Solid-pseudopapillary neoplasm of the pancreas – comparisons between magnetic resonance and histological findings

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Solid-pseudopapillary neoplasm is a rare pancreatic tumor typically observed in young adults. A new case of the tumor was diagnosed in a 22-year-old woman. An abnormal mass connected with the pancreatic body was found on ultrasound and computed tomography. Magnetic resonance revealed weak homogeneous contrast enhancement and a low ADC value (0.824 mm/s^2; b1000). Primary radiological diagnosis suggested a solid pancreatic neoplasm, which was confirmed during histopathological assessment after resection of the pancreatic body with preservation of the spleen and normal drainage through the main pancreatic duct. Histological appearance of the solid-pseudopapillary neoplasm corresponded with its radiological morphology.

Key words: solid-pseudopapillary tumor, pancreatic tumor, diffusion-weighted imaging, magnetic resonance, diagnosis.

Introduction

Solid pseudopapillary neoplasm/tumor, also known as papillary epithelial neoplasm, Hamoudi or Frantz tumor, is a low-grade or borderline epithelial pancreatic malignancy and has been reported in 0.9-2.7% of all neoplasms of the organ [1, 2]. Its incidence is higher among young individuals, especially women with a mean age at diagnosis of 28 years (range from 7 to 79 years). The neoplasm is observed less frequently in males and is diagnosed 5-10 years later [1, 3]. Strong geographical and ethnic implications have also been suggested, since higher incidence was observed in Asians and Afro-Americans [4]. The only genetic marker associated with the tumor is mutation in exon 3 of the *CTNB1* gene encoding β-catenin [5]. Despite extensive study, histogenesis of the tumor is unclear. Recent findings suggested its origin from pluripotent embryonic stem cells of the pancreas and from embryonic neural precursor cells of the neural crest [6].

A new case of solid pseudopapillary neoplasm – preliminarily diagnosed on the basis of ultrasound (US), computer tomography (CT) and magnetic resonance (MR) with supplementary sequences including diffusion-weighted imagining (DWI), apparent diffusion coefficient (ADC) maps, dynamic contrast enhancement and magnetic resonance cholangiopancreatography (MRCP) – is presented in relation to its postoperative gross and microscopic appearance. The main idea of the paper was to compare the tumor's morphology in magnetic resonance imaging with histological findings.

Case description

A 22-year-old Caucasian woman with no remarkable past family or personal medical history (gravid 0)

was admitted to hospital due to mild epigastric discomfort for a few days. During physical examination a tumor located in the upper umbilical area was found. All clinical laboratory tests, including various tumor markers, were unremarkable.

A well-circumscribed homogeneous mass (50 mm × 60 mm) directly connected with the pancreatic body was revealed during abdominal ultrasound examination (Voluson E6; General Electric; USA). Single, large vascular trunks were visible in power Doppler US (Fig. 1). All other abdominal and pelvic organs had typical morphology. The chest radiograph was normal.

Pre-contrast CT (Lightspeed Pro 32; General Electric; USA) confirmed the localization and presence of the abnormal hypoattenuating mass (25-35 HU) with a size approximately 50 mm × 65 mm. Inho-

mogeneous, mainly peripheral enhancement (80-100 HU) was visible (Fig. 2). The strongest enhancement was observed in the area adherent to the unchanged part of the pancreatic body. Hypoattenuation or lack of any changes in the post-contrast phase was also found in selected internal areas. No dilatation of the main pancreatic duct, vessel invasion, calcification, infiltration of adherent pancreatic parenchyma and surrounding organs, or enlargement of abdominal lymph nodes were observed. However, the margin between the lesion and pancreas was unclear.

