EUS Imaging in the Diagnosis of Pancreatic Masses

8

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EUS Imaging Features of Solid Pancreatic Lesions

Pancreatic Adenocarcinoma

Pancreatic adenocarcinoma, an aggressive form of cancer, usually presents at an advanced stage, resulting in a very disappointing prognosis for these patients. Typically, a 5-year survival rate is less than 5 % [1]. Surgical removal is currently the only curative treatment. Only small pancreatic tumors without significant invasion into surrounding organs are suitable for a complete surgical resection [2]. Unfortunately, the majority of pancreatic cancer presents at an advanced stage and cannot be treated curatively.

Given that operable pancreatic cancers are small in diameter and that they tend to be asymptomatic, the current noninvasive techniques, including computed tomography (CT) and magnetic resonance imaging (MRI), cannot provide sufficient resolution to reliably detect these small lesions [3]. Hence, endoscopic ultrasound (EUS), which has a significantly higher resolution, plays a significant role in the identification of these small pancreatic lesions [4]. Moreover, EUS also enables tumor staging together with a capacity for fine-needle aspiration (FNA); thus, it is commonly used for the evaluation of pancreatic adenocarcinoma [5]. Therefore, to provide the best management for patients, the abilities to recognize and to be familiar with EUS imaging features of pancreatic adenocarcinoma are valuable although EUS-FNA is needed to make a definite diagnosis of pancreatic adenocarcinoma.

A normal pancreas typically shows endosonographic features with a homogeneous "salt–and-pepper" appearance (Fig. 8.1). Pancreatic adenocarcinoma commonly displays as a heterogeneous hypoechoic mass with an irregular border during EUS examination, and it may be readily differentiated from the normal surrounding pancreatic parenchyma (Fig. 8.2). Solid pancreatic masses with these endosonographic features are suspected as pancreatic adenocarcinoma. However, results from a prospective study that used EUS images to diagnose 115 pancreatic lesions showed sensitivity and specificity rates for diagnosing malignant pancreatic masses that were 95 % and 53 %, respectively. Thus, EUS imaging alone is nonspecific for pancreatic cancer [6]. Upon retrospective analysis of results

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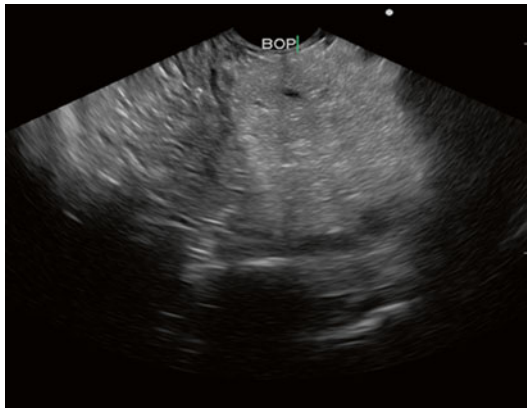

Fig. 8.1 A normal pancreas typically shows a homogeneous "salt-and-pepper" appearance

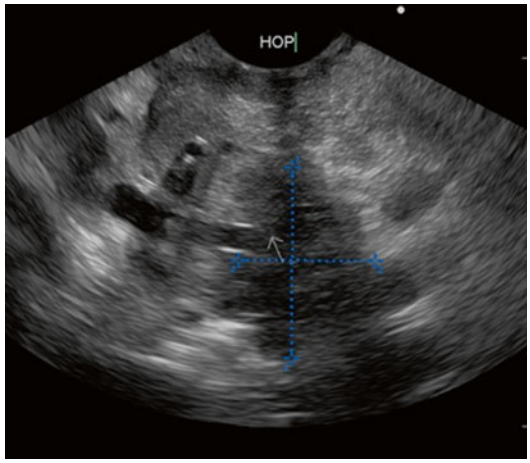

Fig. 8.2 A hypoechoic mass measuring 26 mm × 18 mm at its maximal diameter is demonstrated in the head of the pancreas

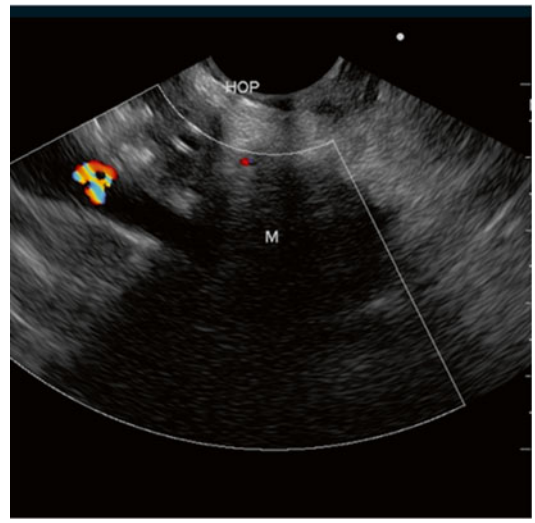

Fig. 8.3 A hypoechoic mass at the head of the pancreas with invasion into the main portal vein is demonstrated. A plastic biliary stent was endosonographically demonstrated by the couple of linear echogenic lines in the left upper corner of the figure

from that study, features associated with pancreatic cancer were lesions larger than 2 cm in diameter, vessel ingrowth, an absence of cystic spaces, and an absence of diffuse pancreatitis [6].

