Contrast-enhanced ultrasound of pancreatic tumours

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Abstract

Indication/purpose: To review contrast-enhanced ultrasound features of the most common pancreatic tumours.

Methods: Contrast-enhanced ultrasound (CEUS) can provide distinctive features of pancreatic tumours that are reported in the present paper, providing radiologic-pathological correlations and clarifying the main differential diagnosis.

Conclusion: Contrast-enhanced ultrasound plays a well-established role in the evaluation of pancreatic tumours. When possible, CEUS should be always performed after the initial US diagnosis, in order to improve the accuracy of the first line examination.

Keywords: contrast-enhanced ultrasound, pancreas, tumours.

Introduction

Ultrasonography (US) is a widely available, relatively inexpensive and easy to perform imaging method; as such, it is often the first imaging modality for the evaluation of pancreatic diseases. Contrast-enhanced ultrasonography (CEUS) leads to considerable improvements in US diagnostic capabilities, due to its high contrast and spatial resolution and the possibility of a dynamic evaluation of the enhancement. As reported in literature, CEUS should be performed when possible immediately after the detection of a pancreatic lesion, thus providing a significant improvement in the accuracy of the first line examination.[1,2]

The 2011 European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines[3] recommend the use of CEUS for focal pancreatic lesions identified with US in order to improve:

1 Characterisation of ductal adenocarcinoma (recommendation level: A;1b)
2 Differential diagnosis between pseudocysts and cystic tumours (recommendation level: A;1b)
3 Differentiation of vascular (solid) from avascular (liquid/necrotic) components (recommendation level: A;1b)
4 Definition of dimensions and margins, including relationship with adjacent vessels (recommendation level: B;2b)
5 Distinction between solid and cystic lesions (recommendation level: C;5)
6 Diagnosis in indeterminate cases at CT (vascularisation of solid pancreatic lesions; Differential diagnosis between pseudocysts and pancreatic cystic tumours, especially mucinous cystic tumour) (recommendation level: C;5).

This paper reviews the main pancreatic oncologic applications of CEUS, describing distinctive features of pancreatic tumours, providing radiologic-pathological correlations, and reporting the main differential diagnosis.

Contrast-enhanced ultrasound of the pancreas: physical basis and technical background

The use of US contrast agents has been approved in several countries, but the Food and Drug Administration in the United States has not yet approved their application for non-cardiac use. US contrast agents consist of microbubbles with a diameter comprised between 2 and 6 microns, a shell of biocompatible materials (proteins, lipids or biopolymers) and a filling gas, such as air or a gas with high molecular weight and low solubility, as perfluorocarbon or sulfur hexafluoride.

The small diameter of microbubbles (< 7 microns) allows their passage through the pulmonary microcircle; microbubbles are exhaled 10–15 minutes after injection, while the kidney and the liver metabolise the components of the shell.

Shell and gas influence the time of circulation and the acoustic behavior of microbubbles. The shell has a thickness of 10–200 nm and a high elasticity: this allows the passage of the microbubbles through the pulmonary capillary circle with a consequent systemic effect and a prolonged contrastographic effect. The filling gas produces a vapor concentration inside the microbubbles higher than the surrounding blood, increasing their stability in the peripheral circulation.[1,4]

Both the shell and the filling gases have been modified over the years. A stiff shell made of denatured albumin and air as filling gas characterised the first generation contrast media. The second-generation contrast media are filled by gases other than air and have a flexible shell (phospholipids) that provides more stability and

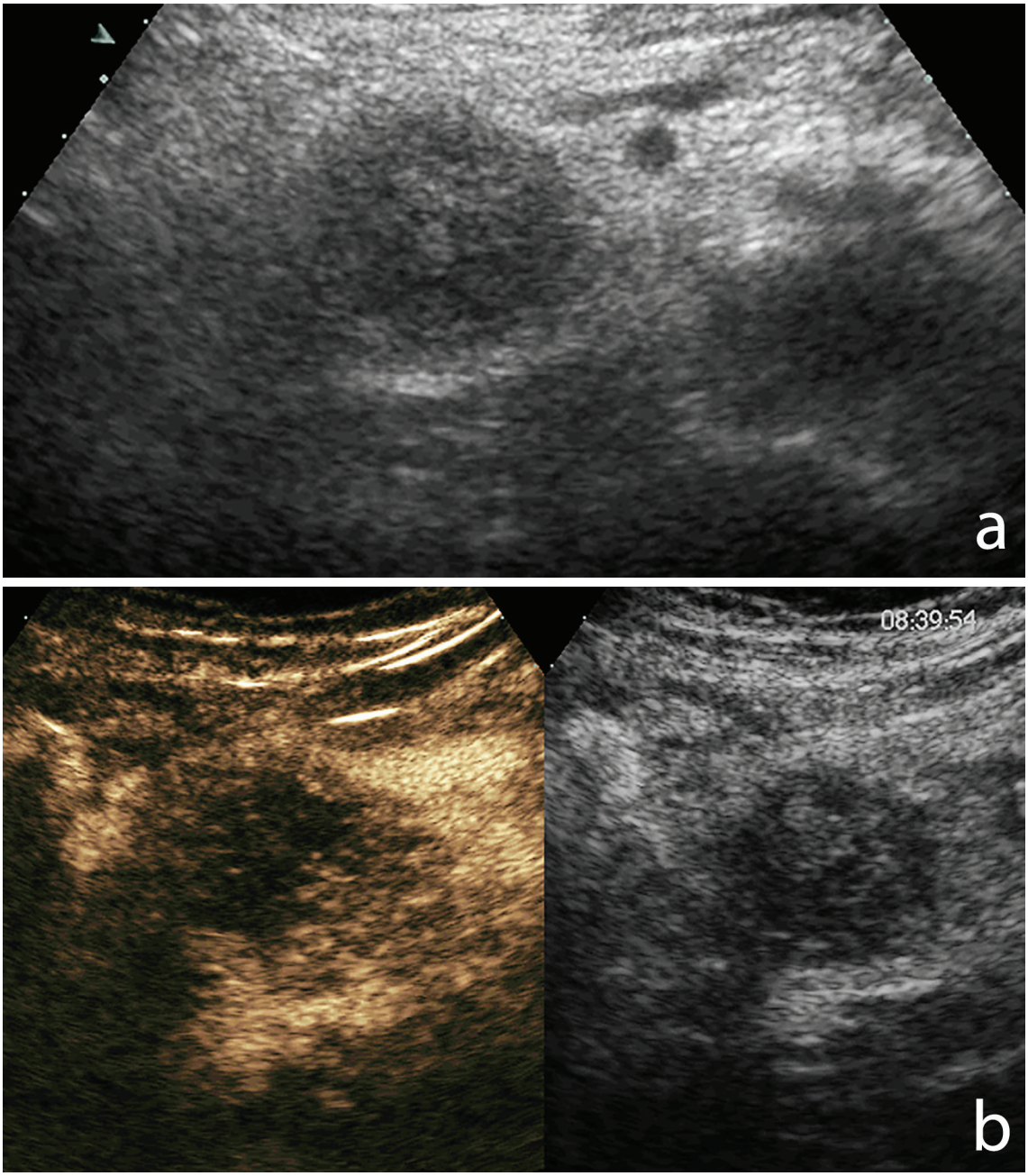

Figure 1: Ductal adenocarcinoma. (a) B-mode US examination shows a solid hypoechoic rounded lesion with ill-defined margins in the pancreatic head; (b) CEUS shows the typical markedly hypovascular pattern of ductal adenocarcinoma.

resistance; the shell allows also the prevalence of a nonlinear behavior after US insonation.