The lesion (52 mm × 63 mm × 60 mm) had a slight heterogeneous signal on both T1- and T2-weighted MR images (1.5T Achieva; Philips Medical Systems; The Netherlands). It was surrounded by a thin capsule with a low signal on both principal series that
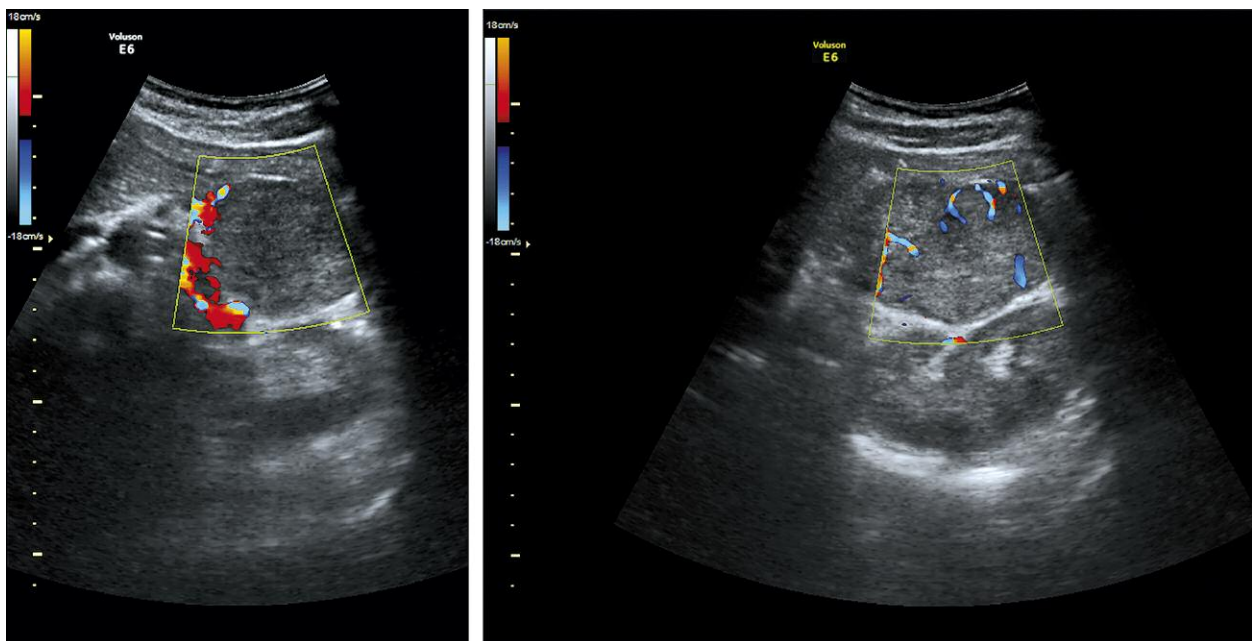

Fig. 1. Hypoechoic heterogeneous mass of pancreas with well-visible internal vascular structure in Doppler ultrasonography
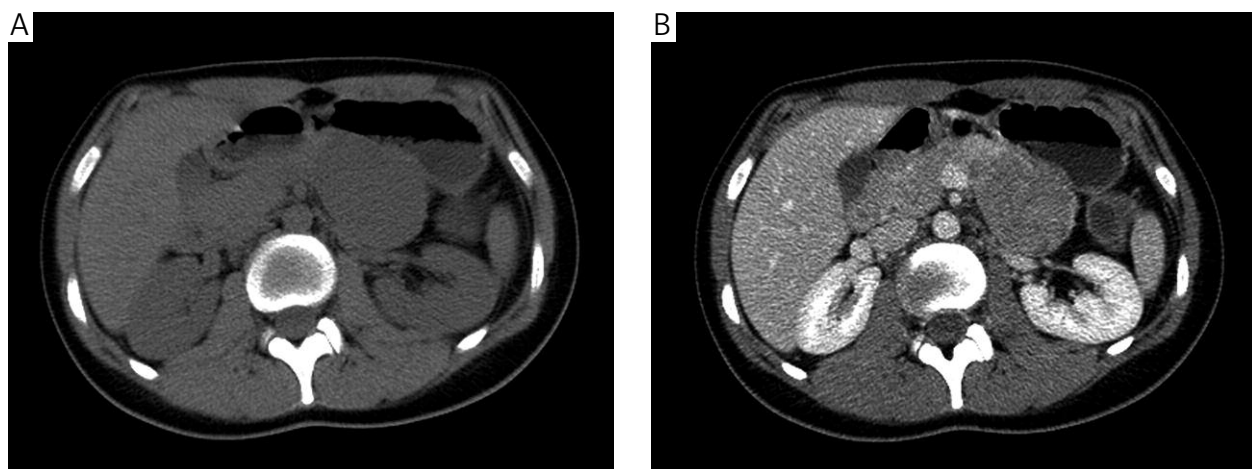