As discussed above, the only curative treatment for pancreatic cancer is complete surgical resection. If preoperative tumor staging suggests that the patient is a potential candidate for resectable pancreatic cancer, most surgeons would not hesitate to perform an exploratory laparotomy to remove the tumor completely. One of the critical points involved in making the decision is vascular invasion. To demonstrate invasion, either CT or MRI is used in practice. Unfortunately, a recent meta-analysis of eight studies ($n = 296$) reported that the pooled sensitivity rates of CT vs. MRI for the staging of pancreatic cancer were 71 % vs. 67 %, respectively, although their specificity rates were higher than 90 % [7]. In comparison, EUS was reported highly sensitive for detecting portal vein and confluence invasion [8, 9]. When three EUS parameters (visualization of tumor in the lumen, complete obstruction, or collateral vessels) were used, the overall sensitivity and specificity of EUS for diagnosing venous invasion were 43 % and 91 %, respectively; however, when another parameter of irregular tumor–vessel relationships was added to the criteria listed above, the sensitivity rate increased to 62 %, but the specificity rate dropped to 79 % [9]. EUS imaging features of portal vein invasion and celiac artery involvement are demonstrated in this chapter (Figs. 8.3, 8.4, 8.5 and 8.6). However, currently, the accuracy rate of EUS vs. CT for the staging of pancreatic cancer cannot be directly compared due to heterogeneity of design, quality, and results in relevant studies [10].

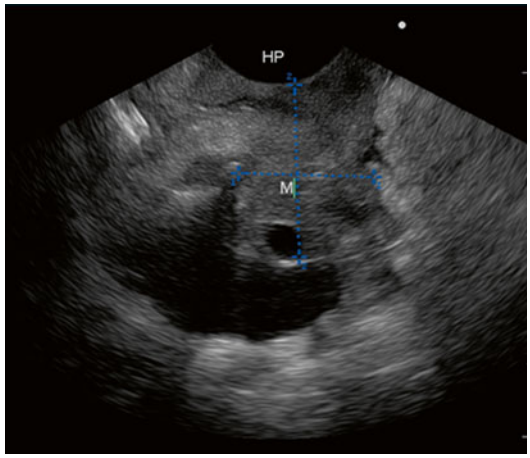

Fig. 8.4 The irregular relationship between the solid mass of pancreatic adenocarcinoma (M) and the portal vein is endosonographically demonstrated

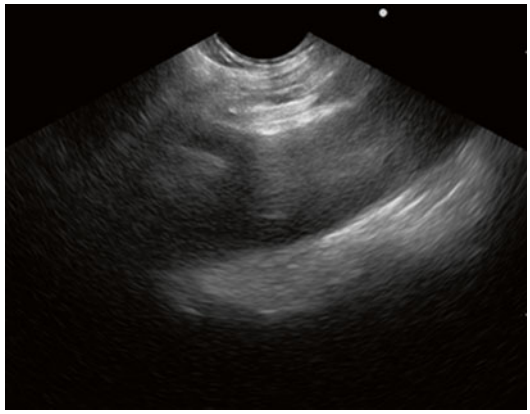

Fig. 8.5 The abdominal aorta demonstrated as a long tubular anechoic structure with the celiac artery originating from the aorta

Pancreatic Neuroendocrine Tumors

Pancreatic neuroendocrine tumors (PNETs) are rare pancreatic neoplasms that account for less than 10 % of all pancreatic cancers [11]. In general,)prognoses for PNETs are more favorable than for pancreatic adenocarcinoma, given that they show a more indolent course and thus a slower rate of growth. Nonetheless, these tumors have the potential to be aggressive; therefore, when identified, they must be removed.)Currently, surgical removal is the only curative treatment. Early detection, when the tumor is relatively small, is the only method of ensuring complete surgical removal. EUS plays a significant role in both the diagnostic management and, more recently, the therapeutic management of PNETs.

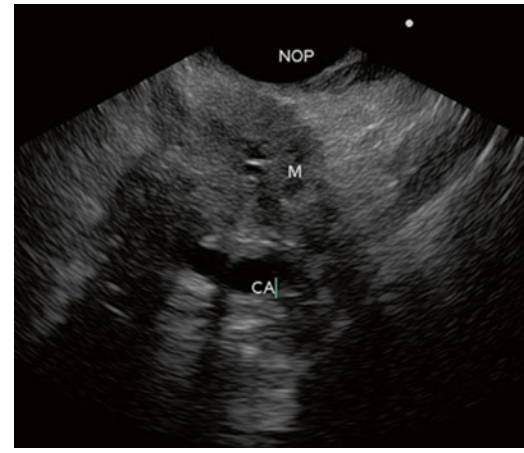

Fig. 8.6 A hypoechoic solid pancreatic mass (M) encases the celiac artery (CA). This mass was subsequently diagnosed as pancreatic adenocarcinoma

The management of)PNETs requires a multidisciplinary approach including expertise from endosonographers, radiologists, and surgeons. This section will focus on the EUS imaging features of PNETs.

