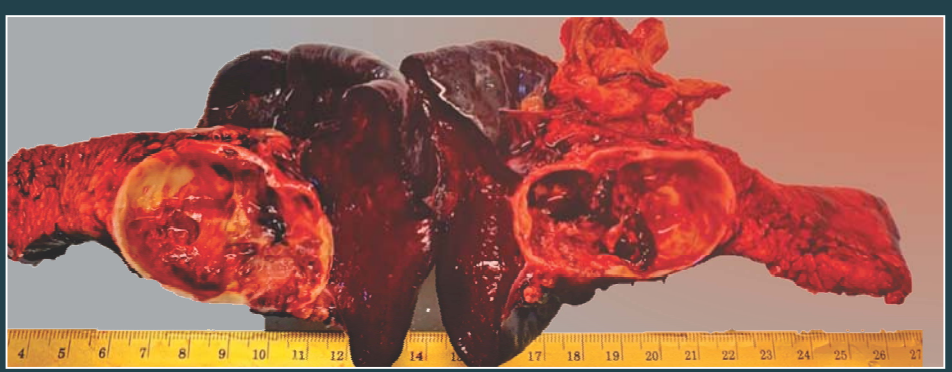


Figure 5. *The macroscopic aspect of the tumor shown in Figure 2 is that of a solitary mass, with an average size of 5,5 cm, fluctuant, well-demarcated, encapsulated. The cut section reveals lobulated brown-yellow solid areas and cystic, necrotic and hemorrhagic degeneration with necrotic debris.*

5). However, some tumors may appear either completely solid, especially the ones that are smaller in size, or completely cystic.

Solid-pseudopaplillary neoplasm has different growth patterns, with a combination of solid and pseudocystic structures, pseudopapillary and haemorrhagic-necrotic in different proportions (Figure 6). Pseudopapillae are formed by delicate vessels surrounded by loosely cohesive cells. Sometimes the cells resemble ependymal rosettes, surrounding minute fibrovascular stalks (Figure 6 - HE 20 x). Tumoral cells have either eosionophilic or vaculoated cytoplasm, central/ excentric round to oval nuclei with finely dispersed chromatin[11,12].

Immunohistochemical analyses are compulsory for the final pathological diagnosis, using a variety of antibody panels[13].

A core panel of markers that includes Beta-catenin, Vimentin and Chromogranin is recommended for establishing the diagnosis of solid- papilary neoplasm. The immunophenotype of this tumor is characterised by positivity for Vimentin, Synaptophysin, Beta-catenin, Progesterone and Androgen receptor and negativity for markers such as E-cadherin, Chromogranin and Pancreatic hormones, which are positive in neuroendocrine tumors, or Trypsin, Lipase and Amylase, which are characteristic for acinar cell carcinoma (Figure 7,8)[13, 14,15,16,17].