Fig. 2. Well-circumscribed pathological mass of the pancreas before (A) and after (B) contrast enhancement in computed tomography
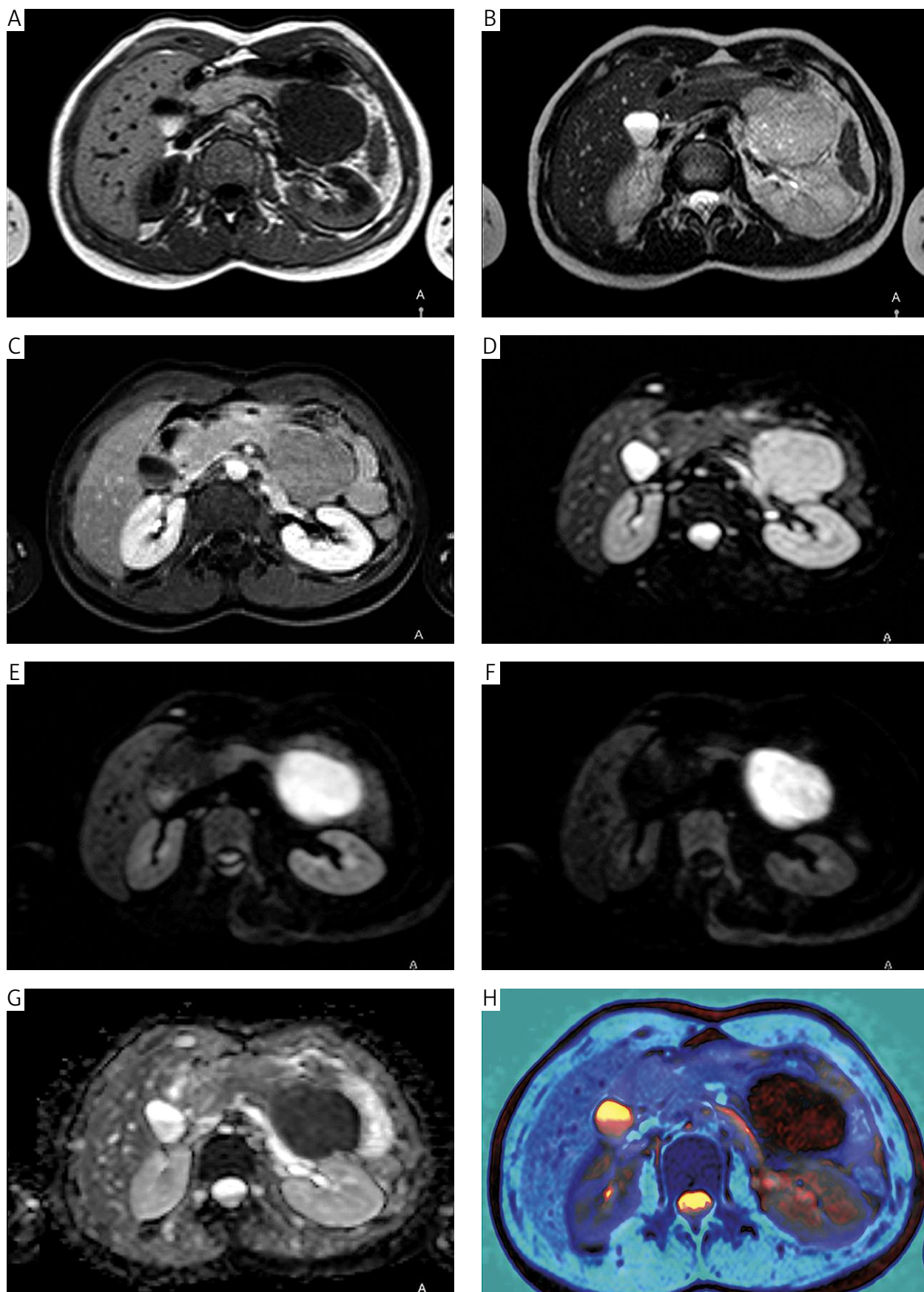
Fig. 3. Well-circumscribed pathological mass of the pancreas in magnetic resonance. T1- (A) and T2-weighted images (B); T1-weighted image with post-gadolinium contrast enhancement (C); DWI images with b0 (D), b500 (E) and b1000 (F); ADC b1000 map (G); fusion of T2-weighted and DWI b100 images (H)