Diagnostic Role of EUS

Functioning)PNETs generally present with hormonal symptoms; hence, they mostly present with small-diameter masses. It is generally recognized that any pancreatic mass smaller than 20 mm in diameter is at risk of being overlooked when using noninvasive imaging, particularly CT, which is the most widely available imaging technique [12]. EUS has the ability of enabling the detection of functioning PNETs lesions that are not identifiable using CT [13]. In studies comparing the sensitivity of EUS vs. CT scans to identify insulinomas, result showed that the former had a sensitivity rate of 79–87 % for the detection of fPNETs whereas the latter shows only 14–30 % sensitivity [14–17]. A recent large retrospective study reported an accuracy rate of 90.1 % (73/81) for EUS-FNA for the diagnosis of PNETs [18]. Other large series reported a sensitivity rate of 87 % in 89 patients [19] and 90 % in 86 patients [20]. In general, the use of EUS-FNA to confirm a diagnosis of PNETs

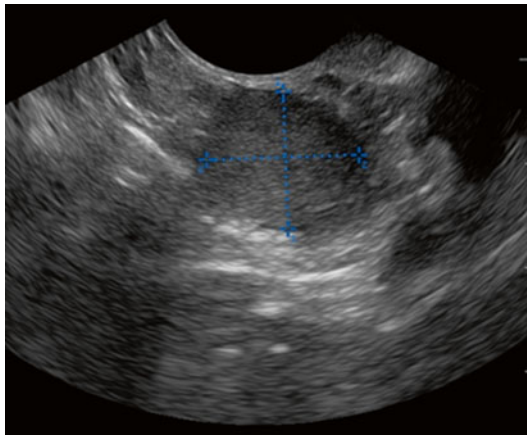

Fig. 8.7 A well-defined border of a homogeneous hypoechoic mass was identified in the tail of the pancreas. The final diagnosis was insulinoma

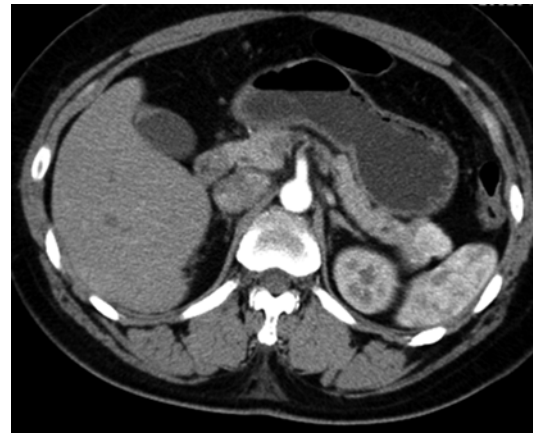

Fig. 8.8 A 2.1-cm × 1.8-cm early and late arterial-enhancing lesion at the tail of pancreas is shown

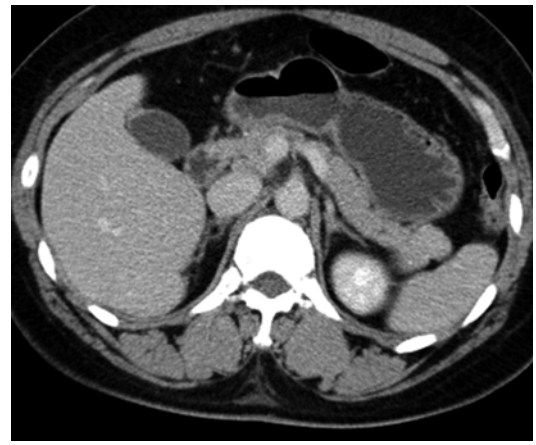

Fig. 8.9 An isodense lesion at the tail of the pancreas was identified. It was difficult to identify the lesion without information from a CT scan in arterial phase

is strongly recommended due to its high accuracy rate. Specific immunohistochemical staining is required for the diagnosis. Because a small pancreatic lesion is a well-known risk factor for inadequate sampling when using EUS-FNA [21], if tissue from the EUS-FNA of a small pancreatic lesion is insufficient to make a diagnosis of PNET but other clinical and laboratory parameters, including obtaining typical endosonographic lesion features, support the diagnosis, definite treatment may be considered. Typical endosonographic features of a small PNET are a homogeneous, slightly hypoechoic mass with a well-defined border (Fig. 8.7). One of the reasons that CT misses diagnoses of fPNETs is that CT shows enhanced lesions only during the arterial phase, whereas the lesion shows an isodensity during the venous phase (Figs. 8.8 and 8.9). Despite studies reporting this impressive capability of identifying fPNETs, in practice, EUS requires a high degree of technical expertise and experience because the echogenicity of fPNETs is generally slightly hypoechoic or even isoechoic compared with surrounding parenchyma. Not only the expertise and experience of endosonographers determine the efficacy of EUS but also other important factors, including the resolution of the ultrasonographic images and, in particular, the period of prediagnostic time that has elapsed prior to the point of clinical presentation of the patient.

