Review

Endoscopic Ultrasound

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Comments and illustrations of the European Federation of Societies for Ultrasound in Medicine contrast-enhanced ultrasound guidelines. Rare pancreatic tumors, imaging features on transabdominal ultrasound and EUS with contrast enhancement: Rare epithelial pancreatic tumors: solid pseudopapillary neoplasm, acinar cell carcinoma, mixed neuroendocrine-non-neuroendocrine neoplasms, some rare subtypes of pancreatic adenocarcinoma and pancreatoblastoma

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ABSTRACT

Rare malignant pancreatic lesions are systematically reported in this review. The focus is on the imaging appearance of the rare epithelial pancreatic tumors such as the solid pseudopapillary neoplasm, acinar cell carcinoma, rare subtypes of adenocarcinoma, and pancreatoblastoma as seen on ultrasound, EUS, and contrast-enhanced ultrasound or EUS. The present overview summarizes the data and shows that not every pancreatic tumor is likely to be the most common entities of ductal adenocarcinoma or neuroendocrine tumor.

Keywords: Solid pseudopapillary tumor; Rare subtypes of pancreatic adenocarcinoma; Acinar cell carcinoma; Imaging; US; EUS; Contrast-enhanced US; Contrast-enhanced EUS; Ultrasound; EUS

INTRODUCTION

The World Federation for Ultrasound in Medicine and Biology has published guidelines on the use of contrast-enhanced ultrasound (CEUS) for the evaluation of focal liver lesions[1–5] and the European Federation of Societies for Ultrasound in Medicine for the evaluation of nonhepatic indications.[6,7]

Improved detection and characterization of common focal pancreatic lesions such as ductal adenocarcinoma, neuroendocrine tumors, and pancreatic metastases are the main topics of these guidelines. In recent years, conventional ultrasound (US) and CEUS features of less common focal pancreatic lesion have been described as well in detail including autoimmune pancreatitis,[8–11] pancreatic tuberculosis,[12,13] pancreatic ascariasis,[14,15] pancreatic hydatid cysts,[16,17] and intrapancreatic metastases.[18]

The World Health Organization (WHO) classification of pancreatic neoplasms in the fifth edition (2019)[19] is based on the lines of cellular differentiation (ductal, acinar, neuroendocrine, or other),

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as well as their predominant morphology (solid, cystic, or intraductal). Up to 90% of pancreatic neoplasms in adults are carcinomas, including 85% ductal adenocarcinomas or related subtypes. Pancreatic neuroendocrine neoplasms (PanNENs) account for 3% to 4%, and acinar cell carcinomas (ACCs) and other rare entities account for the remaining. Tumors of the pancreas are rare in childhood. The most common neoplasms in the first decade of life are pancreatoblastomas, ACCs, and PanNENs. In the second decade of life, solid pseudopapillary neoplasms (SPNs), PanNENs, and ACCs occur most frequently.[19,20] Epithelial tumors according to the WHO classification fifth edition (2019)[19] are listed in Table 1.

The current article on the appearance of rare malignant pancreatic tumors on imaging with criterion-standard histology includes SPN; ACC; mixed neuroendocrine-nonneuroendocrine neoplasms, formerly mixed adenoneuroendocrine carcinoma (MANEC); some rare subtypes of pancreatic adenocarcinoma (pancreatic clast-like–giant cell carcinoma, sarcomatoid carcinoma, and others); and pancreatoblastoma.

Although solid pseudopapillary neoplasia has good data on imaging including EUS with EUS-guided sampling and CEUS, much of the very rare tumors have few descriptions of the tumor on imaging. Many of the rare tumors are initially suggestive of adenocarcinoma based on imaging of a tumor with pancreatic duct dilatation and common bile duct dilatation if present. In general, the rare tumors described are already very large at diagnosis, and the diagnosis is not uncommonly only made on cytohistologic assessment.

The aim of the present review is to comprehensively present rare primary predominantly solid malignant tumors of the pancreas apart from typical ductal adenocarcinoma and neuroendocrine neoplasms. For some of the very rare entities, the engagement of a variety of authors has helped demonstrate the appearance on US with examples.

NEOPLASTIC PANCREATIC DISEASES

Solid pseudopapillary neoplasm

Solid pseudopapillary neoplasm is a rare exocrine pancreatic neoplasm, with a low potential of malignancy, accounting for 1% to 2.7% of all pancreatic tumors in adults and approximately 5% of all cystic pancreatic neoplasms.[20,21] First cases of SPN have been reported as early as 1911 and 1934.[22] The pathologist Virginia Kneeland Frantz described the typical characteristics of the tumor in 1959.[23] Various terms have been used to describe this tumor, such as "Frantz tumor," "Hamoudi tumor,"[24] papillary epithelial neoplasm, and solid and papillary tumors.[25–28] In 1996, the WHO, defined them as "solid pseudopapillary neoplasm." Probably due to the increasing use of modern imaging techniques, SPN has been increasingly diagnosed over the last 2 decades.[26] Solid pseudopapillary neoplasms mainly affect young women in the third and fourth decades of life,[25,26] although patients of any other age can develop this tumor. Solid pseudopapillary neoplasm can also affect children and represent the majority of pancreatic neoplasms in children.[21,29] The proportion of male patients is approximately 12%. Solid pseudopapillary neoplasms in male patients tend to have an onset 5 to 10 years later than female patients.[28] Lipase and CA-19-9 are typically not elevated.[28] The tumor has a good prognosis after surgery with a 5-year survival rate of up to 97%.[30] In a large meta-analysis, Law et al.[26] evaluated 2744 reported cases in 484 studies from 1961 to 2012. Women were affected in 87.8%[26]; 38.1% of the patients were symptom-free. Abdominal pain or discomfort was reported in 63.6%. Other signs and symptoms included

Table 1

Pancreatic malignant epithelial tumors in WHO classification 2019.[19]

Malignant epithelial tumors	Related terminology	Acceptable	Subtypes
Ductal adenocarcinoma	Ductal adenocarcinoma	Duct cell adenocarcinoma; infiltrating duct carcinoma; tubular adenocarcinoma	Colloid carcinoma; poorly cohesive carcinoma; signet-ring cell carcinoma; medullary carcinoma; adenosquamous carcinoma. hepatoid carcinoma; large cell carcinoma with rhabdoid phenotype; carcinoma, undifferentiated; undifferentiated carcinoma with osteoclast-like giant cells
	Adenosquamous carcinoma		
	Colloid carcinoma	Mucinous noncystic carcinoma	
	Undifferentiated carcinoma, anaplastic type	Giant cell carcinoma; anaplastic carcinoma; pleomorphic large cell carcinoma	
	Undifferentiated carcinoma, sarcomatoid type	Spindle cell carcinoma; sarcomatoid carcinoma	
	Undifferentiated carcinoma with osteoclast-like giant cells	Osteoclastic giant cell carcinoma	
ACC	None		Acinar cell cystadenocarcinoma; mixed acinar-neuroendocrine carcinoma; mixed acinar-endocrine ductal carcinoma
Pancreatoblastoma	None		None
SPN		Solid pseudopapillary tumor; solid-cystic tumor; papillary-cystic tumor; solid and papillary epithelial neoplasm; Frantz tumor	SPN with high-grade carcinoma

WHO: World Health Organization; ACC: acinar cell carcinoma; SPN: solid pseudopapillary neoplasm.

palpable mass, nausea, vomiting, and weight loss. Five percent of patients had pancreatitis, and 10.3% jaundice. The mean tumor size was 8.6 cm, but in later years with increased use of cross-sectional imaging, mean tumor size has been smaller.[26] More recent studies report a higher proportion of incidentally detected SPN, >50%.[28,31,32] In 59.3%, the tumor was located in the pancreatic corpus or tail, in 36% in the area of the pancreatic head/processus uncinatus.[26] Vascular involvement was identified in 4.6%, lymph node metastases in 1.6%, and distant spread in 7.7% of all cases.[26] Even if the tumor was located at the head of pancreas, it rarely caused obstructive jaundice.[33] The tumors are usually round or oval and well demarcated from the rest of the parenchyma by a pseudocapsule. The tumors consist of varying degrees of solid, cystic, hemorrhagic, and necrotic parts and pseudopapillary structures.[31,34,35] In smaller tumors, the solid parts usually predominate. Larger tumors have more cystic, hemorrhagic, and necrotic parts.[28,31] Malignancy within SPNs does not correlate with tumor size.[31] An incomplete capsule is highly suggestive of a malignant SPN.[34] Further signs predictive of malignancy are metastases, capsular, parenchymal, vascular, and perineural invasion.[28,31,36] Li et al.[28] described pancreatic tissue infiltration and focal capsular invasion in 32.4% of the patients on computed tomography (CT) and magnetic resonance imaging (MRI), but none of them developed tumor recurrence on follow-up. Ten percent to 15% of SPNs metastasize to the peritoneum or liver, whereas lymph node metastases are rare.[21,26,35,36] Hao et al.[37] reported in a meta-analysis 59 patients with aggressive SPN (metastasis, 81.4%; local recurrence, 11.9%; and deep tissue invasion, 6.8%) with remarkable disease-free survival of 45 ± 6.28 months and 5-year disease-free survival rate of 26.8%. Lack of resectability and occurrence of metastases or local recurrence within 3 years had a statistically negative impact on survival.[37] Important differential diagnoses are other solid, cystic-solid, or cystic tumors and lesions such as pancreatic ductal adenocarcinoma (PDAC), cystadenocarcinoma, neuroendocrine tumors, mucinous cystadenoma, serous-microcystic cystadenoma, pseudocysts, and focal autoimmune pancreatitis.[38]