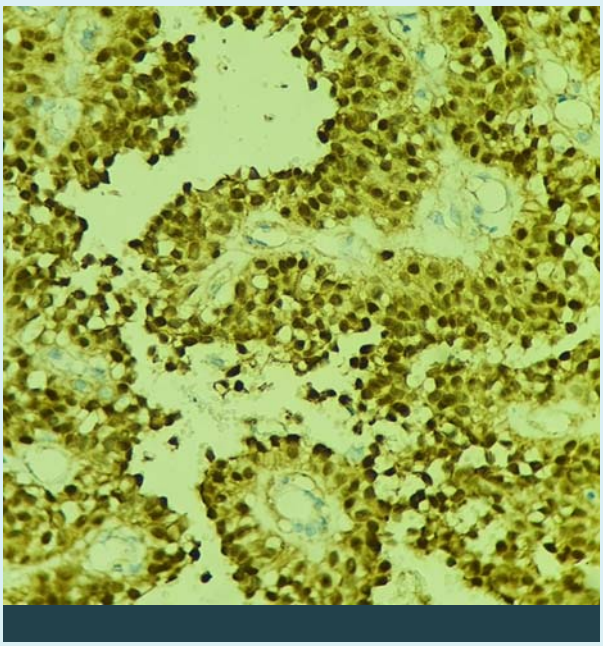


Figure 7. *Beta catenin 40 x: the neoplastic cells show nuclear positivity*

Differential diagnosis

The pathological entities that SPN must be differentiated from include both neoplastic and non-neoplastic lesions: pancreatic adenocarcinoma, cystadenoma and cystadenocarcinoma, islet cell tumor, neuroendocrine neoplasm, acinar cell carcinoma, papillary mucinous carcinoma, pancreatic pseudocyst, teratoma, hydatid cyst, pancreatoblastoma[3,6,13].

Apart from the imaging features that may suggest an alternative diagnosis, certain pathological findings can guide the pathologist towards different histological entities, such as:

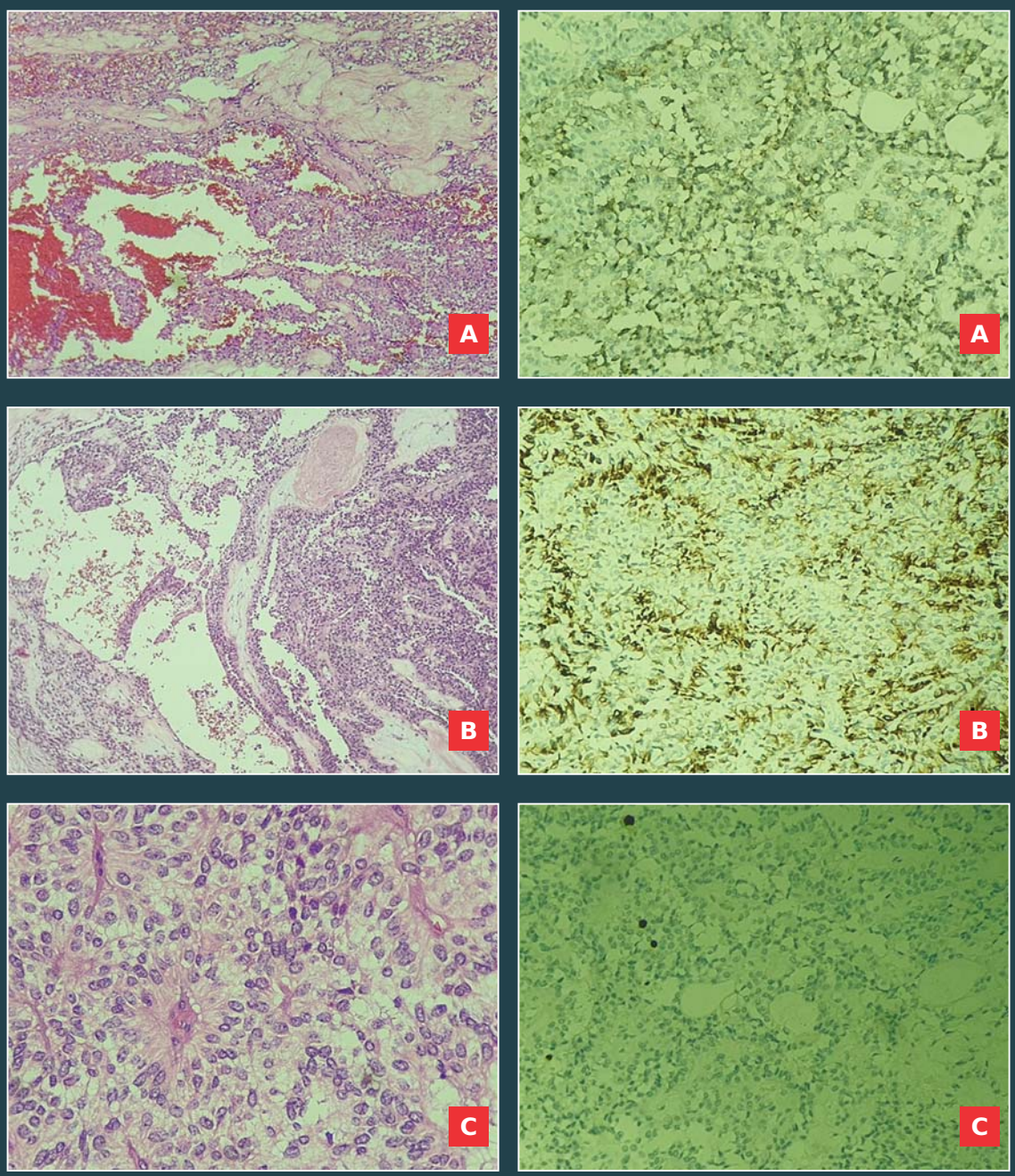


Figure 6. *Hematoxylin-Eosin* ***Figure 6.a*** *10x,* ***Figure 6.b*** *10x,* ***Figure 6.c*** *20x. Solid papillary neoplasm with heterogeneous growth pattern with a combination of solid, pseudopapillary and hemorrhagic-necrotic (a), pseudocystic structures in different proportions (b). Delicate vessels surrounded by poorly cohesive monomorphic cells with eosinophilic and clear vacuolated cytoplasm, round to oval nuclei with finely dispersed chromatin and grooved or indented nuclei. Mitoses are rare (c).*

Figure 8. *Synaptophysin 20x* ***(Figure 8a)*** *and vimentin 10x* ***(Figure 8b)*** *show cytoplasmic positivity for these markers. Ki 67 40x* ***(Figure 8c)*** *shows less than 1% positivity in neoplastic cells in this patient.*



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- Neuroendocrine tumors: small to medium-sized cells with uniform nuclei and salt and pepper chromatin, with organoid, trabecular, nested patterns, positive for neuroendocrine antibody, but negative for Beta- catenin
- Acinar cell carcinoma: prominent acinar pattern and cells with finely granular cytoplasm, positive for pancreatic enzymes. Trypsine, Chymotrypsin and Lipase and variable positivity for Beta-catenin
- Pancreatoblastoma: acinar, ductal and neuroendocrine patterns and squamoid corpuscles, more common in children younger than 10 years; positive for beta catenin (80%), neuroendocrine and pancreatic enzymes[18,19,20].

Treatment

Surgical resection is the therapy of choice in SPN patients, since approximately 95% of patients can be *cured* by this means alone.
In cases where the tumor is located in the tail and pancreatic corpus, distal pancreatectomy with spleen preservation is performed, whereas in the cases that present a lesion in the pancreatic head a pylorus-preserving pancreaticoduodenectomy is performed. Since there has been evidence that SPN does not metastasize to the lymph nodes, formal lymphadenectomy is not recommended[21].
Resection of both local and distant metastases is beneficial and completely justified, considering the fact that the prognosis is favorable even in the presence of metastatic disease, with the most common locations being the liver, mesentery and peritoneum[21,22].
In patients that present a locally invasive tumor, with vascular involvement (affecting the portal vein, superior mesenteric artery and vein) or extension to the adjacent organs (spleen, duodenum), en bloc resection has proved to be the best surgical approach[21].
The recurrence rate after surgical resection is estimated to be around 10-15%, suggesting that patients need to be followed-up over an extended period of time, considering that late recurrences (7-14 years post-surgery) have been described[21,22].
Neoadjuvant treatment is generally unnecessary, but there have been case reports that related the use of cisplatin, 5-fluorouracil and gemcitabin for tumor reduction[23,24]. *Radiotherapy* was also suggested as an option of treatment[25]. However, surgery remains the treatment of choice, while the rest of the therapeutic options need to be further defined.

Conclusion

Solid papillary neoplasm of the pancreas is an infrequently-encountered tumor that occurs mainly in young females and does not cause significant symptoms. Its diagnosis

comprises both imaging studies, with CT and MRI playing important roles in tumor characterization, and pathological analyses. SPN is cured by surgical resection in most cases, with an excellent prognosis and survival rate, but follow-up examinations are required.

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