Because approximately 90 % of PNETs present as solid lesions, it is often falsely presumed that any cystic lesions are not PNETs. This fact underscores the need to perform FNA for any cases clinically suspected of PNETs where cystic lesions have been identified by EUS. Based on the few existing studies reporting on cystic PNETs, these lesions do not display the typical characteristics of cystic tumors because they may present as simple cysts, mixed solid–cystic lesions, or cysts with septation; thus, endosonographic images are not recommended as the sole means of diagnosis (Fig. 8.10). FNA should

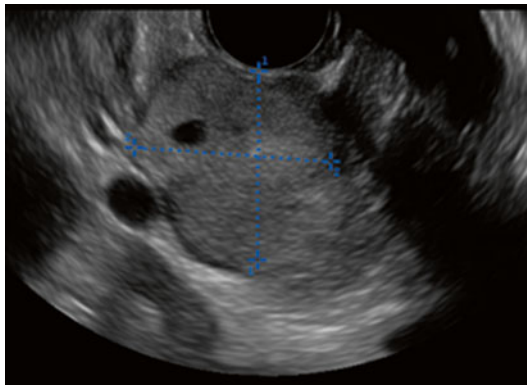

Fig. 8.10 A well-defined homogeneous hypoechoic solid pancreatic mass with a small cystic area inside the mass is shown. The final diagnosis was a cystic pancreatic neuroendocrine tumor

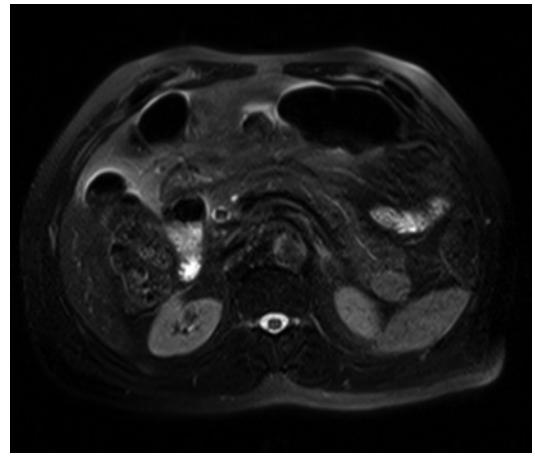

Fig. 8.11 Magnetic resonance imaging (MRI) showed a solid, well-defined, hypervascular lesion in the tail of the pancreas. The lesion was located close to the spleen. It showed a similar enhancing pattern to the adjacent spleen. All these features are typical when diagnosing an intrapancreatic accessory spleen

always be performed for the definitive identification of PNETs [22–26].

In summary, for fPNETs displaying typical endosonographic features, a presumptive diagnosis of PNETs may be made based on the endosonographic features alone. Nonetheless, to confirm the diagnosis preoperatively, EUS-FNA should be performed whenever possible because, together with its relatively low complication rate, the efficacy of FNA has been reported in several studies as being approximately 80 %. However, in atypical lesions, such as mixed solid–cystic lesions, preoperative diagnosis is required, and it is readily performed via EUS-FNA).

Accessory Spleen

The accessory spleen is a congenital anomaly caused by failure of the splenic anlage to fuse with the spleen during embryogenesis. It is found in 10–15 % of the general population and mostly shows no symptoms. Anatomically, it may either be a lesion connecting the main spleen or a separate nodule. In general, lesions are typically smaller than 2 cm; however, they can be as large as the spleen itself [27]. Approximately 80 % of accessory spleens are located adjacent to the splenic hilum, with the majority of the remaining located at the tail of the pancreas. However, occasionally, they may locate along the length of the splenic artery or anywhere in the abdominal cavity. Lesions are solitary or multiple in 80 % and 10 % of cases, respectively [28].

Intrapancreatic accessory spleens are solid, well-defined, hypervascular lesions in CT and MRI images (Fig. 8.11). These lesions should be differentiated from well-differentiated adenocarcinoma, mucinous cystic neoplasm, solid pseudopapillary neoplasm of the pancreas, neuroendocrine tumor, and metastases [29]. Endosonographically, the accessory spleens are generally round or oval-shaped lesions with a regular and sharp margin. They are usually homogeneous hypoechoic lesions with similar echogenic patterns to the major spleen (Fig. 8.12). It is difficult to differentiate from a splenic lobule. In equivocal cases, EUS-FNA may provide a definite diagnosis [30]. Classic cytopathological features include a heterogeneous population of lymphocytes, traversing small vascular structures, and a background of mixed inflammatory cells and blood [29].