IMAGING

Solid pseudopapillary neoplasms typically appear at imaging as mixed solid or cystic lesions because of the presence of extensive hemorrhage and necrosis. Usually, SPNs are round or oval with well-defined margins. A typical sign is the tumor capsule.[28,29,39–41] Another feature is calcifications inside the tumor or the capsule. Li et al.[28] described punctate calcifications and chunky, nodular, or annular calcifications on CT imaging. De Robertis described calcifications in 10% of cases on MRI.[31] The pancreatic and the bile duct usually are not or rarely affected. For this reason, jaundice rarely occurs even when the tumor is localized at the head of the pancreas.[28,29,40]

Ultrasound

On B-mode US, SPNs appear as well-defined, hypoechoic, homogeneous, or heterogeneous lesions. The cystic or hemorrhagic parts are anechoic or hypoechoic.[42,43] In the CEUS, solid and cystic/hemorrhagic parts can be better differentiated.[39,42,43] In the study by Xu et al.,[40] 70% of the SPNs were spherical, 21% ellipsoidal, 9% were irregular. For echogenicity of SPN on B-mode US, 23.3% were hypoechoic, 9.3% were hyperechoic, and most of them (67.4%) were mixed. Most SPNs (81.4%) had a well-defined tumor border. Color Doppler imaging identified 14% of the lesions with intralesional abundant blood flow, 81.4% of the lesions with scarce blood flow, and 4.7% of the lesions with no blood flow signal. Calcifications were present in 11.6% of the lesions; fluid in 39.5% of the lesions; mural nodules in 9.3% of the lesions; and separation (fiber strip within the lesion) in 4.7% of the lesions.[40] Jiang et al.[39] detected calcifications in the rim in 29.4% of SPNs on B-mode US alone.

Contrast-enhanced US

D'Onofrio et al.[42] describe in the early phase of CEUS a slight peripheral rim enhancement, suggesting the diagnosis of a small SPN with peripheral pseudocapsule deriving from the compression of the adjacent pancreatic parenchyma. At pathological examination of the resected lesions, it was possible to show a thin pseudocapsule, derived from compression of a few millimeters of the perilesional parenchyma, which determined an increase in vessel concentration.[42] The authors conclude that the identification of a peripheral hypervascularized rim could be helpful in differentiation of SPN from other tumors.[42] Jiang et al.[39] also describe a ring-like enhancing rim around the tumor during arterial phase in CEUS. Tang et al.[41] describe large SPNs with isoenhancement on CEUS in the peripheral rims of the tumors during the early arterial phase, and the interiors of the masses showed heterogeneous enhancement consisting of regions of isoenhancement, hypoenhancement, and nonenhancement. Progressive washout of the contrast agent during venous phases revealed hypoenhancement compared with normal adjacent pancreatic parenchyma.[41] The authors conclude that the findings of both a capsule and intratumoral hemorrhage are important diagnostic indicators for a solid pseudopapillary tumor, because these features are rarely found in other pancreatic neoplasms.[41] On CEUS with SonoVue (Bracco, Konstanz, Germany), 90.7% of SPNs demonstrated inhomogeneous enhancement.[40] In CEUS with SonoVue, SPNs in the early phase showed hyperenhancement in 18%, isoenhancement in 44%, and hypoenhancement in 37%. In contrast-enhanced CT, this was comparable to 30%/37%/32%, respectively. In the portal venous phase, the CEUS showed hyperenhancement in 0%, isoenhancement in 25%, and hypoenhancement in 74%. In comparison, the contrast-enhanced CT showed 14%/48%/37%, respectively.[40] The most common enhancement levels of SPN on CEUS were isoenhancement and hypoenhancement. The 4 most enhanced patterns were hypo-hypo (37.2%), iso-iso (25.6%), hyper-hypo (18.6%), and iso-hypo (18.6%).[40] In the comparison of CEUS and CT, isoenhancement was the most common enhancement characteristic during the early phase and hypoenhancement in the portal venous phase.[40] Xu et al.[40] found 3 common CEUS features of SPNs: lesion membrane (69.8%), intralesional vessel (62%), and intralesional compartmentalization (23.2%), especially in those lesions >3 cm. The authors conclude that these signs could be used to differentiate SPNs from other pancreatic tumors.

Computed tomography

On enhanced CT images, solid tumors and solid parts of mixed tumors had slight contrast enhancement in the arterial phase and showed as hypodense to normal pancreatic parenchyma. In portal venous phase, solid tumors and solid parts of mixed tumors had progressive enhancement and slightly increased or decreased enhancement in delayed phase and showed as slight hypodense or isodense to pancreatic parenchyma. The cystic part of tumors had no obvious enhancement, but the wall enhanced similar to solid tumors.[28] Li et al.[28] divided SPN into 5 types according to the ratio of solid and cystic parts: type I is completely solid, type II had few cystic parts, type III was cystic-solid (solid portions accounted for >50%), type IV consisted predominantly of cystic parts with few solid parts, and type V is completely cystic. Types

III and IV were the most common. Type III/IV/V tumors were larger than types I and II. This suggests that with increasing size, more cystic, hemorrhagic, and necrotic parts develop. Men are more likely to have types I and II, whereas women are dominated by types III and IV.[28]

Magnetic resonance imaging

In the study by Li et al.,[28] the SPNs were T2 hyperintense and T1 hypointense on MRI and with heterogeneous enhancement on contrast-enhanced T1-weighted images (T1WIs). Cystic degenerations present as intratumoral T2 hyperintense and T1 hypointense. Hemorrhage was found as hyperintense within the lesion on T1WIs. Capsule was seen as a peripheral hypointense rim on T1WI and T2WI.[28] De Robertis et al.[31] describe the SPNs with slight hyperintensity on T1WIs, heterogeneously hyperintense appearance on T2WIs, and an enhancing and minimally thickened capsule. Magnetic resonance imaging is more accurate than CT in differentiating the cystic or solid components inside the tumor.[43,44] In MRI, SPNs can also be distinguished into 3 types according to the extent of the solid and hemorrhagic parts[43,45]:

(1) Type 1: SPN with completely solid part. T1-weighted image revealed homogenously hypointense and slightly hyperintense than pancreas parenchyma on T2WI. Strong and rapid enhancement and gradually fading pattern could be observed.
(2) Type 2: SPN with solid mass with hemorrhage. T1-weighted image revealed hypointensity with heterogeneously hyperintense area. The hyperintense areas on T1WI appeared slightly hyperintense on T2WI, meaning hemorrhage while there is enhancement of the capsule and gradual enhancement of the solid part.
(3) Type 3: SPN with massive hemorrhage. T1-weighted image revealed mainly hyperintensity with intermediate and hypointense areas. The hyperintense areas on T1WI appeared slightly hyperintense on T2WI. Only capsular enhancement could be detected.

Type 1 SPN is exclusively solid, showing diffuse hypointensity on the T1WI and slight hyperintensity on the T2WI when compared with normal pancreatic parenchyma. Type 2 SPN has a solid portion associated with hemorrhage, which shows central hypointensity with surrounding heterogeneously hyperintense areas on the T1WI, and the central hypointense areas show hyperintensity on the T2WI. Type 3 SPN shows massive hemorrhage, appearing as a predominantly hyperintense area with some hypointense areas on the T1WI, and these areas of hemorrhage show hyperintensity or hypointensity on T2WI image, depending on the age of hemorrhage.[45]

EUS

The diagnostic workup of pancreatic lesions is a domain of EUS, including contrast-harmonic EUS and EUS-guided fine-needle sampling for obtaining cytology/histology. EUS has the highest spatial resolution of all imaging methods. In an EUS study by Jani et al.,[32] 89.5% of the SPNs were well-defined, 95.7% were hypoechoic, 50% were solid, 39% were mixed solid and cystic, and 11% were only cystic. Calcifications were seen in 21.4%. A preoperative diagnosis was possible in 75% by EUS-FNA.[32] A similar appearance was described by Law et al.[46] on EUS. The SPNs were predominantly solid and cystic (67.8%) or solid (32.4%). No SPN was exclusively cystic. The margins were well defined in 91.2%. Infiltrations were seen in 8.8% and calcifications in 17.6%. A definitive diagnosis could be made by EUS-guided sampling in 82.4%, similar to PDAC.[46] Stoita et al.[47] achieved a preoperative diagnosis of SPN in 83% by EUS-guided sampling. In an international EUS multicenter study of 106 patients, no pathognomonic features were described on EUS imaging. However, EUS-guided sampling was conclusive in 97.2% regardless of needle type.[48] On immunohistochemistry, SPN is typically positive for β-catenin, E-cadherin, α1 antitrypsin, synaptophysin, CD10, CD56, and progesterone receptors and negative for chromogranin, epithelial membrane antigen, and cytokeratin.[47] Researches had suggested that positive staining of Ki-67 may correlate with the malignant potential and poor outcome of SPT.[49] In an EUS study of pancreatic tumors with contrast-enhanced EUS using Sonazoid (Daiichi-Sankyo, Tokyo, Japan; GE Healthcare, Milwaukee, WI), 13 patients with SPN were examined.[50] These were not evaluated separately but together with 31 pancreatic neuroendocrine neoplasms (PanNEN). The result with prolonged hypervascular patterns is more typical for the PanNEN and does not coincide with the flow patterns in percutaneous CEUS as reported by Xu et al.[40]

Table 2

Solid pseudopapillary neoplasm on imaging and EUS-guided sampling.