indicated its fibrous structure. The best view of the tumor margin was observed on T2- weighted images, opposed phase as well as on their fusion with DWI images. Scattered internal hypointense areas in the upper part of the tumor on T1- and T2-weighted images were interpreted as vessels (Fig. 3). A similar type of inhomogeneous signal was also observed on DWI images (b 0, 500, 1000). The mean apparent diffusion coefficient (ADC) obtained for the lesion on the ADC map was lower (0.824 mm^2/s; b 1000) than unchanged parenchyma of the pancreatic head (1.469 $\times$ 10^{-3} mm^2/s). A lower ADC value was established for the area located near the unchanged part of the pancreatic body (0.607 $\times$ 10^{-3} mm^2/s) but higher for the surrounding capsule (0.845-1.773 $\times$ 10^{-3} mm^2/s). Both parts were also characterized by significant contrast enhancement. However, the perfusion curve, established for the whole lesion, was typical for malignant tumor (type III). All other findings were similar to those in US and CT examination.

Based on radiological data and clinical information, a primary diagnosis of a solid pseudopapillary neoplasm was made and surgery was suggested. Formal middle segment pancreatic resection with spleen preservation was performed. The cross-resection of pancreatic parenchyma was covered by the posterior wall of the stomach. The isolated main pancreatic duct was preserved but the entero-pancreatic anastomosis was not completed.

A surgical specimen of the pancreas showed a well-circumscribed tumor (65 mm $\times$ 66 mm $\times$ 30 mm) covered by a thin capsule. It was solid, yellow and focally brownish in cross-section (Fig. 4). Microscopically, the tumor was composed of monomorphic, small, polygonal cells with an eosinophilic cytoplasm and round nuclei with dispersed chromatin and small nucleoli (Fig. 5). PAS-positive globules were noted in the cy-toplasm. Occasionally, small hemorrhages were seen in the tumor mass (Fig. 5A). The cells formed solid masses with numerous rosettes arranged around blood vessels and pseudopapillary structures with fine fibrovascular stalks (Fig. 5B, D). The tumor was surrounded by a thin fibrous capsule (Fig. 5C). Infiltration of the pancreas beyond the capsule, vascular or perineural involvement and massive necrosis were not observed. Neoplastic cells were immunoreactive for progesterone receptor (Fig. 6A), vimentin (Fig. 6B), CD10, neuron-specific enolase and CK MNF116. The lymph node located next to the hepatic artery was not involved.

The patient had an uncomplicated recovery. Eight months after the operation, no signs of metastasis or local recurrence were found.

Discussion

In the currently reported case, all classic radiological and histological features of solid pseudopapillary neoplasm were seen, except for clinical symptoms. Although the size of the tumor was relatively large when compared with the data from the available literature [1, 4], the patient complained only of abdominal discomfort and negated all other typical symptoms, such as abdominal pain, early satiety, loss of appetite, nausea or vomiting, that are related to intra-abdominal mass and compression on surrounding organs. Less than 10% was diagnosed secondary to a rupture of the tumor accompanied by hemoperitoneum. However, one third of cases were incidental findings without any clinical symptoms {3].