Mass-Forming Chronic Pancreatitis

Chronic pancreatitis is a well-known risk factor for pancreatic cancer. A large prospective study following 373 patients with chronic pancreatitis

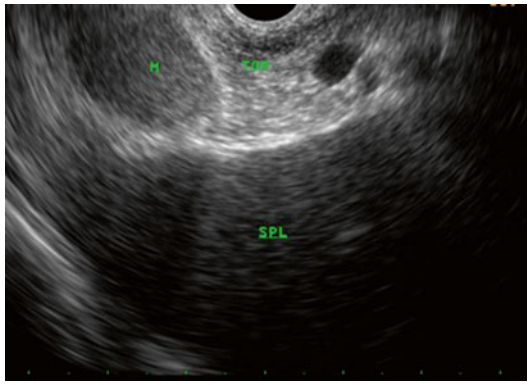

Fig. 8.12 A homogeneous hypoechoic solid mass (M) with an echogenic pattern similar to the major spleen (SPL) was identified in the tail of the pancreas (TOP). Endosonographically, the accessory spleens are usually round or oval-shaped lesions with regular and sharp margins

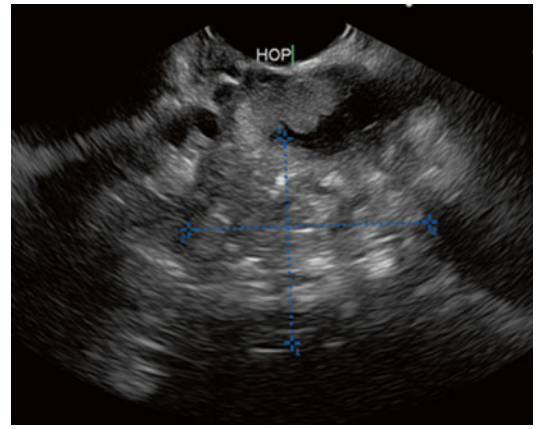

Fig. 8.13 An ill-defined heterogeneous hypoechoic calcified solid pancreatic mass is identified in the head of the pancreas. The final diagnosis of the mass was a mass-forming chronic pancreatitis

for at least 2 years observed four cases of pancreatic adenocarcinoma (1.1 %). The authors concluded that patients with chronic pancreatitis are at a markedly increased risk of pancreatic cancer compared with the general population [31]. Thus, when patients with baseline chronic pancreatitis develop a solid pancreatic mass, it is very challenging to differentiate between a mass-forming chronic pancreatitis or a de novo pancreatic cancer in addition to chronic pancreatitis.

Several technologies have been developed to assist the physician to diagnose solid pancreatic masses in the context of chronic pancreatitis. To date, the gold standard is EUS-FNA. Currently, EUS-FNA is recognized as the best test for diagnosing solid pancreatic masses, with reported sensitivity and specificity rates of 91 % and 94 %, respectively [5]. However, in the context of a solid mass with baseline chronic pancreatitis, the sensitivity of EUS-FNA drops from 89–91 % to 54–73 %, respectively [32, 33]. Thus, with this significant limitation, it is valuable for clinicians to recognize and be familiar with the typical EUS imaging features of mass-forming chronic pancreatitis; perhaps these data may assist in managing patients with solid pancreatic masses.

Radiographically, compared with pancreatic cancer, mass-forming chronic pancreatitis shows less severe main pancreatic ductal dilation, a more irregular main pancreatic duct contour, and more dilated side branches [34]. Endosonographically, a diagnosis of chronic pancreatitis is conventionally based on five parenchymal criteria (calcification with shadowing, echogenic foci without shadowing, echogenic strands, lobulation, and cystic change) and four ductal criteria (main pancreatic ductal stone, dilation or irregular contour of the main pancreatic duct, increased echogenicity of the main pancreatic ductal wall, and side-branch dilation). An international consensus has weighted each EUS criterion of chronic pancreatitis as being major or minor for the diagnosis of more solid lesions and to help standardize terminology. Major criteria include (1) echogenic foci with shadowing and main pancreatic duct calculi and (2) lobularity with honeycombing. Minor criteria include cystic changes, a dilated main pancreatic duct (≥3 mm), an irregular pancreatic duct contour, dilated side branches (≥1 mm), a hyperechoic ductal wall, strands, nonshadowing hyperechoic foci, and lobularity with noncontiguous lobules. This consensus is known as the Rosemont classification and is used for the diagnosis of chronic pancreatitis in several institutions [35]. Therefore, classically, mass-forming chronic pancreatitis shows imaging features including an inhomogeneous echogenic pattern, calcification, peripancreatic echorich stranding, and cysts (Fig. 8.13) [36, 37].