Methods	Appearance
Prevalence	Mostly women, third and fourth decades of life
Morphology	Round or oval shape; pseudocapsule; solid, cystic, hemorrhagic, and necrotic parts, pseudopapillary structures; calcifications
	Pancreatic duct and common bile duct are mostly not affected
B-mode in US and EUS	Well-defined margins; solid, cystic-solid, or cystic appearance; mostly heterogeneous or homogeneous, mixed hypohyperechoic or hypoechoic; cystic parts are anechoic, necrotic parts are hypoechoic or anechoic[26,32,42,43,46]
	Calcifications, calcifications in the rim[32,39,46]
Color Doppler imaging	Mostly with scarce blood flow[40]
CEUS	Enhancing capsule: slight peripheral rim enhancement[39,42]
	Inhomogeneous enhancement[42]
	Arterial phase: mostly isoenhancement or hypoenhancement[40]
	Portal-venous phase: usually hypoenhancement[40,41]
Contrast-enhanced CT	Wall enhanced similar to solid tumors[28]
	Nonenhancing cystic or necrotic parts[28]
	Arterial phase:
	In equal proportions hyperenhancement, isoenhancement, or hypoenhancement[40]
	Slight contrast enhancement, hypodense to normal pancreatic parenchyma[28]
	Portal-venous phase:
	Predominant isoenhancement or hypoenhancement[40]
	Progressive enhancement of solid parts[28]
	Delayed phase:
	Slight hypodense or isodense to pancreatic parenchyma[28]
MRI	Capsule: a peripheral hypointense rim on T1WI and T2WI[28,31]
	T2 hyperintense and T1 hypointense, heterogeneous enhancement on contrast-enhanced T1WIs; cystic degenerations and hemorrhage present as intratumoral T2 hyperintense and T1 hypointense[28]
	Heterogeneously hyperintense appearance on T2WIs[31]
EUS-guided sampling	Preoperative diagnosis in 82%–83%[39,40]

CEUS: contrast-enhanced ultrasound; CT: computed tomography; MRI: magnetic resonance imaging.

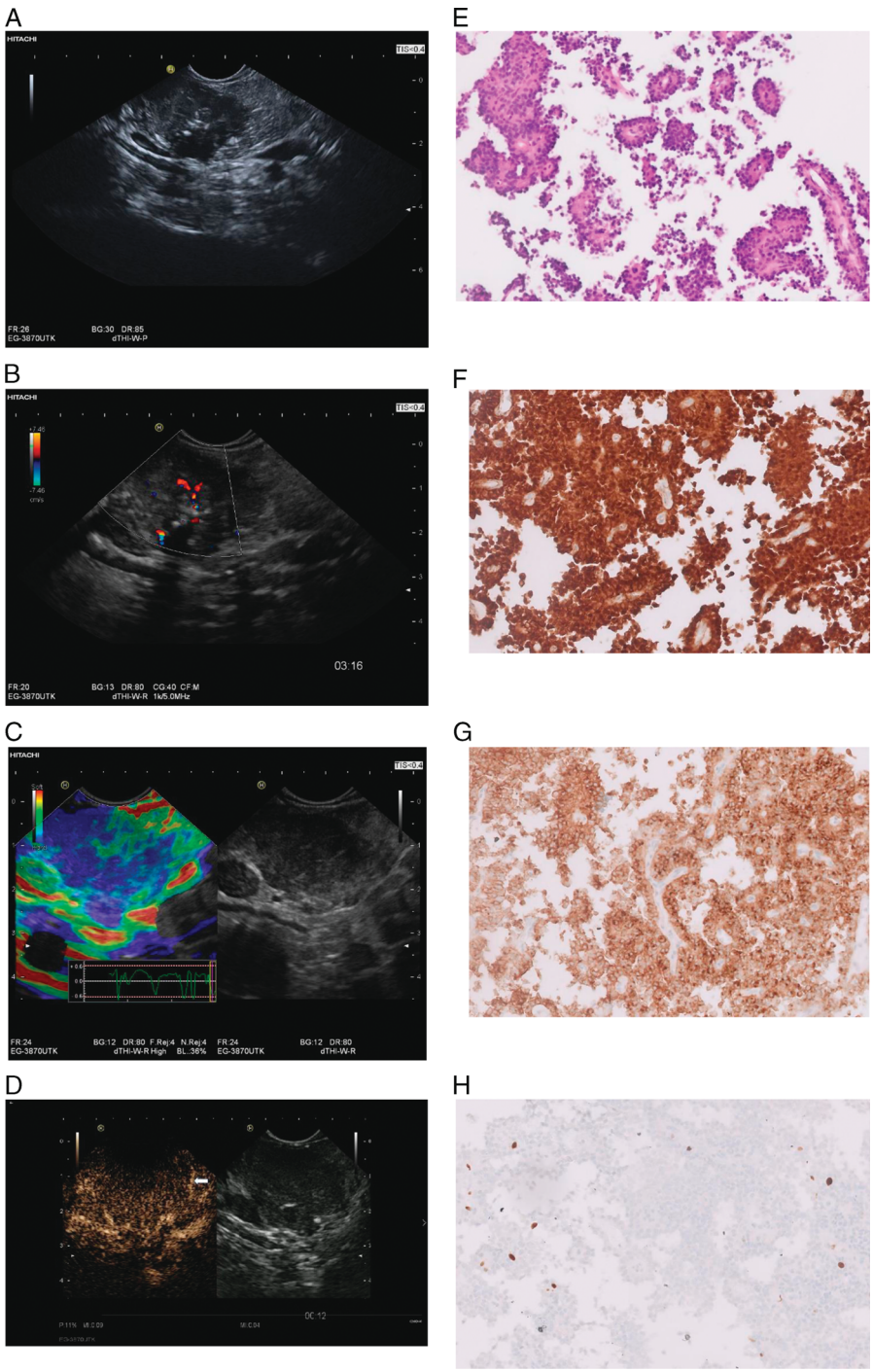

Figure 1. Solid pseudopapillary neoplasm of the left pancreas (pancreatic body and tail). A 38-y-old man. Nonspecific upper abdominal complaints. Normal lipase and CA-19-9. Left pancreatic mass on CT and MRI. Native EUS shows a 34-mm, sharply demarcated, solid, hypoechoic lesion with central calcifications at the junction of the pancreatic corpus and the pancreatic tail. Echogenic internal septa are visible (A). EUS with duplex shows central star-shaped macrovessels (B). Elastography shows the lesion to be stiffer than the surrounding area (C) In CE low-mechanical-index EUS, the lesion is isoenhanced in the early phase compared with the adjacent parenchyma. A contrast-enhancing rim is seen, comparable to a capsule (narrow) (D). Histologic examination of the particles of EUS-guided sampling diagnosed solid pseudopapillary neoplasia; hematoxylin-eosin stain 200-fold (E). Immunohistological examination was performed. Tumor cell strongly expressed vimentin, cytoplasmic and nuclear strongly expressed β-catenin (F) and CD10 (G). Synaptophysin and chromogranin were negative. Progesterone receptor was nuclear varying degrees positive in most tumor cells. Ki-67 was positive in single cells (H; all histopathological images are displayed with 200× magnification). Image source of histological images courtesy of Dr Daniel Bethmann and Dr Uwe Schlichting, Institute of Pathology, Sana-Klinikum Berlin-Lichtenberg. Metastases were not reported in the staging. Pancreatic left resection with splenectomy was performed. Four years postoperatively, the patient was in good health without recurrence or metastases.