Our experience is mainly based on the use of a sulfur-hexafluoride contrast medium (Sonovue, Bracco, Milan, Italy): a 2.4 mL bolus of this second-generation microbubble contrast agent is injected intravenously, followed by a 5 mL saline flush. Other commercially available contrast media have different composition and dosage, but the effect in terms of US response is similar.

The US response of microbubbles to an ultrasound beam is complex, because gases are much more compressible than soft tissue thus, when exposed to the compression-rarefaction sequence of an ultrasonic pulse, they undergo alternate contraction and expansion; particularly, they vibrate most readily at a particular resonance frequency corresponding to the frequencies used in diagnostic ultrasound (2–10 MHz). This coincidence accounts for the extraordinary effectiveness of microbubbles as ultrasound contrast agent: they return much stronger signals than tissue reflectors having similar size such as red blood cells.[5] US insonation mainly produces nonlinear harmonic frequencies, since at low acoustic power (30–70 kPa), the degree of microbubble expansion is greater than its compression.[4]

US contrast agents have a purely intravascular distribution without interstitial phase; CEUS-specific equipments filter all the background signals, thus visualising only vascularised structures.[6] Several contrast-specific software applications have been developed for CEUS examination, even though the most used techniques are phase and amplitude modulation. Pulse inversion is the most common phase modulation technique,[7] while power modulation is a well-known amplitude modulation software application.[4] Cadence contrast pulse sequencing (CPS) is a more advanced combined phase and amplitude modulation technique.[1,8] In each case, microbubble-specific imaging with a low acoustic pressure (mechanical index < 0.2) is required for CEUS examination, so that microbubbles are not destroyed and

a continuous real time scanning is possible.

The CEUS examination of the pancreas must be performed after an accurate conventional US of the whole abdomen, in order to correctly localise the pancreatic lesion and to provide a detailed evaluation of the whole liver in order to map focal liver lesions, particularly cysts and hemangiomas, as better explained below.[6] The pancreatic examination requires the use of the same multifrequency curved array transducer (at least from 3 to 4 MHz) used for conventional US. The dual screen visualisation should be used to adequately and continuously compare B-mode and contrast enhanced images. Focus and depth should be regulated simultaneously in both images and low acoustic US pressures should be selected (mechanical index lower than 0.2). It is also possible to use high frequency bursts, which destroy the microbubbles thus allowing assessment of new microbubbles flow into the lesion vasculature.

The dynamic evaluation begins immediately after the intravenous administration of the bolus of microbubble contrast agent. Since the pancreatic blood supply is exclusively arterial, its enhancement begins almost at the same time of the aorta (from 10 to 30 seconds after contrast injection). The arterial phase is followed by the portal venous phase (from 30 to 120 seconds after injection), defined by the enhancement of the spleno-mesenteric-portal veins. Arterial and portal phases are used to characterise lesions and to assess resectability by evaluating their relations with peripancreatic vessels.[9]

The late phase begins about 120 seconds after injection and lasts for about 4 minutes, which is the mean lifetime of microbubbles; it is defined by hyperechogenicity of the hepatic veins: during this phase a complete evaluation of the liver must be performed to identify metastases, which appear hypoechoic during this phase, an extremely specific pattern for malignant liver lesions.[10,11] It must be kept in mind that cysts and hemangiomas, which are the most common focal liver lesions, may also present during the late phase; therefore a detailed pre-contrast B mode evaluation of the liver must always be performed. Sometimes, a second contrast medium administration may be helpful for thorough liver examination.

Solid pancreatic lesions

Solid pancreatic lesions mainly comprise of ductal adenocarcinoma (ADK) and neuroendocrine tumours (P-NETs); these two entities must be characterised and differentiated at imaging, because they have in most cases completely different management and prognosis.

Ductal adenocarcinoma – ADK

Epidemiology, pathology and clinical findings

Ductal adenocarcinoma (ADK) is the most common primary malignancy of the pancreas (about 80%).[12] Its incidence ranges from 1 to 10 in 100,000 people, with highest prevalence between 60 and 80 years of age. It is a highly aggressive tumour with an overall five-year survival rate < 5%.[13] About 70% of ductal adenocarcinomas arise in the pancreatic head, while 30% are located in the body/tail. In up to 95% of cases, regardless of the site, ADK is diagnosed at an advanced stage, with locally advanced (stage III) or metastatic disease (stage IV). Only 10–20% of patients are deemed resectable at diagnosis.[14] Non-resectability depends not only on the presence of metastases and/or involvement of adjacent organs, but also on the infiltration of celiac, common hepatic, and superior mesenteric arteries, as well as on circumferential extension to the superior mesenteric vein and superior mesenteric–portal vein confluence.[15]

Microscopically, ADK is composed of neoplastic tubules or glands embedded in a dense fibrous tissue with poor vascularisation. The massive stromal reaction determines the scirrhous and firm macroscopic aspect, and explains the low vascular density that leads to the radiological detection as a hypovascular mass. Macroscopically, ADK is a white-yellow mass with infiltrative, ill-defined margins and hard consistency owing to the presence of fibrosis and desmoplasia. The main pancreatic duct is often infiltrated and upstream dilated.[16]

Pancreatic head cancers generally present with jaundice because of common bile duct infiltration, associated with abdominal discomfort and weight loss; body-tail tumours usually present with nonspecific pain due to the infiltration of peri-pancreatic vessels and nervous structures, and also with newly onset diabetes. Infiltration of the pancreatic duct can cause acute or chronic pancreatitis.

CEUS

Every solid hypoechoic pancreatic lesion identified at US must be considered a ductal adenocarcinoma until otherwise proven; when possible, CEUS should immediately follow B-mode US, thus providing fast characterisation and staging of the lesion[3].

At CEUS, ADK usually presents as an ill-defined mass, showing poor enhancement during all dynamic phases; this behavior reflects the low mean vascular density of the tumour[6,17,18] (Figure 1).

As reported in the Pancreatic Multicenter Ultrasound Study (PAMUS), this hypovascular pattern is typical of ductal adenocarcinoma: among the 987 ADKs included in this study, 891 (90%) were hypovascular.[19] CEUS allows better visualisation of tumour margins as well as its relations with peripancreatic vessels (local staging – Figure 2).