In the reported patient, all applied radiological techniques presented similar localization and morphology of the tumor. Generally, the lesions are usually solitary, without predominance to any particular part of the pancreas [1, 3]. Moreover, the abnormal mass usually grows
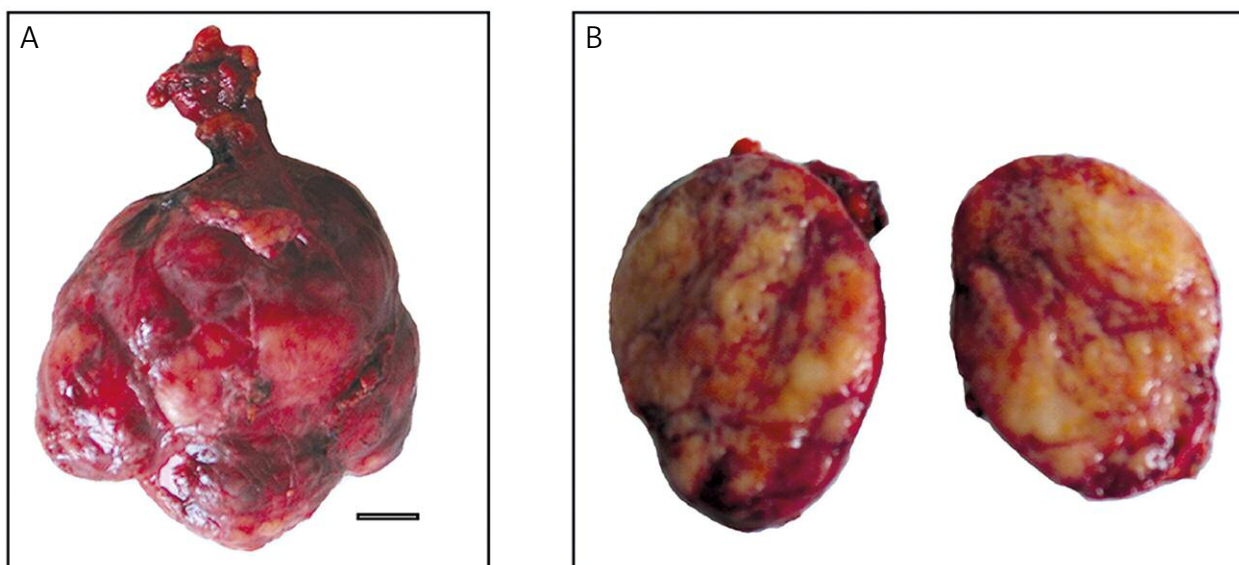

Fig. 4. Gross appearance of the surface (A) and cross sections of the tumor (B) (bar = 1 cm)

forward and is presented between intestinal loops and the stomach. However, incidental retroperitoneal position and tumor arising from the ectopic pancreas and localized in the transverse mesocolon was described [7].