Autoimmune Pancreatitis

Autoimmune pancreatitis may present as either diffuse enlargement of the pancreas or focal pancreatic mass or enlargement [38]. In practice, differentiation between the focal mass of autoimmune pancreatitis and pancreatic adenocarcinoma is a challenging issue. Certainly, pathological diagnosis remains the gold-standard criterion; unfortunately, obtaining adequate tissue for a diagnosis is not straightforward. Therefore, clinically, the combination of various clinical findings is used to differentiate these two conditions. A recent review from Japan proposed that the following clinical parameters may suggest autoimmune pancreatitis rather than pancreatic adenocarcinoma. These findings include fluctuating obstructive jaundice; elevated serum IgG4 levels; diffuse enlargement of the pancreas; delayed enhancement of the enlarged pancreas and the presence of a capsule-like rim on dynamic CT; low apparent diffusion coefficient values on diffusion-weighted MRI images; irregular narrowing of the main pancreatic duct upon endoscopic retrograde cholangiopancreatography (ERCP); less upstream dilation of the main pancreatic duct upon magnetic resonance cholangiopancreatography (MRCP); the presence of other organ involvement, such as bilateral salivary gland swelling, retroperitoneal fibrosis, and hilar or intrahepatic sclerosing cholangitis; negative workup for malignancy, including EUS-guided FNA; and steroid responsiveness [39].

As discussed above, the diagnosis of autoimmune pancreatitis cannot rely solely on EUS findings; however, it is valuable to learn the typical endosonographic imaging features of autoimmune pancreatitis. Endosonographically, both diffuse and focal forms of autoimmune pancreatitis show echo-poor pancreatic parenchyma with echogenic interlobular septa (Fig. 8.14) [40]. In the diffuse form, a thickened gland border may be noted. These changes may vary based on the degree of pancreatitis as shown in a study that

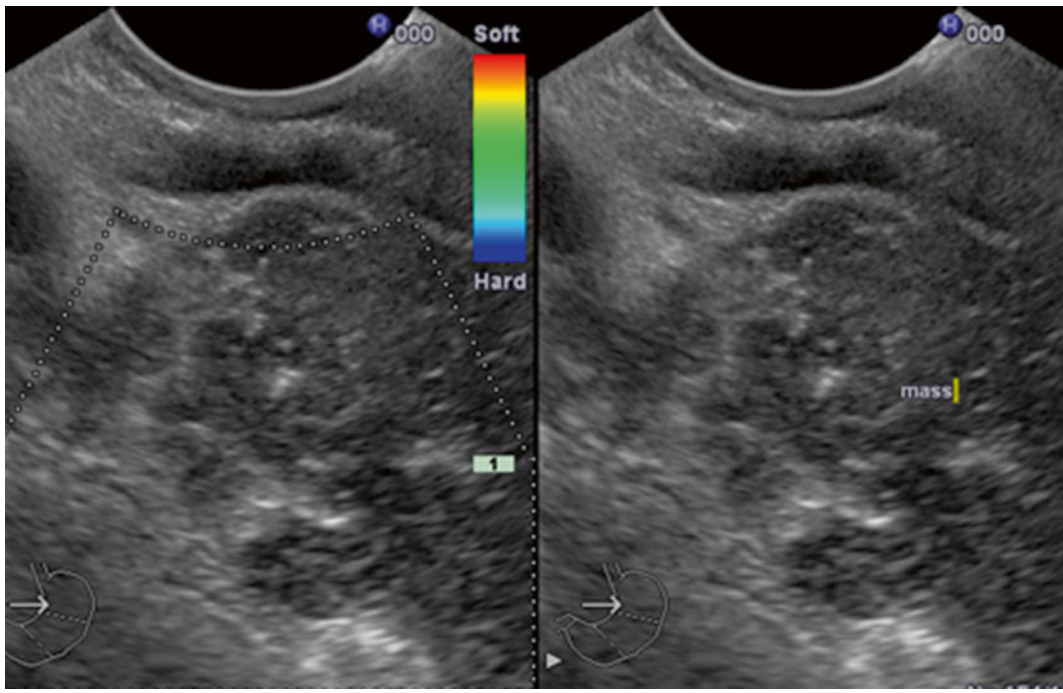

Fig. 8.14 A hypoechoic pancreatic mass in a patient with a final diagnosis of a focal form of autoimmune pancreatitis is shown. Endosonographic findings of echo-poor pancreatic parenchyma with echogenic interlobular septa are demonstrated

compared endosonographic findings in nine patients with early-stage and ten patients with advanced-stage autoimmune pancreatitis who were classified based on the Cambridge classification. Endosonographic findings of lobularity and a hyperechoic pancreatic duct margin were detected at a significantly higher frequency in early-stage compared with advanced-stage autoimmune pancreatitis [41].

Pancreatic Lymphoma

Primary pancreatic lymphoma is rare. From a retrospective review of 2397 patients with solid pancreatic masses over a 10-year period, only 12 patients (0.5 %) with pancreatic lymphoma were finally identified [42]. Based on results from this study, at the time of diagnosis, masses of primary pancreatic lymphoma were large and more than 80 % were located in the head of the pancreas. Heterogeneous versus homogeneous hypoechoic masses were found in 75 % and 25 % of patients, respectively (Fig. 8.15). The margins of all masses were ill defined, with vascular invasions in 41.7 %. Peripancreatic lymphadenopathy was noted in 58.3 % of patients. Neither EUS imaging features of chronic pancreatitis nor main pancreatic ductal dilation was noted [42]. However, to the best of our knowledge, EUS imaging features of pancreatic lymphoma have only been reported on a few series; thus, it is difficult to conclude the characteristic endosonographic findings [43, 44].