In addition, CEUS improves hepatic staging, allowing a higher accuracy in the detection of metastases.[20,21] CEUS sensitivity in diagnosing pancreatic ductal adenocarcinoma does not statistically differ from that of MDCT; CEUS sensitivity seems to be higher for small and medium lesions, while MDCT sensitivity is higher for larger lesions: by combining both imaging methods a higher accuracy in diagnosing pancreatic ductal adenocarcinoma can be expected.[22] CEUS quantitative perfusion analysis of ductal adenocarcinoma of the pancreas can provide its objective characterisation: peak of enhancement and ascending curve values are significantly different between the tumour and the adjacent parenchyma;[23] this can be a potential tool to detect well-differentiated ADKs, which tends to have a different enhancement pattern other than markedly hypovascular.[24–26]

Differential diagnosis

Any solid pancreatic mass must be differentiated from ductal adenocarcinoma. The second most frequent pancreatic solid neoplasms are neuroendocrine tumours, which are usually hypervascular; moreover, associated findings as upstream main pancreatic duct and common bile duct dilation and parenchymal atrophy are less common in neuroendocrine tumours. CEUS

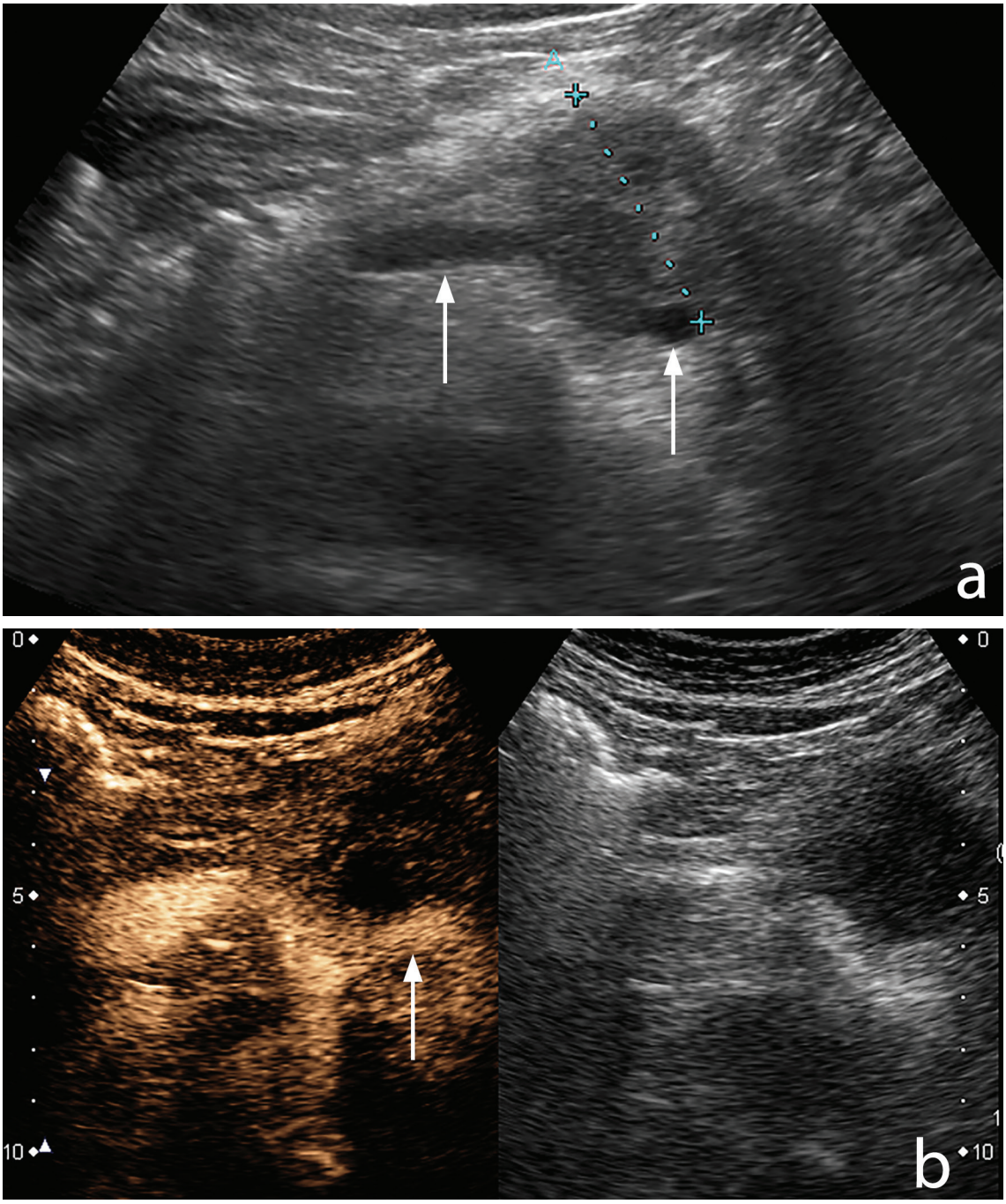

Figure 2: Ductal adenocarcinoma. (a) B-mode examination shows a solid hypoechoic mass with infiltrative margins in the pancreatic body, which seems to diffusely infiltrate the celiac trunk and its branches (arrows - non resectable lesion); (b) CEUS provides a better local staging showing the real extension of the neoplasms, which infiltrates only the splenic artery (arrow - resectable lesion).

improves the differential diagnosis between ADK and mass-forming pancreatitis: while ductal adenocarcinoma remains hypovascular during all the dynamic phases, mass-forming pancreatitis has an isovascular appearance ('parenchymographic' enhancement).[27]

Pancreatic neuroendocrine tumours – PNETs

Epidemiology, pathology and clinical findings

Pancreatic neuroendocrine tumours arise from neuroendocrine cells. They represent about 1–2% of all pancreatic neoplasms and are the second most common pancreatic solid tumours. P-NETs may cause specific symptoms related to an abnormal hormonal secretion (functioning endocrine tumours) or non-specific symptoms due to their expansive growth (nonfunctioning endocrine tumours).[1] Whether functioning or non-functioning, they are in most cases less aggressive than ductal adenocarcinoma, despite the presence of metastases at diagnosis.[28] P-NETs are usually sporadic but may also be part of hereditary syndromes as multiple endocrine neoplasia type 1, von Hippel Lindau, type 1 neurofibromatosis and tuberous sclerosis complex; sporadic P-NETs are usually solitary lesions, whereas hereditary forms tend to be multifocal.[29] Insulinomas and gastrinomas are the most common functioning P-NETs: they cause specific syndromes (hypoglycemia with hyperinsulinemia and Zollinger-Ellison syndrome, respectively), therefore they are usually diagnosed at an early stage.[30] Other functioning P-NETs such as VIPoma, glucagonoma and carcinoid are extremely rare (about 20%); in studying functioning tumours, imaging has two roles: identification and staging.[31] Nonfunctioning tumours account for about 30% of P-NETs and have a higher malignancy rate.[32] They are usually large at presentation;[31] the main aim of