Tumors are usually encapsulated, occasionally with foci of dystrophic calcification that, depending on their size, could be easily visible in about 30% of cases [8] during CT or less commonly US and MR examinations.
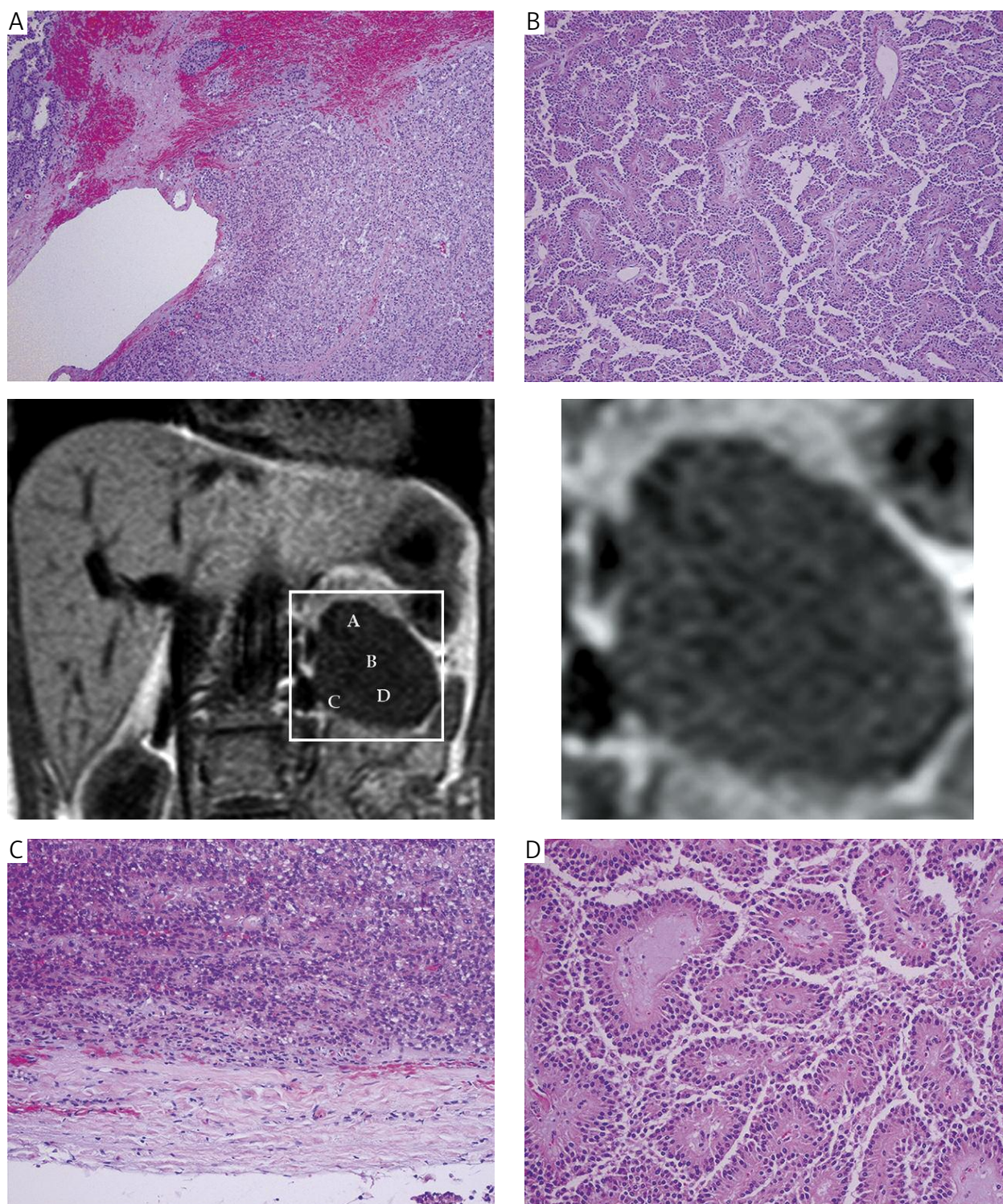