Pancreatic Metastases

Pancreatic metastases are relatively rare. Of these types of metastases, renal cell carcinoma is the most common primary cancer that metastasizes to the pancreas. It is difficult to differentiate pancreatic metastases from pancreatic adenocarcinoma based on EUS imaging alone. Nevertheless, a few studies have reported on the EUS imaging features of pancreatic metastases. Most lesions are solid, are likely to have well-defined margins, and are mostly present in patients with a known history of primary malignancy (Fig. 8.16) [45, 46]. Another retrospective study of 28 and 60 patients with pancreatic metastases and primary pancreatic adenocarcinoma, respectively, reported that the presence of regular borders, the absence of retention cysts, and the presence of a nondilated main pancreatic duct detected by EUS indicated the former rather than the latter disease [47]. However, because pancreatic metastases may present with other features, including solid pancreatic masses with irregular margins or _cys-

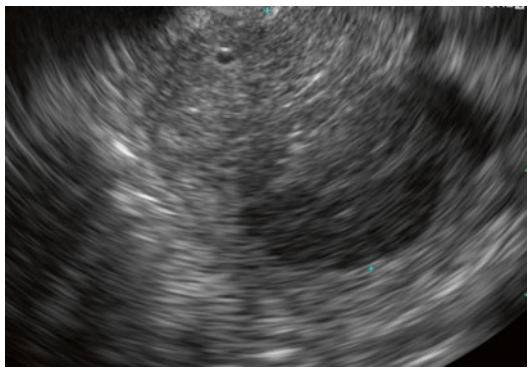

Fig. 8.15 A well-defined heterogeneous hypoechoic pancreatic mass was identified in the pancreas with a final diagnosis of primary pancreatic lymphoma

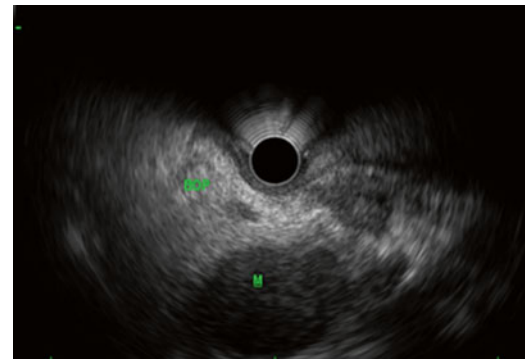

Fig. 8.16 A well-defined homogeneous hypoechoic pancreatic metastatic solid mass (M) from gastric adenocarcinoma is located in the body of the pancreas (BOP)

tic lesions, it is recommended that accurate diagnoses should be made based on pathology rather than EUS imaging features alone.

EUS Imaging Features of Cystic Pancreatic Lesions

Cystic pancreatic lesions are being increasingly identified worldwide due to the increased use of radiological imaging, including CT scans and MRI.

In comparison with other cross-sectional imaging including CT and MRI, EUS is considered a more invasive technique. Advantages of EUS include higher magnification of pancreatic cysts and the ability to perform EUS-guided diagnostic procedures. Those procedures include cystic fluid analysis for tumor markers and pancreatic enzymes, cytology, and direct visualization of the cystic wall.

Pseudocyst

Diagnosis of a pseudocyst should be made only when the clinical course and imaging features are compatible. Clinical and radiological evidence of either acute or chronic pancreatitis supports a diagnosis of pseudocyst although they are not entirely specific. Imaging features alone are not sufficient to confirm a diagnosis of a pseudocyst because it can mimic cystic neoplasms of the pancreas (Fig. 8.17). In questionable cases of pseudocysts, cystic fluid features and analysis help in differentiating pseudocysts from cystic neoplasms of the pancreas [48]. Cystic fluid may be obtained using transabdominal ultrasound or CT or EUS guidance. EUS is the most preferable due to its proximity to the pancreas. Low-viscosity, low-cystic-fluid CEA levels and significantly higher cystic-fluid amylase levels are suggestive of a pseudocyst [49].

Serous Cystadenoma

Serous cystadenoma may present with either a microcystic or honeycomb appearance or an oligocystic appearance, the latter of which is less common. A microcystic serous cystadenoma

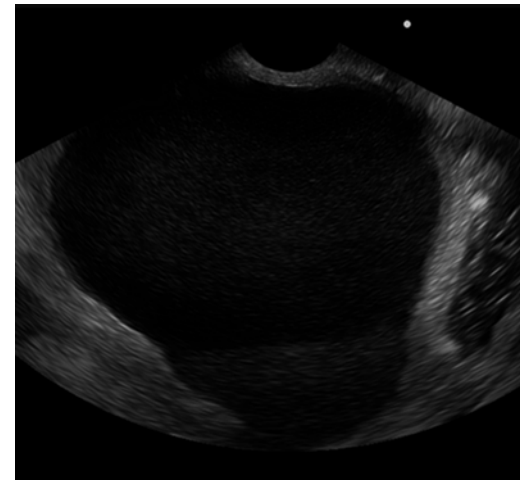

Fig. 8.17 A large pancreatic cyst with a regular border and echogenic content at the bottom of the lesion was identified in the tail of the pancreas. The lesion was finally diagnosed as a pseudocyst