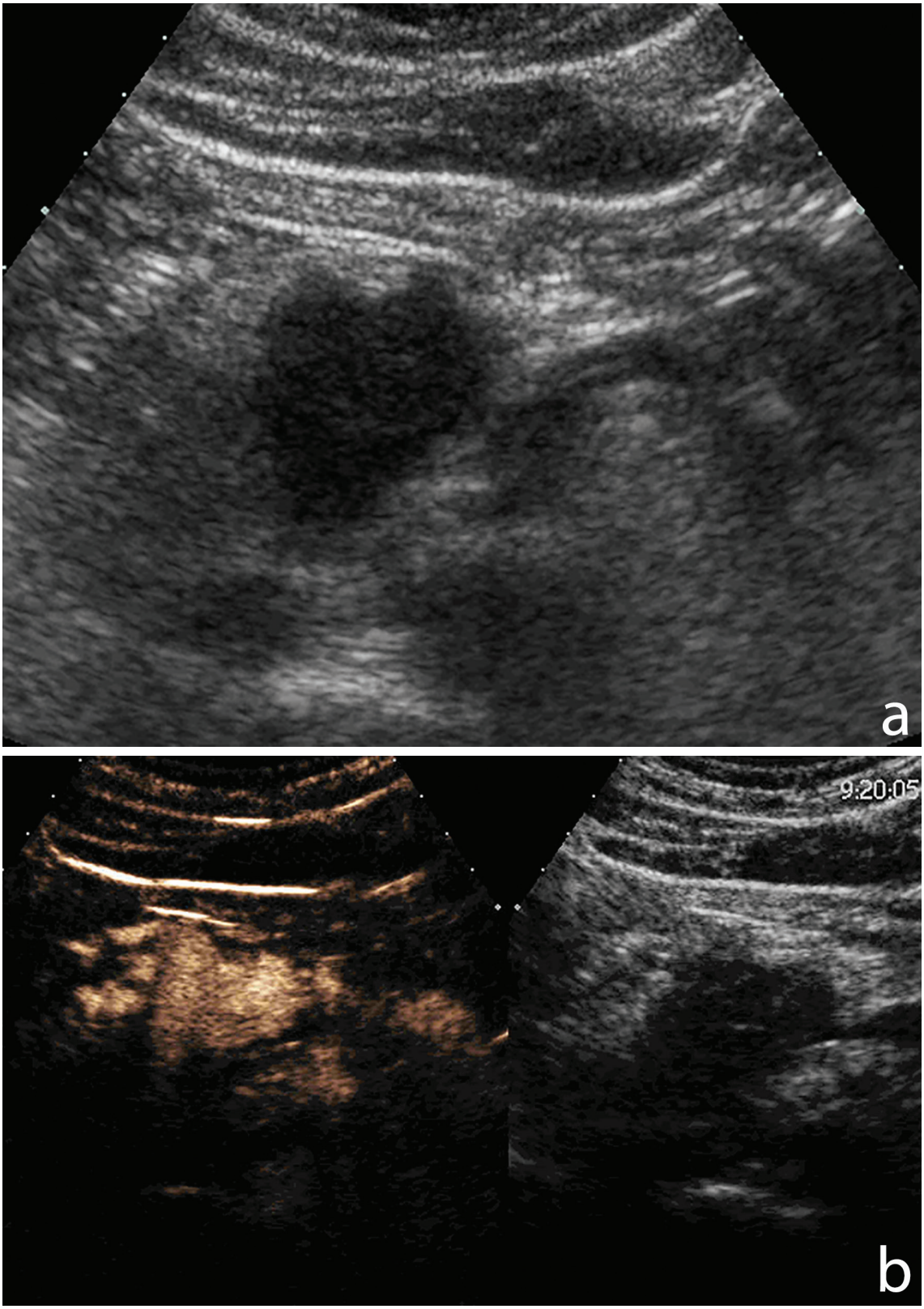

Figure 3: Pancreatic neuroendocrine tumour. (a) B-mode US examination shows a solid hypoechoic well-defined lesion in the pancreatic head; (b) CEUS shows the typical hypervascular pattern of neuroendocrine tumours.

imaging in regard to these tumours is characterisation. P-NETs have different degrees of differentiation and are classified according to the ENETS grading system, which is based on the proliferative activity of the neoplasm, into G1 (ki-67 < 2% and/or < 2 mitosis/10 CFI), G2 (ki-67 3–20% and/or 2–20 mitosis/10 CFI) and G3 (ki-67 > 20% and/or > 20 mitosis/10 CFI) tumours; G3 P-NETs are invariably malignant and should be defined neuroendocrine carcinomas (NECs).[33]

Rich microvascularisation characterises the majority of P-NETs and is responsible for their common hypervascular radiological appearance. Typically, numerous small vessels, surrounded by a variable amount of stroma, encircle the clusters of neoplastic cells.[29] Macroscopically, P-NETs are usually solid, well-circumscribed round-shaped lesions with sharp margins.

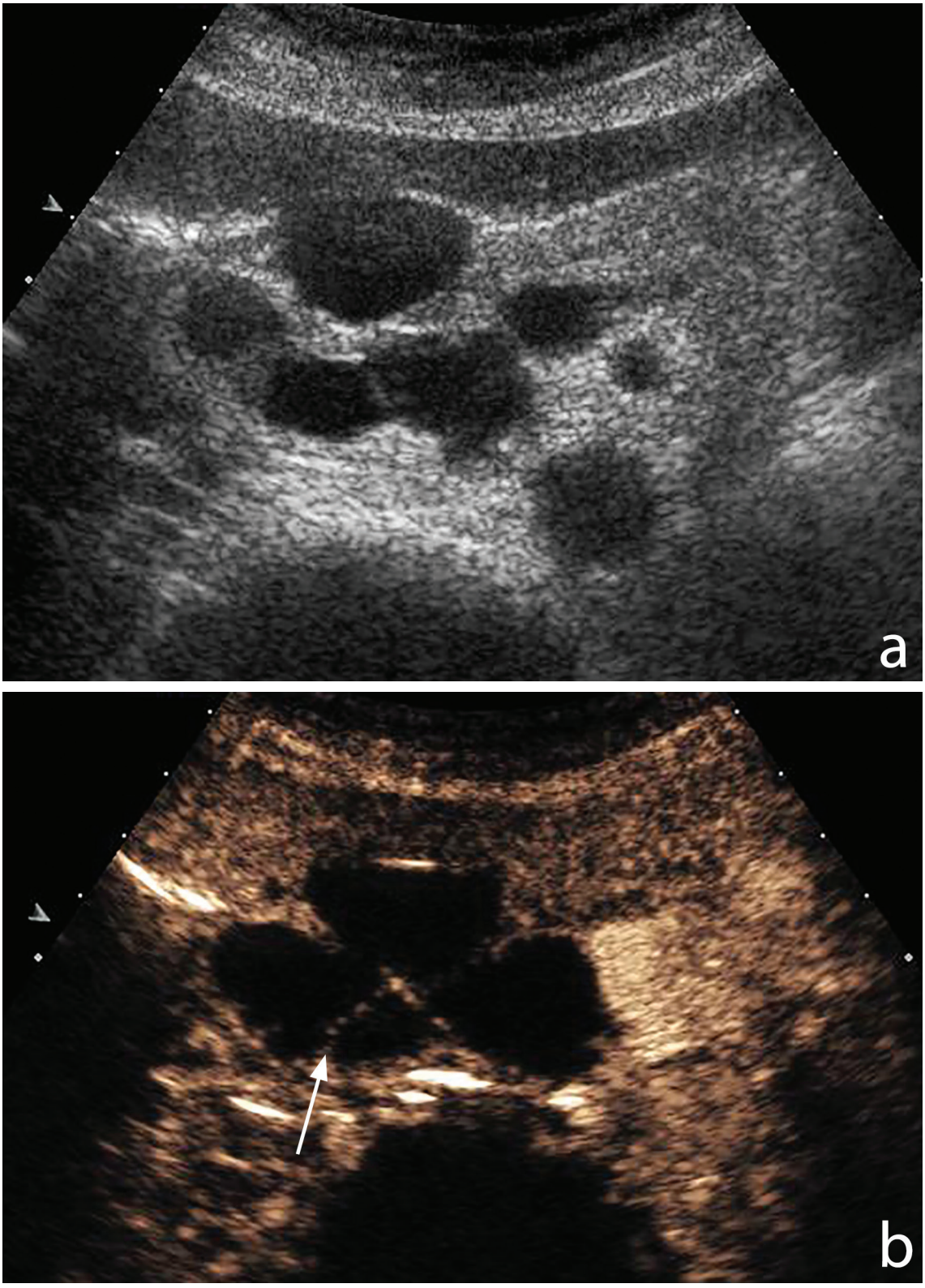

Figure 4: Serous cystadenoma. (a) B-mode US examination shows a cluster of cysts in the pancreatic head, with homogeneous anechoic content; (b) CEUS depicts the classical cloud-shaped appearance with multicystic architecture of a serous cystadenoma, with thin enhancing, centrally oriented septa (arrow).