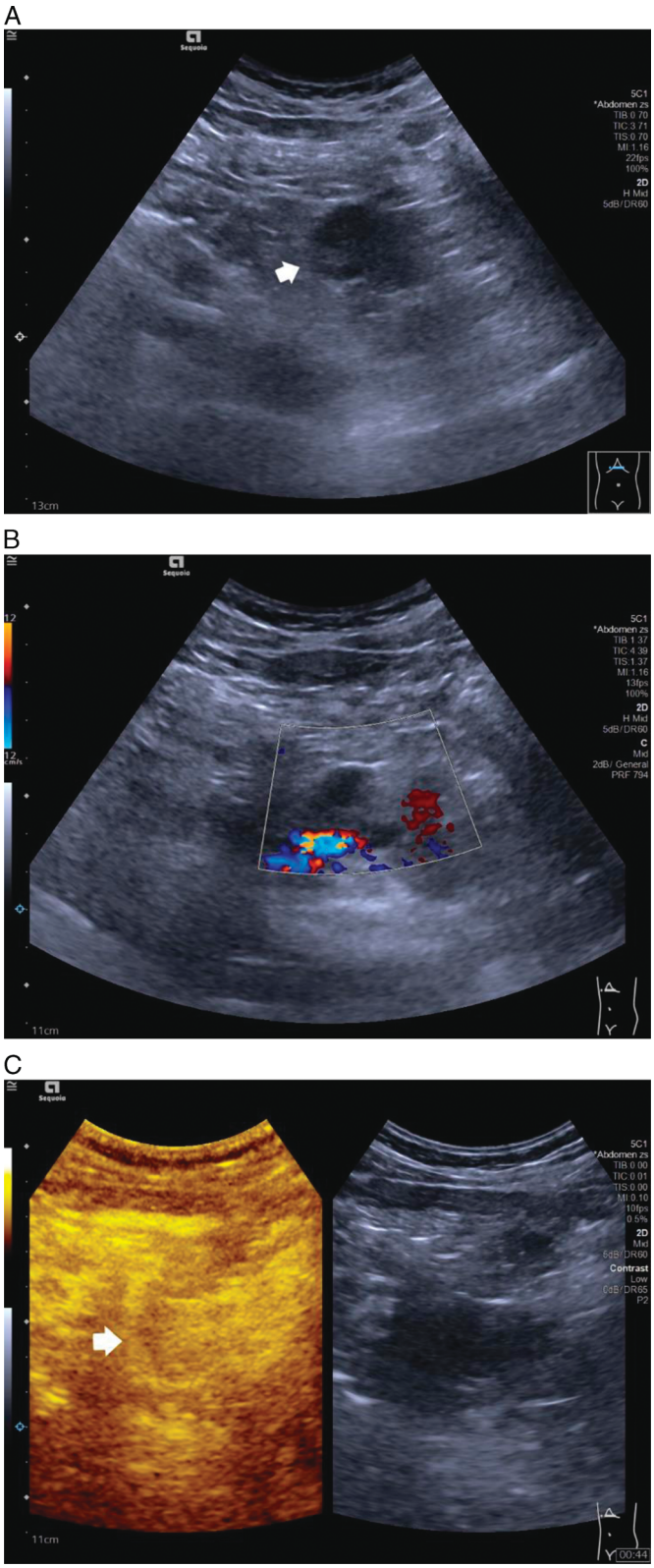

Figure 2. Solid pseudopapillary neoplasm of the pancreas (body and tail) in a 30-y-old man. A hypoechoic and heterogeneous lesion was visible in B-mode US (A). No blood vessels could be found inside the tumor on color Doppler imaging (B). Compared with perilesional pancreatic tissue, the lesion showed hyperenhancement in CEUS (C).

Further reports are awaited here. Although EUS-FNA is considered a safe method, and tumor seeding is exceptionally rare,[51] single cases of gastric wall metastasis and rupture of SPNs after EUS-FNA have been reported.[52,53] Typical features of SPN in imaging are summarized in Table 2 [Figures 1-3].

Treatment

Comparing with pancreatic adenocarcinoma, the prognosis of SPN is relatively favorable.[54] Surgical resection is frequently curative and considered the therapeutic method of choice. The postoperative overall resection survival rate is reported in several studies to be 96% and 93% after 5 and 10 years, respectively.[43] Local invasion, recurrence, or limited metastases are not contraindications to resection.

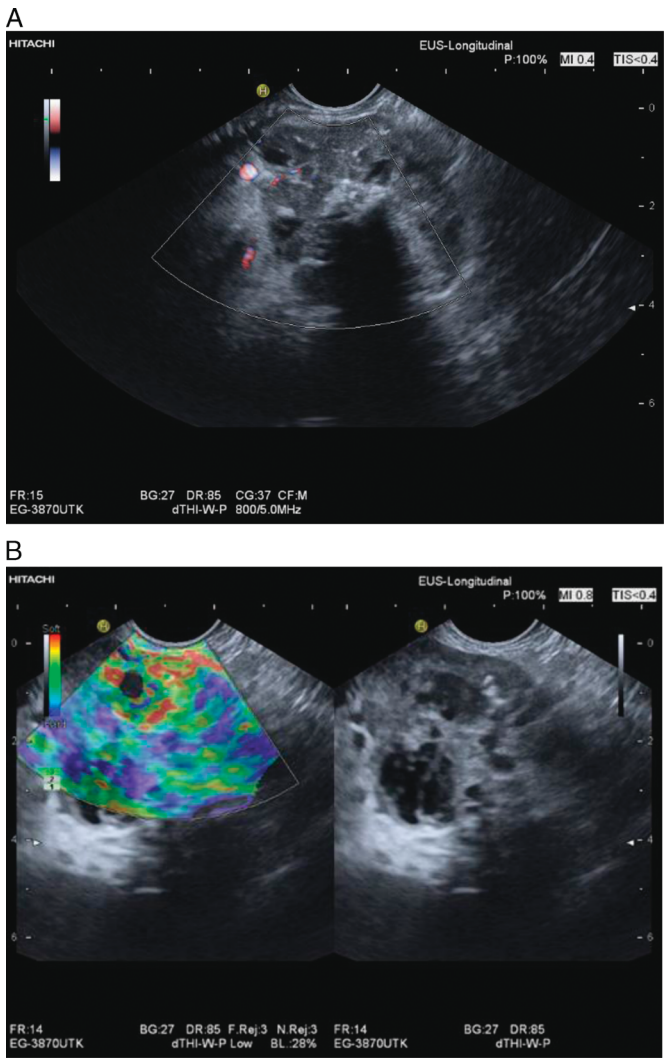

Figure 3. Solid pseudopapillary neoplasm, female, 63 years old. Incidental finding of a 48-mm lesion on the pancreatic head. On EUS, the lesion was smooth bordered, polycyclic contoured, heterogeneous, with cystic portions, and without evidence of vessels on power Doppler Imaging. Centrally, conspicuous calcifications were observed (A). On elastography, the lesion had both softer portions and harder portions. The latter projected onto the cystic areas (B). Assignment as SPN was performed by EUS-guided sampling with a 22-gauge needle. Curative surgical resection was then performed.

Table 3

ACC on imaging.

Feature	Appearance
Prevalence	Predominantly men around 60 y old
Morphology	Larger masses, round, pancreatic duct enlargement in approximately 50%
	Bile duct dilatation in 26% in case of pancreatic head tumors
	Pseudocapsule, calcifications, less vascularized tumors. hemorrhages, cystic parts
Contrast-enhanced CT and MRI	Enhancing pseudocapsule; uneven enhancement
	Degree of enhancement in each phase is less than that of the adjacent pancreatic parenchyma, but the enhancement in the arterial phase is greater than that of the surrounding pancreatic parenchyma[59]
	Central lower density[59]
CEUS	Heterogeneous enhancement pattern,[61] no sufficient data

ACC: acinar cell carcinoma; CEUS: contrast-enhanced ultrasound; CT: computed tomography; MRI: magnetic resonance imaging.

Acinar cell carcinoma

Approximately 1% to 2% of adult pancreatic neoplasms and 15% of pediatric neoplasms are ACCs.[55] Adult patients average 58 years of age, and men are approximately 3 times more likely to be affected.[56] Acinar cell carcinoma is derived from acinus pancreaticus, which is responsible for formation and secretion of digestive enzymes. Acinar differentiation is defined as the production of pancreatic exocrine enzymes by the neoplastic cells. Symptoms are usually nonspecific, and weight loss and abdominal pain may occur. Some patients (10%–15%) develop lipase hypersecretion syndrome. This is due to the fact that a large amount of lipase is released by the tumor and involves massive elevations of lipase in the serum. These may be accompanied by subcutaneous fat necrosis, polyarthralgia, and eosinophilia.[57,58] Increases in serum α-fetoprotein (AFP) in ACC have been reported, particularly in younger patients.[55] In a study of 39 patients with ACC, CA-19-9 and carcinoembryonic antigen were normal in all cases. α-Fetoprotein was elevated in 12.8% of cases.[59] In another study, CA-19-9 was elevated in 45%, carcinoembryonic antigen in 15%, and AFP in only 7.5%.[56] Acinar cell carcinoma can arise in all areas of the pancreas. However, in a study of 39 patients with ACC, nearly half of the tumors were located in the pancreatic head.[59] They are usually large at diagnosis. Tumor size is described from 1.48 to 13.2 cm, with an average of 5.77 cm.[59] In a study of 45 confirmed ACCs, 53.3% were localized, 11.1% were locally advanced, and 35.6% were primary metastatic.[56] Most ACCs are round and only rarely lobulated or irregular. They exhibit a pseudocapsule.[59] The pseudocapsule may be contrast-enhanced.[59,60] Disruption of enhancement of the pseudocapsule indicates infiltration of the surrounding area.[59] Approximately 20% of ACCs have calcifications on CT.[59] As a consequence of acinar secretion, ACCs may show cystic changes.[55] The pancreatic duct and common bile duct are not affected in every case.[55,59,60] When tumor localization was at the head of the pancreas, only 26.31% showed a slight dilatation of the bile ducts. In more than half (52.63%), the pancreatic duct was slightly dilated.[59]