Fig. 5. Correspondence of magnetic resonance image (coronal section in T1-weighted images) and histological findings (HE) of the solid-pseudopapillary neoplasm of the pancreas: A) large non-infiltrated vessel with local fibrosis and hemorrhage inside the upper part of the tumor (objective magnification 10×); B, D) pseudopapillary structures covered by monomorphic cells (objective magnification: B – 10×; D – 20×); C) pseudocapsule of the tumor (objective magnification 20×)
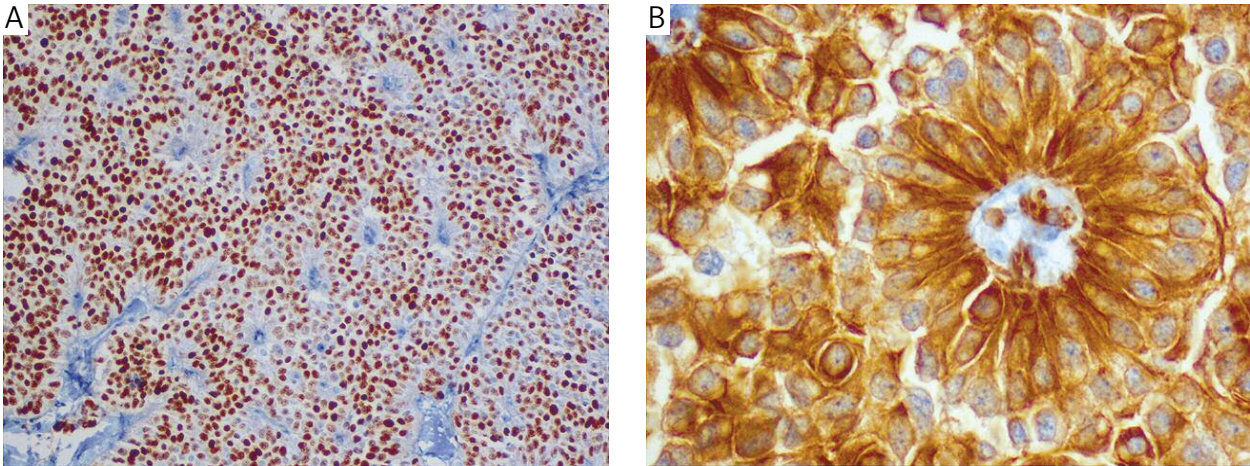
Fig. 6. Positive immunostaining for progesterone receptor (A) and vimentin (B) (Dako, EnVision+System-HRP; objective magnification A – 20×; B – 60×)

Calcifications are secondary to previous necrosis or hemorrhages. Non-encapsulated lesions have also been reported, but they were probably detected in an early stage, before formation of the capsule [2]. The capsule composed of fibrous connective tissue has a unique morphology in all radiological techniques. It is usually hypoechogenic in ultrasound examination, hypo- or isodense in CT and hypointense in T1- and T2-weighted MR images [9].

According to their name, tumors are usually solid but often, especially in large lesions, cavities filled with necrotic masses or blood as a result of acute or remote hemorrhages are also noted. In an extreme situation they may imitate a classic cystic pancreatic lesion and histopathological evaluation is crucial to prove their true nature [3]. Due to their soft consistency, tumors rarely cause obstruction of bile and pancreatic ducts, which may be examined by MRCP.

Despite the relatively benign nature of the tumor, solid parts are usually enhanced after contrast injection in both CT and MR, with an early "wash-in" effect during the dynamic phase. Progressive, heterogeneous enhancement in portal venous and equilibrium phases but less than the surrounding and unchanged part of the pancreas has been also observed [10]. Moreover, the tumor has a low or isointense signal on T1- and a high signal on T2-weighted images.

In solid pseudopapillary neoplasm, the ADC value – which depends on the degree of water restriction diffusion and cellularity – usually is higher than that observed for malignant tumors (0.9-1.2×10^{-3} mm²/s). Higher signal on T1-weighted images and high ADC value are typical for hemorrhage. Observations mentioned above were not confirmed in our patient due to the small size of hemorrhages. The heterogeneous intensity in the upper part of the lesion on T2-weighted images, DWI and on ADC maps is probably secondary to large internal vasculature, proven in Doppler US. Furthermore, even using different *b* values (50, 400, 800) than in our MR protocol, Rodrigues-Duarte *et al.* [9] presented a high mean ADC value (1.8×10^{-3} mm²/s) for a small solid pseudopapillary neoplasm (45 mm) in a 13-year-old boy. However, focal areas with a lower ADC value (1.3×10^{-3} mm²/s) were also observed but, in that case, large cystic, hemorrhagic and necrotic areas were found in histological examination. Lack of such changes and solid form of the currently reported tumor may explain the relatively low ADC value.