There may be necrotic foci, especially in large masses, which appear as yellowish areas with a soft, infarct-like consistency.[34]

CEUS

Both functioning and non-functioning P-NETs usually appear as hypervascular solid masses (Figure 3).

The main pancreatic duct is usually not infiltrated and upstream dilated.[35] Larger lesions show a rapid, intense and heterogeneous enhancement during the early contrast-enhanced phase, due to the presence of avascular necrotic intralesional areas; moderate-size lesions may show a capillary blush enhancement in the early contrast-enhanced phase; then they can become hypoechoic during the late phase.[36] As with ductal adenocarcinoma, CEUS examination of P-NETs must include liver evaluation during late phase to exclude metastases.[1,36]

Differential diagnosis

The main radiologic differential diagnoses are ductal adenocarcinoma, pseudosolid serous cystadenoma, and pancreatic metastases.[37] The hypervascularity of P-NETs is fundamental to differentiate them from adenocarcinoma, which is hypovascular.[36] Extremely microcystic serous cystadenoma may have a pseudosolid aspect and appear hypervascular, owing to the homogeneous enhancement of the extremely compacted internal septa: the differentiation from neuroendocrine tumours needs MRI, which usually clearly depicts the true cystic nature of the cystadenoma on T2-weighted images.[5,38] Hypervascular pancreatic metastases usually arise from renal cell carcinoma, and may be identical to P-NETs; clinical history of a primary malignancy can help the distinction.[39] Endocrine tumours with cystic changes may show intracystic solid complex components (irregular thick wall, septa and nodules); this aspect can be also found in some other cystic pancreatic tumours as mucinous cystic neoplasms and in other solid pancreatic neoplasms with cystic component or cystic degeneration, as solid pseudopapillary tumour, adenocarcinoma, and metastases.[12,40]

Cystic pancreatic neoplasms

Cystic pancreatic lesions comprise several different tumours that range from non-surgical lesions, such as serous cystadenoma (SCA) and branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs), to surgical lesions, such as mucinous cystic neoplasms (MCNs), solid pseudopapillary tumours (SPTs), main duct and mixed IPMNs (MD- and MIX-IPMNs). Imaging therefore plays a fundamental role in their characterisation and differentiation in order to provide the best management for the patient.

Serous cystadenoma

Epidemiology, pathology and clinical findings

Serous cystadenoma (SCA) is generally diagnosed in 50–60 year-old females. It is usually solitary but can be multifocal in patients with Von-Hippel Lindau disease.[41] SCA has a benign nature, with a typical slow growth and a slow and uncommon progression to malignancy; however, because malignant change is possible, US or MRI follow-up is required.[42] The typical aspect of SCA is that of a multilocular honeycomb lesion due to the presence of multiple small cysts (< 20 mm) separated by thin centrally oriented septa and thin wall (micro-/macro-cystic SCA). SCA never communicates with the main pancreatic duct. In 15% of cases, a central scar, sometimes calcified, is present.[43] Less common variants of SCA are the extremely microcystic (pseudosolid), the macrocystic and the unilocular. Cysts have a "clear watery" content and are lined by cuboidal monostratified glycogen-rich epithelial cells without atypia. Septa have an abundant subepithelial microvessels network.[44]

CEUS

The typical 'cloud-shaped' morphology of SCA is usually depictable at B-mode US; nevertheless, CEUS can improve the US characterisation of SCA, showing enhancement of the internal septa and of the central scar, when present[5] (Figure 4).

Differential diagnosis

Extremely microcystic SCAs may mimic at CEUS a solid hypervascular lesion such as a NET: in this case MRI can provide the correct diagnosis.[5,38]

SCA never communicates with the pancreatic ductal system: this finding, not visible at US, is crucial for the differential diagnosis in respect to branch duct intraductal papillary mucinous neoplasms (BD-IPMNs) that may have a similar appearance.[45] The macrocystic variant must be differentiated from mucinous cystic neoplasms, side-branch and mixed type IPMNs and solid tumours with cystic degeneration.[46] Mucinous cystic neoplasms are more common among females and are usually located in the pancreatic body/tail; they usually present an internal complex architecture with thick enhancing septa and mural nodules.[47] Unilocular SCA must be differentiated from pseudocysts and IPMNs.[46] A clinical history of pancreatitis is crucial for the differential diagnosis with pseudocyst; this diagnosis is reinforced by the absence of internal or parietal enhancement.[46]

Mucinous cystic neoplasms

Epidemiology, pathology and clinical findings

Mucinous cystic neoplasms (MCNs) represent about 10% of all cystic pancreatic lesions.[48] They have female sex predilection (F:M = 9:1) and generally occur at 50–60 years of age.[49] MCNs encompass lesions with benign (mucinous cystadenoma – MCA) or malignant (mucinous cystadenocarcinoma) biological behaviour; as MCNs are potentially malignant they always require surgical resection, even if asymptomatic, therefore differential diagnosis between mucinous and non-mucinous cystic pancreatic lesions is mandatory. MCNs are thick-walled, uni- or multilocular tumours with a dense content (mucin); they usually present as a single rounded mass with a smooth surface, a fibrous pseudocapsule of variable thickness and calcifications. Unilocular tumours usually have a smooth and glossy internal surface. When dysepithelised, the internal surface is irregular and brownish. In high-grade neoplasms papillary vegetations are often recognised. MCNs with an associated invasive carcinoma are generally larger and multilocular, with a higher structural disarrangement with thick septa and mural nodules.[50] The presence of the distinctive ovarian-like stroma is required for the correct diagnosis and represents a fundamental finding especially in case of cysts without epithelial lining.[50]

CEUS

Some lesions appear grossly round and unilocular without septa because, especially at B-mode US, the mucinous content may hide septa and parietal nodules, which are fundamental for the correct diagnosis (Figure 5).

Given that intratumoural septa and nodules have blood vessels, blood-pool microbubbles flow within these portions, producing their typical vascular appearance at CEUS; moreover, since at CEUS all the echogenic avascular intracystic content (i.e. mucine, clots or debris) are not visualised, a higher diagnostic accuracy in comparison to US is obtained.[19,51,52] Frankly malignant mucinous cystic neoplasms usually present a more complex internal architecture (Figure 6).