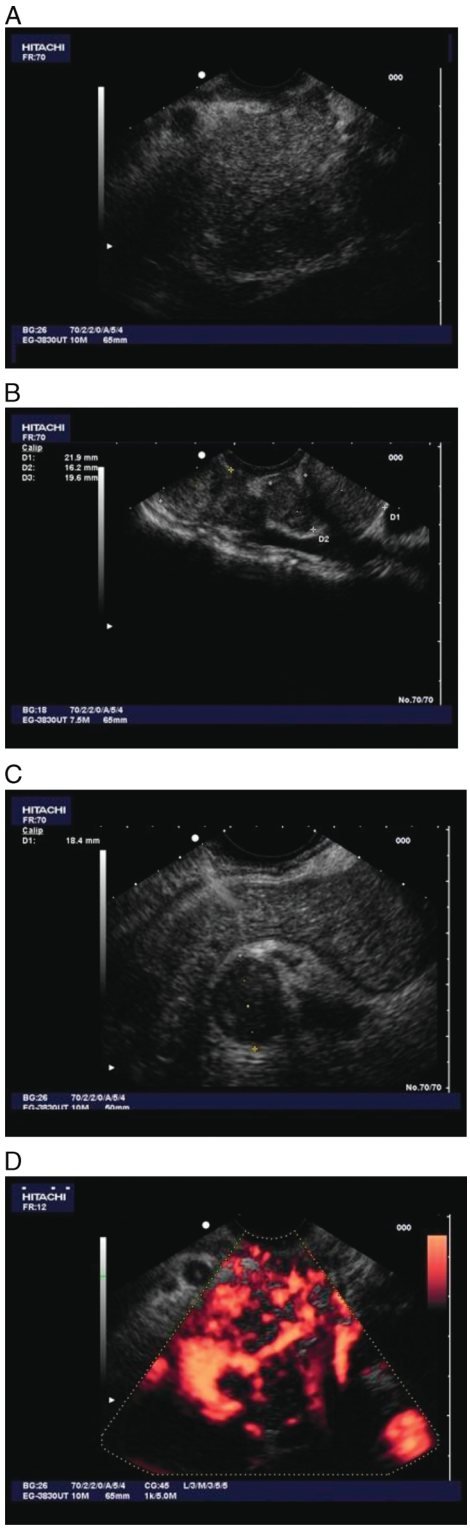

Figure 4. Acinar cell carcinoma. A 73-y-old man. Painless jaundice. Enlarged pancreatic head on US and CT, pancreatic duct slightly dilated (4 mm), with abruption at the pancreatic head. Dilatation of the bile ducts. EUS shows an enlarged hypoechoic pancreatic head (A) and multiple rounded and enlarged lymph nodes in the mediastinum and abdomen (B: paraesophageal and C: paraduodenal lymph nodes). EUS with contrast-enhanced power Doppler with 1 mL SonoVue intravenously administered shows hypervascularity of the pancreatic head. The diagnosis of metastatic ACC was confirmed by EUS-FNA of both the pancreatic head and mediastinal lymph nodes.

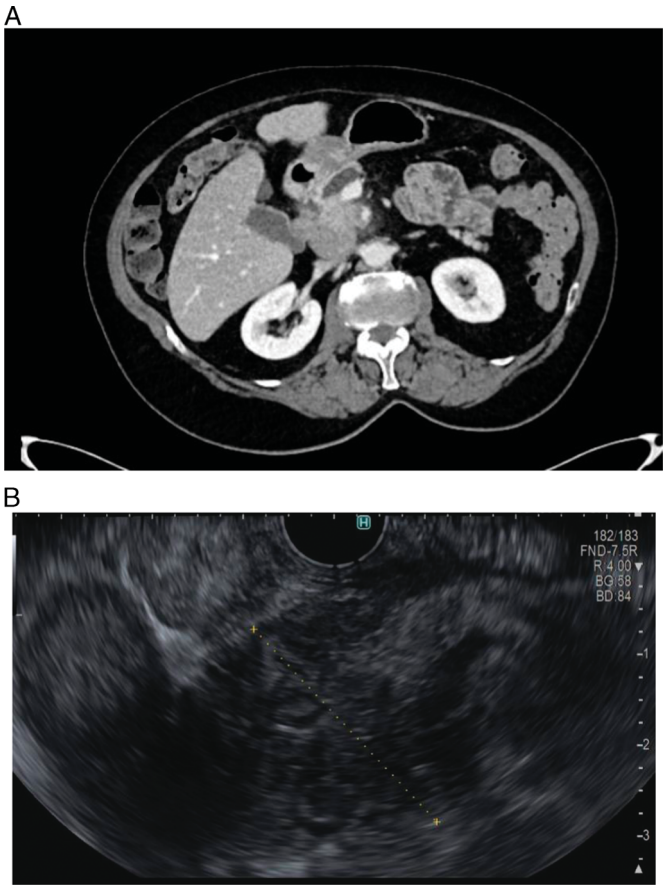

Figure 5. A 84-year-old woman presented with central abdominal discomfort and underwent a CT (A), which demonstrated an ill-defined mass in the head of pancreas causing an abrupt cutoff of the pancreatic duct and common bile duct. She underwent EUS (B), which demonstrated a poorly demarcated, heterogeneous soft tissue mass within the head of pancreas. EUS-FNA confirmed the diagnosis of MINENs.

Imaging

In 3 reported cases, ACC showed a heterogeneous enhancement pattern in CEUS.[61]

On arterial CT and MRI, all tumors showed uneven enhancement.[59] Most tumors are less vascularized compared with the surrounding pancreatic parenchyma. The degree of enhancement in each phase is less than that of the adjacent pancreatic parenchyma, but the enhancement in the arterial phase is greater than that of the surrounding pancreatic parenchyma.[59] In contrast-enhanced CT, 79% of patients had varying degrees of central lower sensitivity of less than 50%; 12.5% were cystic.[59] It may be difficult to identify tumor cells by FNA alone because of high-cellularity nodules composed of monotonous tumor cells with little or no stroma and a lack of desmoplastic reaction.[62]

Treatment

The prognosis of ACC is better than that of PDAC. Patients who have undergone curative surgery have a better prognosis than those who have not undergone resection. Median overall survival in the 45 patients with ACC in the study by Zhou et al.[56] was 18.9 months with a 5-year survival rate of 19.6%. Patients with resected ACC had longer survival compared with the unresected cases (36.6 *vs.* 8.5 months, $P < 0.001$). Typical features of ACC are summarized in Table 3 [Figure 4].

Mixed neuroendocrine-nonneuroendocrine neoplasms (previously mixed acinar-neuroendocrine tumor/MANEC)

The term "mixed neuroendocrine-nonneuroendocrine neoplasms" replaces in the fifth edition of the WHO Classification of 2019 the former term "mixed acinar-neuroendocrine tumor (MANEC)." Mixed neuroendocrine-nonneuroendocrine neoplasm includes a number of neoplasms in the pancreas with mixed differentiation, such as ductal-neuroendocrine carcinomas and some mixed-acinar-neuroendocrine carcinomas.[19] Mixed neuroendocrine-nonneuroendocrine neoplasms of the pancreas comprise the histological and immunohistochemical features of ACC and neuroendocrine tumor.[63] For this reason, the disease is listed here, although PanNENs are not discussed further in this work. These tumors arise from oncogenic proliferation of both endocrine and exocrine components. Acinar cell carcinomas may exhibit expression of neuroendocrine markers[64]; however, when neuroendocrine cells comprise at least 30% of the tumor burden, the tumors can be described as a distinct entity: MANEC.[65] To date, 44 cases of MANEC have been reported in the literature. The occurrence of metastatic disease appears to be high, affecting 20 of 44 patients, with the liver being the commonest metastatic site.[66] In a study of 45 ACCs, in addition to 38 pure ACCs, 6 were mixed acinar-endocrine carcinomas, and 1 was mixed acinar-ductal carcinoma.[56] Mixed adenoneuroendocrine carcinoma has also been demonstrated to be more aggressive compared with PanNENs[67] [Figure 5].

Rare histological subtypes of adenocarcinoma

Morphologically distinct but related entities of PDAC include adenosquamous carcinoma, undifferentiated carcinoma, and undifferentiated carcinoma with osteoclastic giant cells. Unrelated carcinomas of ductal origin comprise colloid carcinoma and medullary carcinoma. Even rarer subtypes are signet-ring cell carcinoma, hepatoid carcinoma, and oncocytic carcinoma.[68] Table 4 summarizes characteristics of the rare subtypes of pancreatic adenocarcinoma.