Having all clinical and radiological findings, an accurate diagnosis of solid pseudopapillary tumor before the surgery is nowadays much more common. Another modern procedure used in preoperative evaluation is endoscopic ultrasound (EUS) with fine needle aspiration biopsy (FNA) [11]. In differential diagnosis acinar cell carcinoma, pancreatoblastoma, neuroendocrine neoplasms, metastatic adenocarcinomas as well as non-neoplastic lesions such as post-inflammatory pseudocyst, parasitic cyst or ectopic spleen also have to be included [4]. Characteristic cytological and histological features of the tumor are usually sufficient for diagnosis (Table I) [12, 13], but some variants with less typical morphology are a diagnostic challenge [14]. In such cases a panel of antibodies is helpful, although overlapping of some immunohistochemical reactions among pancreatic neoplasms is well known (Table I). Nuclear staining with β-catenin is regarded as a specific and sensitive marker of solid pseudopapillary tumor. In the available literature expression of a variety of antigens, e.g., vimentin, CD10 and neuroendocrine markers such as synaptophysin and CD56, was also observed [11, 12]. It should be noted that progesterone receptor expressed by the tumor may be responsible for its rapid growth during pregnancy and puerperium [8]. However, some authors explained such higher occurrence as incidental and related to frequent US examination during gestation.

In the present case, histological findings as well as immunoreactivity were typical and finally confirmed

Table I. Differential diagnosis of solid pseudopapillary neoplasm, acinar cell carcinoma and pancreatic endocrine neoplasm, according to Chakhachiro and Zaatari [12] with own modification

Features	solid pseudopapillary neoplasm	acinar cell carcinoma	pancreatic neuroendocrine tumors
Gross	circumscribed; variegated, hemorrhagic solid and cystic	circumscribed; nodal with or without necrosis and cystic changes	circumscribed; usually solid, possible cystic changes
Cytological	pseudopapillary fragments, cytoplasmic vacuoles, hyaline extracellular material or globules; cercariform cells, retiform nuclei	prominent acinar formation, cells with granular cytoplasm	monotonous, small or medium-sized with granular chromatin (salt-and-pepper) and plasmocytoid morphology
Histological	pseudopapillary structures; discohesive cells, nuclear grooves, hyaline globules	acinar or solid patterns; cells with finely granular cytoplasm	organoid, trabecular, nested patterns; granular chromatin (salt-and-pepper)
Ultra-structural	nonspecific cellular junctions, numerous mitochondria, well-developed rough endoplasmic reticulum, variably sized zymogen-like granules, sporadically neurosecretory-type granules	desmosomes, well-developed rough endoplasmic reticulum, numerous mitochondria, numerous variably sized zymogen granules, elongated bodies composed of filaments	desmosomes, numerous variably sized neurosecretory-type granules, intermediate filaments
Immunoreactivity			
vimentin	+	V	V
wide-spectrum cytokeratins	V	+	+
β-catenin (nuclear)	+	–	V
chromogranin A	–	+	V
synaptophysin	V	+	–
CD56	+	-	+
neuron specific enolase (NSE)	+	V	+
CD10	+	V	V
CD117	+	ND	V
glypican-3	+	ND	–
pancreatic enzymes	V	+	–

(+) – positive; (–) – negative; V – variable; ND – not determined

the radiological diagnosis. Generally, it could be performed using traditional histological staining methods but immunohistochemical reactions have to be applied especially in lesions with cellular pleomorphism, high mitotic activity, vessel invasion or metastases without known location of primary tumor [4, 14]. In such cases components of sarcomatoid or undifferentiated carcinoma could be occasionally revealed. Those lesions are associated with rapid progression [15]. Moreover, in rare cases a direct infiltration of the duodenum, stomach or spleen, metastases to the liver, peritoneum, skin and regional lymph nodes, as well as recurrences after surgical treatment have been reported in otherwise morphologically typical tumors [3].

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