Differential diagnosis

The differential diagnosis mainly includes unilocular serous cystadenoma and pseudocysts. MCNs usually arise in pancreatic body/tail of middle-aged women[47] and, as serous cystadenomas, never communicate with the pancreatic ductal system. The

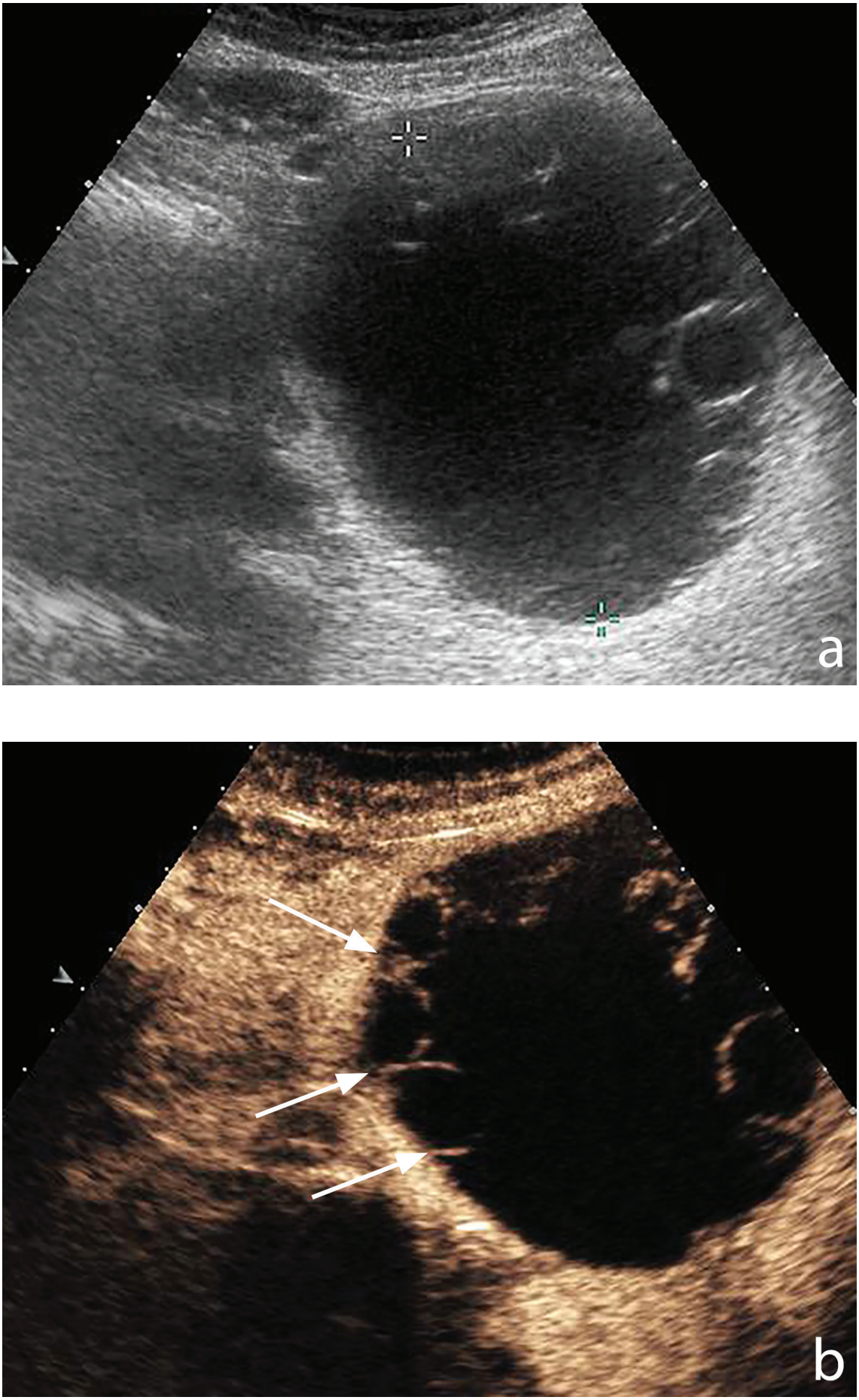

Figure 5: Mucinous cystadenoma. (a) B-mode US examination shows a rounded, well-defined lesion in the pancreatic tail, with thick wall, slightly echoic content and internal echoic septa; (b) CEUS shows the enhancement of multiple vascularised septa (some of those were not visible at B-mode examination – arrows).