Squamous/Adenosquamous carcinoma

Primary squamous cell carcinoma (SCC) of the pancreas is rare. Of 114,000 cases of nonmetastatic pancreatic carcinoma in the National Cancer Database, 0.8% corresponded to adenosquamous carcinoma and 0.16% to pure squamous carcinoma.[70] Normally, squamous epithelium is not present in the pancreas. Nevertheless, squamous metaplasia in the pancreas has been reported in an autopsy study. These were up to 16.4% of cases with squamous metaplasia in which pancreatic cancer was not present.[70,76] Squamous metaplasia was found in chronic pancreatitis and after stent placement.[77,78] Therefore, it has been speculated that chronic inflammation in the pancreas is a possible mechanism for the development of SCC.[79,80]

Imaging

Intrapancreatic metastasis of SCC elsewhere should always be excluded. The appearance on imaging is similar to PDAC.[79] Hypodense mass on CT is described.[81] Pancreatic duct dilatation, corresponding atrophy of the parenchyma, and bile duct stenosis have also been

Table 4

Histological subtypes of adenocarcinoma according to the WHO classification 2019.[19]

Tumor	Characteristics	Prognosis
Adenosquamous carcinoma and SCC	Squamous differentiation is rare in pancreatic carcinomas, usually occurring in the setting of a common ductal adenocarcinoma. Pure SCC of the pancreas is extremely rare; a primary tumor in other organs should be excluded. <1.3% of exocrine pancreatic cancer[19]	Median overall survival 4 mo, significantly higher in patients who underwent surgical resection of the primary tumor (17 *vs.* 4 mo, $P < 0.001$)[69] MS = 6.8 mo without surgery *vs.* 21.3 mo with surgery, $P < 0.001$[70]
Colloid carcinoma	Neoplastic epithelium is in extracellular mucin pools	Better prognosis than ductal adenocarcinomas, 5-y survival rate over 55%[19]
Hepatoid carcinoma	>50% of the neoplasm presents with hepatocellular differentiation 4 histological subtypes[71]: • Pure HCC-like morphology • Neuroendocrine differentiation • True glandular differentiation • Acinar cell differentiation Extremely rare in pancreas Metastatic hepatocellular carcinoma should be excluded.	Overall, 1-y survival rate 71.1% and 5-y 40.4%, with a median survival of 13.0 mo[72]
Medullary carcinoma	Poorly differentiated carcinomas, more common in the ampulla and duodenum and uncommon in the pancreas In the setting of Lynch syndrome	Somewhat better than for those with conventional ductal adenocarcinomas[19]
Invasive micropapillary carcinoma	Most commonly a focal finding, occurring in <5% of pancreatobiliary adenocarcinomas	Become more aggressive[19,73]
Signet-ring cell (poorly cohesive cell) carcinoma	Extremely rare A primary tumor in other organs (especially stomach and breast) should be excluded.	Extremely poor[19] Lower overall 5-y survival rate than pancreatic adenocarcinoma (4%)[74]
Undifferentiated carcinoma Three morphologic patterns: • Anaplastic undifferentiated carcinomas • Sarcomatoid undifferentiated carcinomas • Carcinosarcomas	Extremely rare and extremely malignant. The disease is histologically characterized by a mixture of carcinomatous and sarcomatous components[75]	Extremely poor, mean survival 6 mo[75]
Undifferentiated carcinoma with osteoclast-like giant cells	Mostly in the pancreas but rarely also in the bile ducts and other organs, 3 cell types: • Nonneoplastic osteoclast-like multinucleated giant cells • Mononuclear histiocytic component • Neoplastic mononuclear cell component	The prognosis seems to be better. Unpredictable biological behavior, long-term survival seems possible[19]

described for pure squamous carcinoma.[79] Central necrosis[82] and annular enhancement[83] have been reported casuistically.

Treatment

The prognosis is even worse than that of PDAC[69,84] [Figure 6].

Pancreatic osteoclast-like giant cell carcinoma

Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGCs) is an extremely rare occurrence, accounting for less than 1% of all pancreatic malignancies, being considered a variant of PDAC.[85] Pancreatic UC-OGCs are more commonly found in old patients, with an average age at diagnosis of 63 years, with a female predominance.[86] The symptoms mostly consist of upper abdominal pain and unintentional weight loss; in rare instances, anemia and jaundice have been reported.[87] These tumors typically present as large masses, often found to be unresectable at diagnosis,[88] mostly located in the pancreatic body and tail.[89] However, local invasion and lymph node or distant metastases are not common findings.[90]

Imaging

On cross-sectional imaging, they tend to mimic typical PDAC, except for being usually larger at diagnosis, and for showing a tendency to display a slight peripheral enhancement in the arterial phase, and continuous enhancement on delayed venous phases.[86] On US examinations, these tumors usually appear with a markedly heterogeneous echotexture with well-demarcated hyperechoic and hypoechoic regions, representing focal hemorrhage and necrosis areas, in contrast with other PDAC cases that tend to be more uniformly hypoechoic.[91]

Undifferentiated carcinoma with osteoclast-like giant cell histologically resembles a giant cell bone tumor, containing 2 different types of cells: osteoclastic-like multinucleated nonmalignant cells, interspersed with mononuclear malignant cells.[92] In a retrospective report of 15 cases, EUS-FNA was able to correctly diagnose these

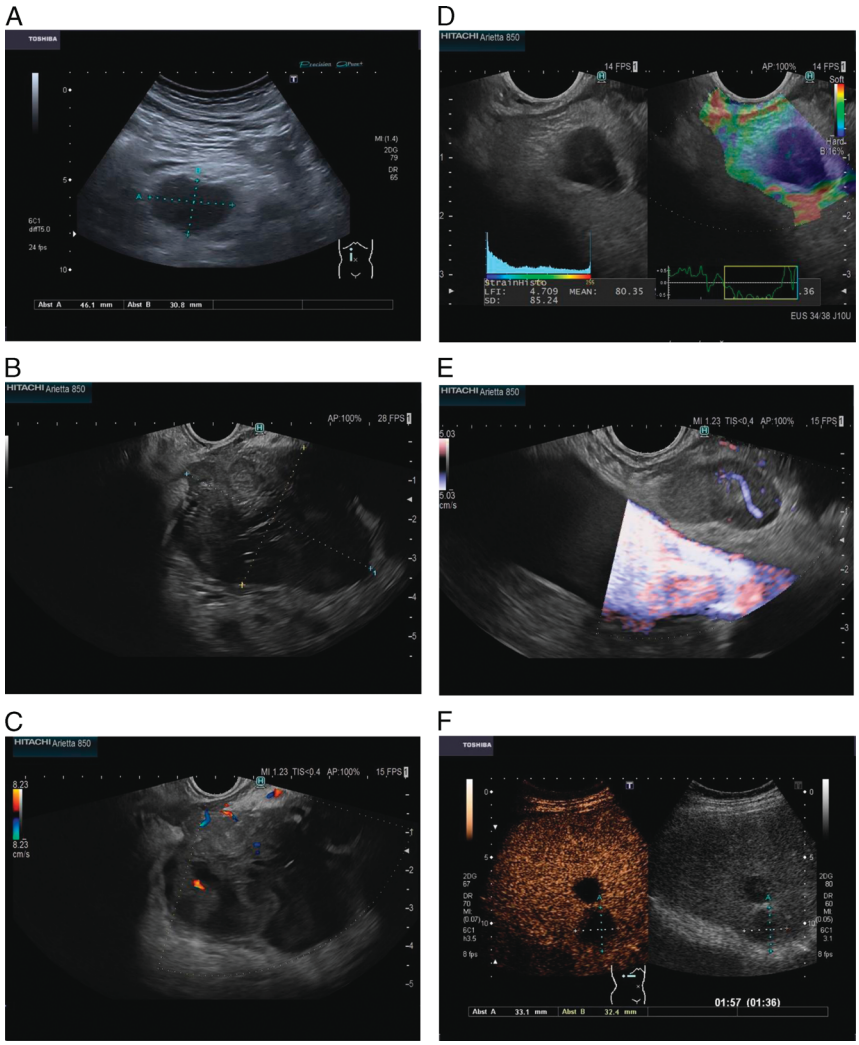

Figure 6. Squamous cell carcinoma. A 64-y-old man, upper abdominal discomfort, no jaundice. Transabdominal US showed a 46 × 30-mm, smooth-bordered, hypoechoic, heterogeneous lesion in the pancreatic head. On EUS, the lesion was smooth-bordered, hypoechoic, and heterogeneous (B); few macrovessels were visible on color Doppler imaging (C). Paraduodenal, a 24 × 12-mm lymph node presented stiff on strain elastography (D) and with visible central vessel on color Doppler imaging (E). Multiple hypoechoic round lesions with hyperechoic rim were found in the liver (not shown). On CEUS of the liver, these nodules were hypoenhanced in the portal venous and late phases and were assigned as metastases (E). EUS-guided sampling was performed from the suspicious lymph node and the pancreatic head lesion. Cytology and histology revealed moderately differentiated SCC in both localizations.

types of tumors preoperatively in only 6 cases (40%), thus highlighting the need for histopathological, rather than cytopathological, sample acquisition for diagnosis.[93]

Treatment

Surgical resection is to this day considered the first line of treatment in resectable cases. Because of the rarity of UC-OGCs, there are insufficient data on prognostic factors in these patients. Limited data, however, suggest a slightly better prognosis than typical PDAC[92] [Figures 7 and 8].

Sarcomatoid carcinoma (adenocarcinosarcoma)

Sarcomatoid pancreatic carcinoma is an extremely rare and extremely malignant variant of pancreatic carcinoma, classified as sarcomatoid undifferentiated carcinoma according to the WHO classification.[20] Sarcomatoid carcinoma has both epithelial and mesenchymal features. The disease is histologically characterized by a mixture of carcinomatous and sarcomatous components.[94] Adenocarcinosarcoma is also reported in the literature[95] with a complex of both carcinomatous and sarcomatous components.[96] It can be assumed that it is the same entity.