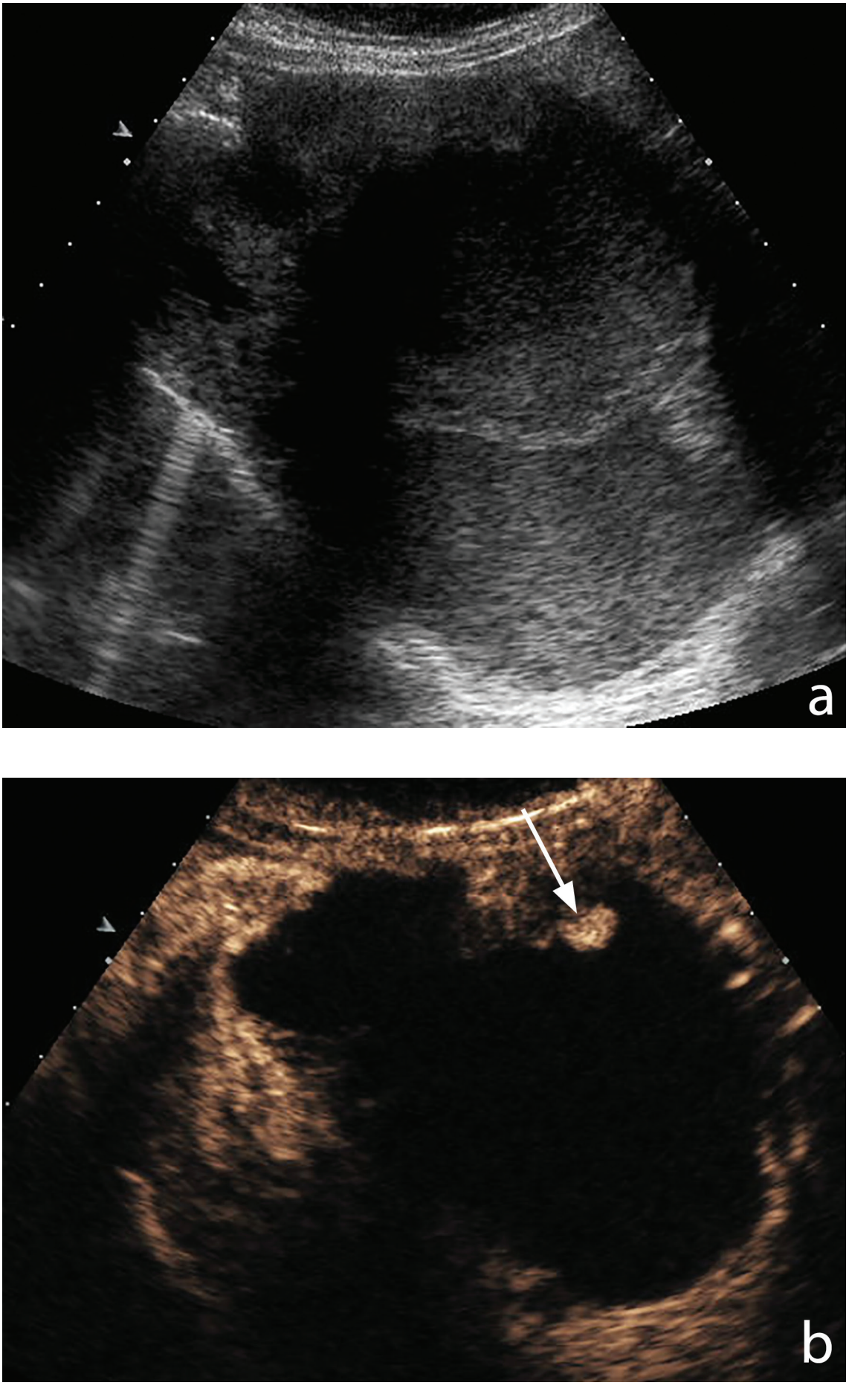

Figure 6: Mucinous cystadenocarcinoma. (a) B-mode US examination shows a huge rounded lesion in the pancreatic tail, with echoic content and diffuse thickening of its ventral wall; (b) CEUS shows the enhancement of the viable tumoural portions, as a small mural nodule (arrow).

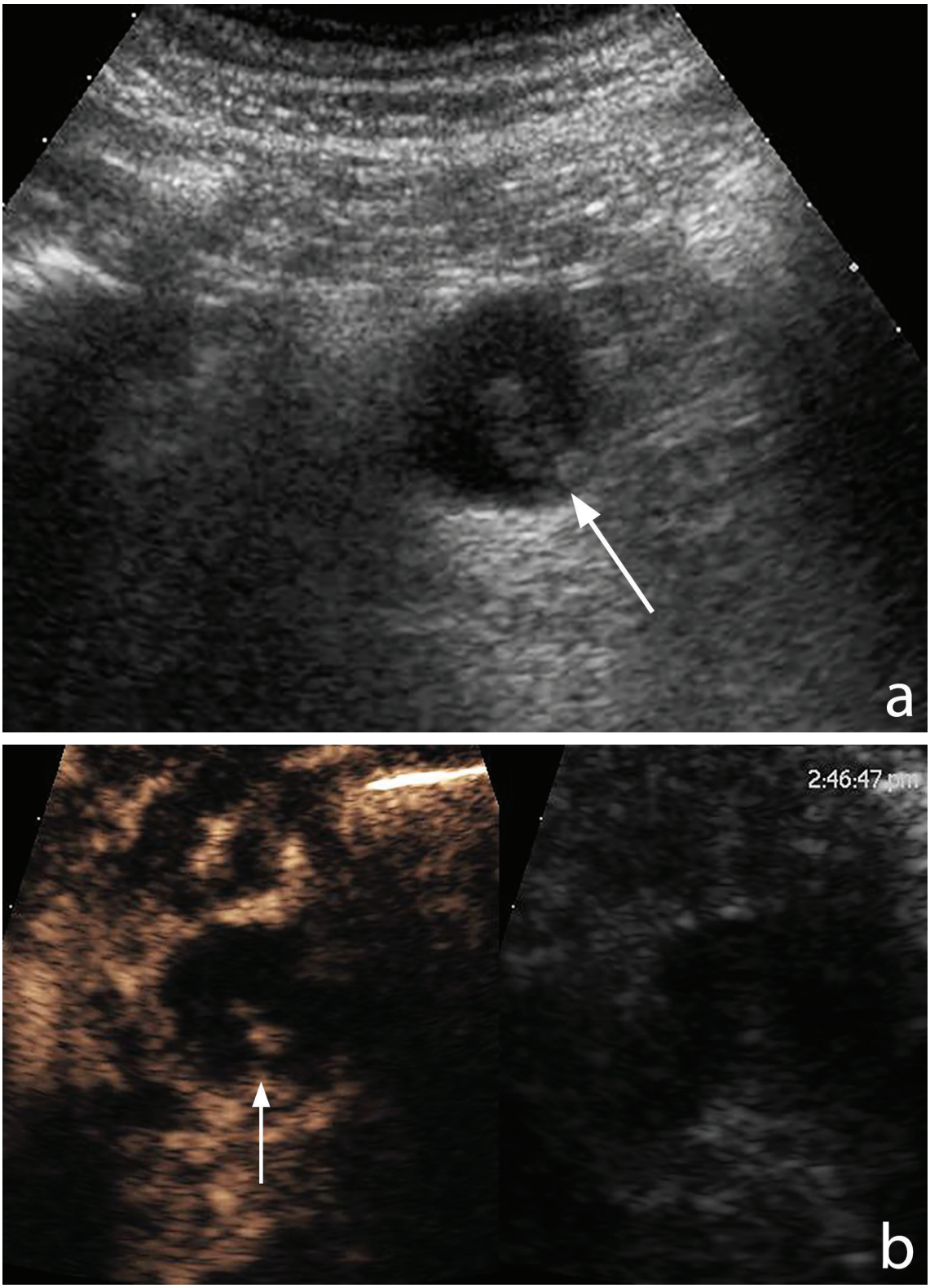

Figure 7: Intraductal papillary mucinous neoplasm. (a) B-mode US examination shows a small solid nodule within a round-shaped BD-IPMN in the pancreatic tail (arrow): the differentiation between a mucin plug and a neoplastic nodule is not possible; (b) CEUS shows enhancement of the solid nodule (arrow - degenerated IPMN).

presence of internal vascularised septa/nodules and the absence of a clinical history of acute pancreatitis are fundamental in differentiating MCNs from pseudocysts.[53]

Intraductal papillary mucinous neoplasms – IPMNs

Epidemiology, pathology and clinical findings

IPMNs are a group of exocrine mucin-producing tumours that arise more often in men at a mean age of 60 years.[43] IPMNs consist of a variety of lesions with different biological behavior, including hyperplasia, adenoma, borderline tumour, in situ or invasive carcinoma, with hyperproduction of mucin and segmental or diffuse dilation of the main pancreatic duct, or cystic dilation of the secondary branches, or both.[54] Most IPMNs involve the pancreatic head, but these tumours can diffusely involve the entire pancreas. Three types of IPMNs have been described: the main duct type (MD-IPMN), with focal or diffuse dilation of the main

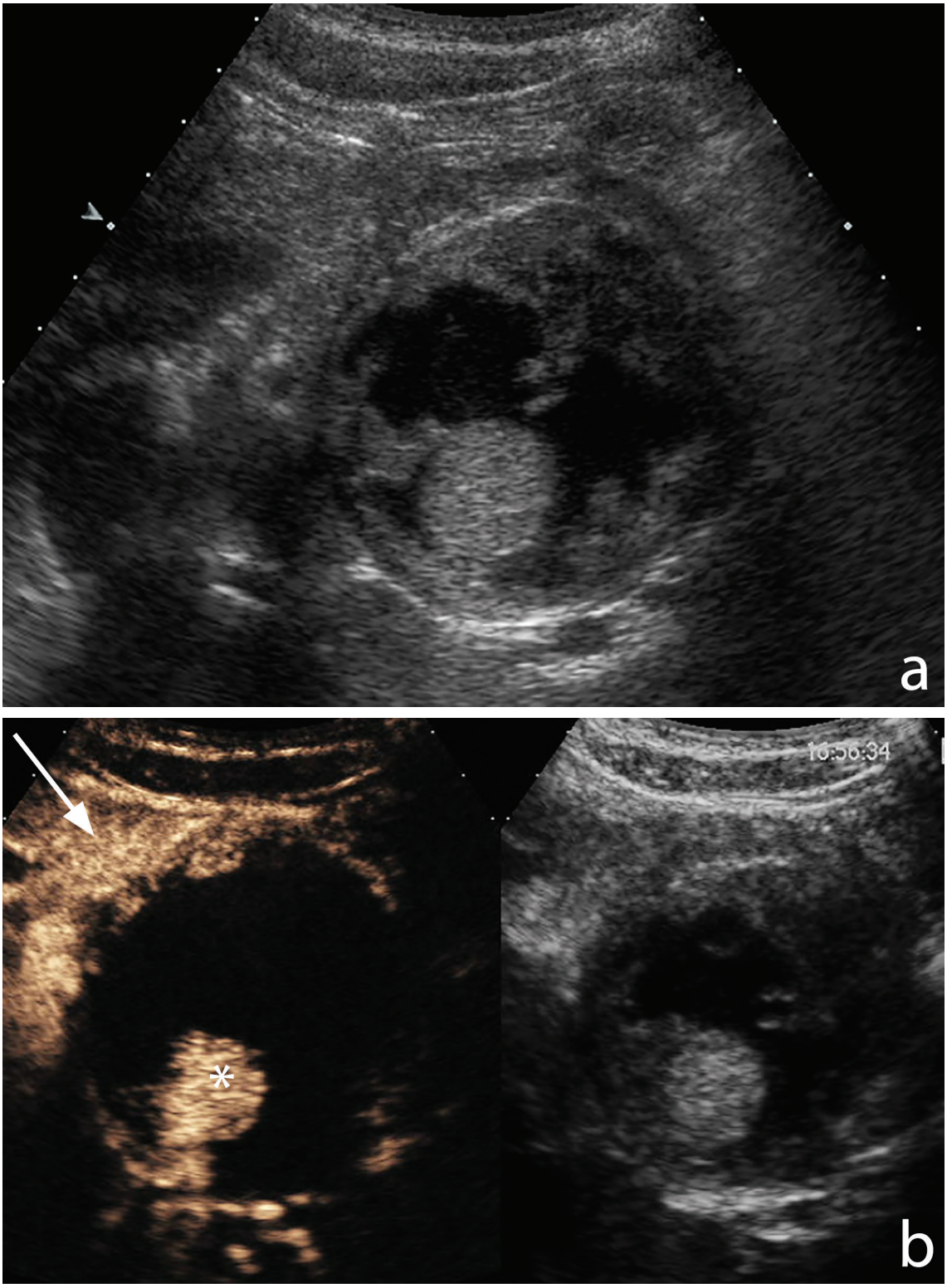

Figure 8: Solid pseudopapillary tumour. (a) B-mode US examination shows a huge, rounded, well defined, and heterogeneous lesion in the pancreatic tail with thick wall; (b) CEUS shows a peripheral enhancement within a thick, irregular wall (arrow) and the vascularisation of a huge solid inclusion (asterisk).

pancreatic duct; the branch-duct type (BD-IPMN), characterised by unilocular or multilocular cystic lesions with grapelike clusters; and the mixed type (MIX-IPMN), which meets the diagnostic criteria for both MD-IPMN and BD-IPMN.[55] Microscopically, IPMNs are characterised by a spectrum of changes, ranging from flat epithelium, microscopic folds, to simple or branching papillae, lined by cells that show different lines of differentiation. Four main histologic subtypes of IPMN exist: gastric-type, intestinal-type, pancreatobiliary-type, and oncocytic-type. High risk stigmata for malignancy are the following: main pancreatic duct diameter >10 mm for MD-IPMN, presence of solid enhancing nodules in BD-IPMN, obstructive jaundice; worrisome features suggesting that the lesion could evolve into malignant are: cyst > 3 cm, thickened enhanced cyst walls, main pancreatic duct diameter 5–9 mm, non-enhancing mural nodules, abrupt change in main pancreatic duct caliber with distal pancreatic atrophy and lymphadenopathy.[56] Other suggested features of malignancy consist in the presence of coarse calcifications[57] and a rapid increase of cyst size.[58]

International consensus guidelines[56] recommend resection in presence of high-risk stigmata, while in presence of "worrisome features" the lesion should be evaluated by EUS to further risk-stratify the lesion. Most IPMNs are asymptomatic and incidentally found during clinical evaluation for other conditions; when symptoms occur, they are generally related to intermittent obstruction of the pancreatic duct caused by thick mucin produced by the neoplasm.[59]

CEUS

MRI with MRCP remains the gold standard for the non-invasive diagnosis and follow-up of patients with IPMNs; CEUS can clearly demonstrate the enhancement of internal vegetations (Figure 7) and can be used to confirm doubtful cases.[5]

3D-CEUS can be used to follow patients with small IPMNs, even if MRI remains the gold standard technique for follow-up: it must be reminded that CEUS cannot be as precise as MRI in the volumetric assessment of these lesions.[60]

Differential diagnosis

MD-IPMN must be differentiated from main duct dilation in the setting of chronic pancreatitis.[55] BD- and MIX-IPMNs may be similar to MCNs and SCAs.[46] The main differentiating feature is the communication with the pancreatic ductal system, only present in IPMNs, but this is not evaluable with CEUS and therefore MRI is needed.[47]

Solid pseudopapillary tumour – SPT

Epidemiology, pathology and clinical findings

SPT is a rare entity (< 10% of the cystic neoplasms of the pancreas), that mainly arises in young women (2nd–4th decade of life) and has indolent biologic behavior characterised by low-grade malignant potential.[61–63] These tumours are usually well defined, round-ovoid shaped lesions with a heterogeneous mixed solid-cystic aspect; they often have large diameter and are well demarcated from the surrounding pancreas. Some tumours appear grossly encapsulated and lamellar calcifications can be observed within their wall. They usually develop as solid tumours and then undergo massive necrotic degeneration giving rise to a cystic/hemorrhagic appearance on radiologic imaging.[62] The microscopic appearance is heterogeneous, with solid areas characterised by nets and sheets of uniform cells or pseudopapillae mixed with cystic hemorrhagic areas, necrotic debris and foamy macrophages.[64] The peripheral pseudocapsule results from the tumoural growth inside the pancreatic gland with compression of the adjacent parenchyma.[65]

CEUS

At CEUS, SPT typically shows inhomogeneous enhancement of the thickened peripheral capsule and of the solid components surrounding cystic and necrotic avascular areas[65] (Figure 8).

Differential diagnosis

Small and solid SPTs may resemble neuroendocrine tumours and acinar-cell tumours. Lesions with more important hemorrhagic-cystic degeneration must be differentiated from other cystic neoplasms.

Conclusions

Contrast-enhanced ultrasound is a relatively widely available imaging method, less expensive than other imaging methods as CT or MRI, that nowadays plays a well-established role in the evaluation of pancreatic tumours. When possible, CEUS should be performed after the initial US diagnosis of a pancreatic lesion, especially if solid, in order to improve the accuracy of the first line examination particularly regarding the diagnosis of ductal adenocarcinoma, which is the most common and most harmful pancreatic neoplasm.

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