Since the first description in 1951,[97] approximately 40 cases have been reported in the literature.[98] Of these, 24 cases were researched by Lim et al.[75] Middle-aged and older patients were affected. Clinical findings were abdominal pain, weight loss, jaundice in some, and incidental findings in others. The tumors occurred in all areas of the pancreas. The majority of the tumors appeared as contrast-enhanced cystic solid masses on imaging. Hyperdense nodules were described in detail. Dilatation of the pancreatic duct was common.[75,94]

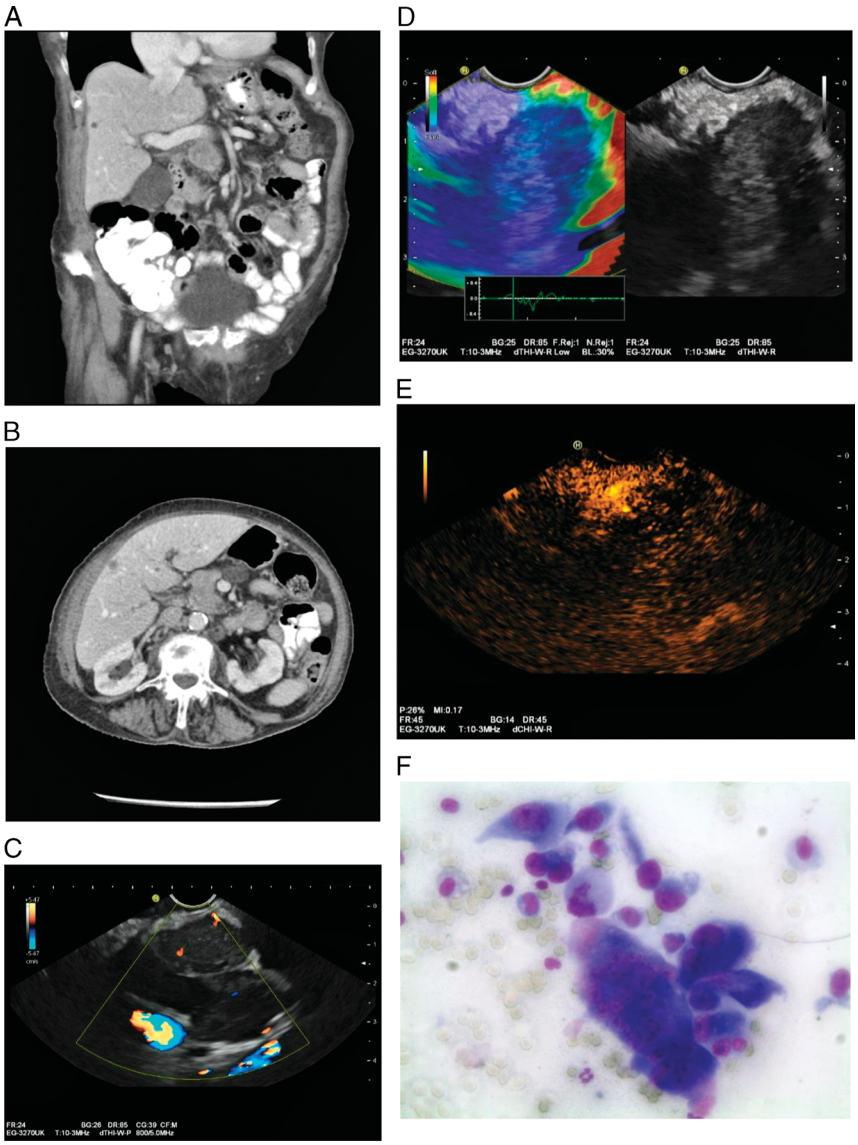

Figure 7. Osteoclast-like adenocarcinoma of the pancreas. Tumor in the pancreatic head on CT on sagittal reconstruction (A) and transversal reconstruction (B). On EUS, the tumor appears well-delineated and in 2 parts (what is down to the scanner's position and not to the tumor itself). The tubular structure coming from the lower bit of the tumor is the massively enlarged pancreatic duct (C). The elastographic image of the tumor has a blue color coding—so the tissue is harder than the tissue in the environment (D). In CH-EUS (Contrast-Harmonic EUS), the tumor is hypoenhanced (E). Hypoenhancement is a typical feature of PDACs. Cytology resulting from an endosonographic FNA (F): the osteoclast-like tumor cell is displayed in the middle and very distinctive because of the multiple cell cores within the massively enlarged cell (PD Dr Hocke, Meiningen). Image source of CT angiogram: Dr H.-J. Hald, Helios Hospital Meiningen, Radiology.

Imaging

Lim et al.[75] reported a multilobulated lesion with mural nodules and septa in enhanced CT, eccentric mural thickening, and calcifications. The pancreatic duct at the pancreatic tail was dilated with parenchyma atrophy. This would typically be interpreted as a mucinous cystic neoplasm. In the short term, the solid portions increased very rapidly. The tumor showed low signal intensity on T1 weighting and heterogeneous intermediate high signal intensity on T2 weighting. Furthermore, there was diffusion restriction and enhancement of the peripheral rim in the arterial phase and progressive enhancement on venous- and delayed-phase images.[75] Compared with cystic solid adenocarcinoma, sarcomatoid carcinoma has more vascularized parts.[75,99]

Treatment

Therapy of choice is radical surgical resection, if possible. The prognosis is poor. In the review by Lim et al.,[75] the mean survival time was approximately 6 months. However, a long-term survival of 10 years has also been reported.[94] Table 5 describes features of the rare subtypes of pancreatic adenocarcinoma on imaging.

Pancreatoblastoma

Pancreatoblastoma is a very rare tumor that originates from pluripotent pancreatic stem cells and mostly affects children up to the age of 10 years, mostly boys.[103,104] In a meta-analysis, pancreatoblastoma was the second most common childhood pancreatic tumor after

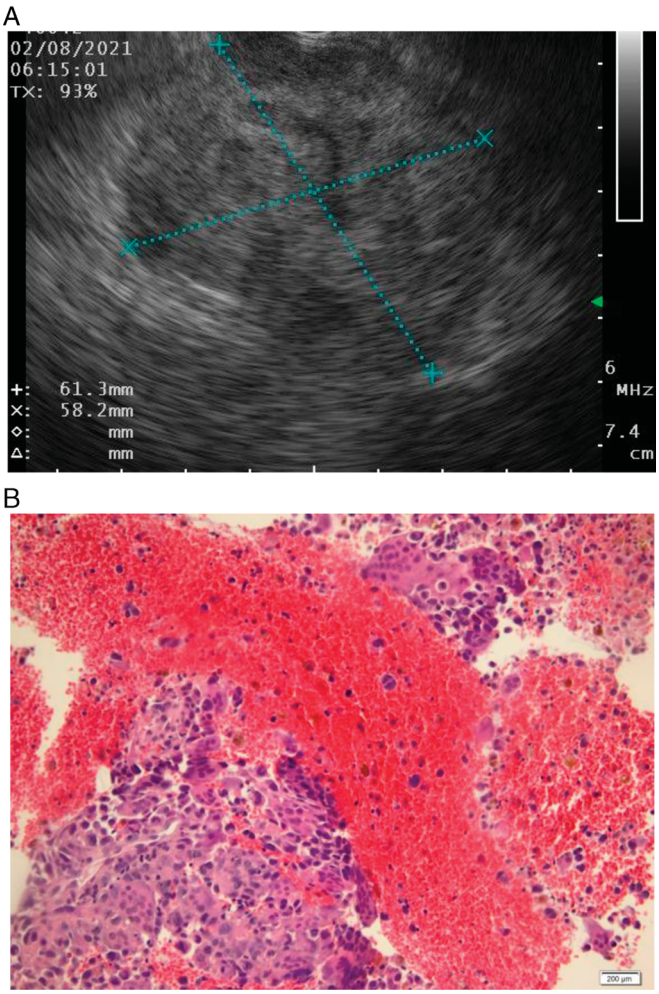

Figure 8. Pancreatic osteoclast-like giant cell carcinoma. EUS evaluation found a large inhomogeneous mass determining splenic vein thrombosis (A). EUS fine-needle biopsy was performed using a 22-gauge Acquire needle (Acquire™ Endoscopic Ultrasound Fine Needle Biopsy (FNB) Device, Boston Scientific corporation, Marlborough, Massachusetts, United States); the smears showed multiple giant cells with many clustered nuclei and prominent nucleoli, along with mononucleated and highly atypical tumor cells, consistent with osteoclastic-like giant cell pancreatic carcinoma. Courtesy of Cristiana Popp, MD, Department of Pathology, Colentina Clinical Hospital, Bucharest (B).

solid pseudopapillary neoplasia at 16.6%.[104] Very rarely, older children or adults may also develop the disease.[105,106] Up to 50% of children also suffer from Beckwith-Wiedemann syndrome (exomphalos macroglossia gigantism syndrome).[103,107] A certain association with familial polyposis coli has been described. Pancreatoblastomas are acinar neoplasms.[103] The tumors are usually large at diagnosis (5–20 cm).[104] They are soft, usually completely or partially encapsulated, and circumscribed.[103,108] Pancreatoblastoma is mostly located at the head (42%) of the pancreas, but also at the body and tail.[104] Among the tumor markers, AFP may be elevated in pediatric patients,[103,104] but not in adults in a study with a limited number of patients.[108] As the tumor is soft, localization to the head of the pancreas does not usually lead to occlusive jaundice. Pancreatoblastomas often compress the surrounding organs without invasion or local invasion, and vascular invasion is infrequent.[103] The pancreatic duct is rarely compressed.[108] Most patients are not symptomatic. Symptoms may include abdominal pain, weight loss, loss of appetite, nausea, diarrhea, and fatigue.[104] Large abdominal masses are diagnosed on imaging. The tumors are mostly lobulated and contain fibrous bands. They may contain varying degrees of hemorrhages, which present as cystic portions. In patients with Beckwith-Wiedemann syndrome, the tumors are usually predominantly cystic. If the tumor grows locally invasive, the margins are poorly circumscribed, and the tumor can infiltrate surrounding structures. At initial diagnosis, up to 35% metastases are described, which are liver and tumor nodes in the first place.[103]

Imaging

Ultrasound is usually the first imaging and is complemented by CT and MRI for further differentiation and treatment decisions. The tumors are large and heterogeneous with mixed echogenicity and lobulated solid and cystic parts. Predominantly cystic tumors appear more hypoechoic with hyperechoic septations. Calcification is not uncommon.[103,109,110] Pancreatoblastoma has been described as both hypervascular[111] and hypovascular.[108]

Li et al.[105] described a pancreatoblastoma in an adult female patient in CEUS as isoenhanced in the arterial phase with slightly more rapid loss of intensity than the surrounding parenchyma in the late phase. Similar to the solid pseudopapillary tumor, the tumor capsule is hyperenhanced. The liver metastasis of pancreatoblastoma was described as hyperenhanced in the arterial phase with hypoenhancement in the portal-venous and late phases. Corresponding quantifications are shown in the time-intensity curve. Histology by US-guided sampling was not immediately conclusive because of necroses. A neuroendocrine neoplasm or a solid pseudopapillary neoplasm remained the suspected diagnoses.[105] Other authors also confirm that the preoperative histological assignment of pancreatoblastoma in adults is difficult as a result of the heterogeneous, variable cellular differentiation and the atypical clinical and imaging features. Pancreatoblastoma should be included in the differential diagnoses when there is a large tumor of the pancreas with both cystic and solid portions.[110] It is important to distinguish pancreatoblastomas from morphological mimics such as ACCs, SPNs, and PanNENs.[112] On MRI, T1-weighted imaging shows a well-circumscribed mass with low to moderate signal intensity; in T2-weighted imaging, necrotic and hemorrhagic components appear with high signal intensity. Magnetic resonance imaging is suitable for visualization of the tumor capsule; the capsule shows signals of medium intensity on T1WI and weak signals on T2WI.[105] EUS can be used to characterize the tumor, describe the vascular relations, and assess local lymph nodes. Tissue collection is performed by means of EUS-guided sampling.

Treatment

Pancreatoblastoma should be completely resected surgically. In case of locally invasive growth or metastases, neoadjuvant therapy with PLADO (cisplatin and doxorubicin) is given for 4 to 6 cycles.[113] Fifty percent to 73% of tumors have a relevant response.[103,114] Patients with an intermediate grade showed a better response to preoperative chemotherapy based on PLADO or ICE (etoposide, ifosfamide, and carboplatin) regimens.[115] Adjuvant therapy is used for incomplete resection or relapse, but the effects are less convincing.[113] Surgical resection is also most important in the case of recurrence or liver metastasis.[103,114]

Table 5

Subtypes of pancreatic adenocarcinoma and features in imaging.

Tumor	Features on imaging
Adenosquamous carcinoma and SCC	Central necrosis and cystic degeneration[82]; Ring enhancement[83] computed tomography (CT): hypodense mass[81] Pancreatic duct dilatation and corresponding parenchymal atrophy[79] EUS: solid, hypoechoic, not well-defined lesion, cytological specimens demonstrated components of both squamous carcinoma and adenocarcinoma[100] EUS-FNA with cytology and immunohistochemistry[81]
Colloid carcinoma	Large and well demarcated, most in intestinal-type intraductal papillary mucinous neoplasms[19]
Hepatoid carcinoma	Tumor capsule,[101] "steatohepatitis-like" areas[101] Tumor sizes from 0.5 to 11.0 cm with median of 6.0 cm[72] AFP abnormally elevated in 60%[72] Heterogeneous hypodense nodule on unenhanced CT, well-enhanced tumor with a rim encapsulation on contrast-enhanced CT, signal drop (fat) on T1 opposed phase MRI image, isointense on T2 weighted MRI image[72] "Sausage-shaped," isointense to hypointense in the fat-suppressed T1WI; isointense to hyperintense in the fat-suppressed T2WI; central necrosis contrast enhanced delayed-phase and mixed signal intensity on diffusion-weighted imaging; hyperintense rim that demonstrated delayed enhancement and a capsule appearance[102]
Medullary carcinoma	The periphery is circumscribed and compresses rather than infiltrates the surrounding fibrous stroma. Tumor-associated inflammatory infiltrates are typical.[19]
Invasive micropapillary carcinoma (IMPC)	Pure IMPC subtype is extremely rare High propensity for lymph node metastasis[73] Hypodense on unenhanced CT, MRI: high signal intensity on T2WI, iso signal intensity on T1WI.[73]
Signet-ring cell (poorly cohesive cell) carcinoma	CT: hypoattenuating mass, bile duct and pancreatic duct stenosis[74] No data
Pancreatic osteoclast-like giant cell carcinoma	Large masses on cross sectional imaging, initially larger than PDAC[88] US: markedly heterogeneous echotexture with well demarcated hyperechoic and hypoechoic regions, representing focal hemorrhage and necrosis areas, more uniformly hypoechoic[91] Contrast-enhanced imaging: tendency to a slight peripheral enhancement in the arterial phase and continuous enhancement on delayed venous phases[86] EUS-FNA with cytology: only 40% of cases with correct diagnoses.[93] Need for histology particle sampling[93]
Sarcomatoid carcinoma/ adenocarcinosarcoma	Multilobulated lesion, eccentric mural thickening, calcifications,[75] dilated pancreatic duct, atrophy of parenchyma[94] Contrast-enhanced cystic solid masses[75] contrast-enhanced CT: mural nodules and septa,[75] MRI: low signal intensity on T1 weighting and heterogeneous intermediate high signal intensity on T2 weighting[75]

Conclusion

Not all malignant pancreatic tumors represent ductal adenocarcinoma, and not all well-vascularized tumors represent neuroendocrine tumors of the pancreas. Ultrasound and EUS with contrast-enhanced techniques and EUS-guided sampling are powerful diagnostic methods to obtain a variety of individual information parameters for the diagnosis of rare pancreatic tumors. In the research of the literature of rare pancreatic tumors described here, it was found that US was mostly used just to make a diagnosis of a pancreatic mass without further characterization. Only for solid pseudopapillary neoplasia, very good descriptions exist for the appearance on US, EUS, and CEUS. For other tumor entities reported here, there are only a few reports. What typical features can be identified? Solid pseudopapillary neoplasm and ACC show a pseudotumor capsule that is contrast enhanced. Both tumors may also show calcifications. Solid pseudopapillary neoplasm tends to affect younger women; ACC tends to affect older men. Solid pseudopapillary neoplasm and ACC may have cystic portions. Adenosquamous carcinoma and ACC often have hemorrhagic parts. Pancreatoblastomas are often very large. Apart from SPN, there are few or no data on the contrast pattern of tumors in CEUS. However, in many rare tumors, there are only a few cases that do not allow for generalization. Using short case studies, the sonographic appearance for some of the very rare tumors could be demonstrated in the present work. In the literature reviewed, imaging was used only to visualize and describe morphology and vascularity of rare pancreatic tumors. Differentiation from ductal adenocarcinoma and neuroendocrine neoplasms based on imaging characteristics alone is not possible, so the diagnosis of the rare tumor entities is usually made histologically or cytologically. If a solid or solid-cystic pancreatic neoplasm has imaging characteristics that are not typical of ductal adenocarcinoma, cytological or histological confirmation should be sought before determining therapeutic consequences, usually by EUS-guided sampling. Comments and illustrations of the European Federation of Societies for Ultrasound in Medicine guidelines. Rare pancreatic tumors, ultrasound and contrast-enhanced ultrasound features. Malignant mesenchymal tumors. Moller et al. Endosc Ultrasound 2024 epub in advance.

Conflicts of Interest

Siyu Sun is the Editor-in-Chief of the journal, and Christoph F. Dietrich is a Co-Editor-in-Chief. Manoop S. Bhutani is a Senior Associate Editor. Christian Jenssen and Michael Hocke are Editorial Board Members. This article was subject to the journal's standard procedures, with peer review handled independently of the editors and their research groups. The authors declare that they have no financial conflict of interest with regard to the content of this report.

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