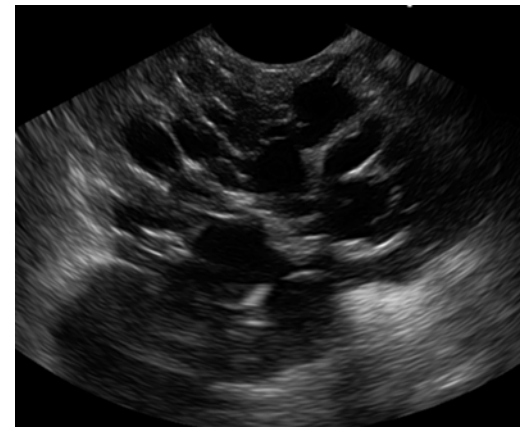

Fig. 8.18 This figure demonstrates a multilocular pancreatic cyst with a characteristic microcystic and honeycomb appearance. These features are characteristic of a serous cystadenoma. A 10-month follow-up period demonstrated a stable pancreatic cyst

comprises multiple small cysts (less than 2–3 mm each) that aggregate (typically more than six cysts) and that are separated by thin-wall septa (Fig. 8.18) [50]. EUS imaging features of a microcystic or honeycomb appearance are strongly suggestive of serous cystadenoma [51]. The microcystic feature is noted in more than 80 % of serous cystadenoma and is very specific when making a diagnosis of this lesion [50]. It is better diagnosed by EUS than other imaging

modalities. However, an oligocystic appearance, which comprises fewer and larger cysts, is difficult to differentiate from a mucinous cystadenoma or an intraductal papillary mucinous neoplasm (IPMN) [52].

Mucinous Cystadenoma

Histologically, a diagnosis of mucinous cystadenoma should be made when a specific finding of ovarian type of stroma has occurred; however, epithelial cells of the cyst may produce mucin, similar to IPMN [53, 54]. Endosonographically, a mucinous cystadenoma may either be unilocular or septated cysts with or without wall calcification. If solid components are identified, they may suggest malignancy (Fig. 8.19) [55]. Diagnosis of mucinous cystadenoma was made based on the criteria elevated cystic fluid CEA and a typical wall thickening and irregularity [56]. Whipple's operation was subsequently performed. A surgical biopsy confirmed mucinous cystadenoma with in situ carcinoma foci.

Pathologically, a malignant mucinous cystadenoma correlates with multilocularity and the presence of a papillary projection or mural nodules, the loss of ovarian-like stroma, and p53 immunoreactivity [54]. Endosonographically, endosonographic signs suggestive of malignancy include intracystic solid lesions, an adjacent solid mass, and an increasing diameter. A mucinous cystadenoma requires surgical resection in all surgically fit patients due to its malignant potential [57]. Unlike IPMN, communication with the pancreatic duct is rarely observed. Therefore, if the communication is clearly demonstrated, IPMN is a more likely diagnosis.

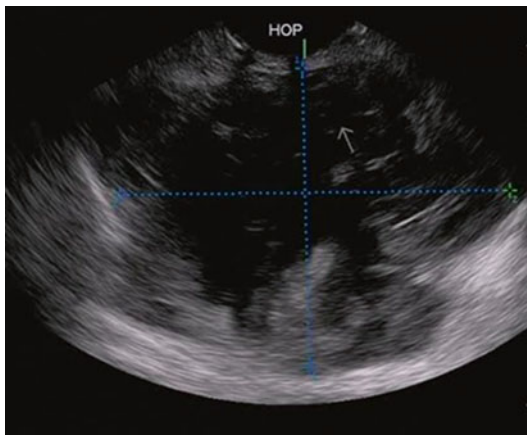

Fig. 8.19 This figure demonstrates a multilocular pancreatic cyst with papillary projection. A large multiloculated pancreatic cyst measuring 55 mm×42 mm in diameter is demonstrated at the head of the pancreas. A papillary projection was demonstrated from the cystic wall. EUS-FNA was performed. The aspirated fluid was a thick mucin

Intraductal Papillary Mucinous Neoplasm

Precancerous lesions of invasive pancreatic ductal adenocarcinoma include pancreatic intraepithelial neoplasms (PanINs), mucinous cystadenomas, and IPMNs. IPMNs are histologically classified as one of three types: main-duct type, branch-duct type, and mixed type [58]. Surgical resection is recommended for the majority of IPMNs. Radiographically, IPMNs are classified as branch-duct IPMN (BD-IPMN), main-duct IPMN (MD-IPMN), or mixed type. From the perspective of imaging, BD-IPMNs and MD-IPMNs are differential diagnoses of cystic pancreatic lesions and obstructive chronic pancreatitis, respectively.

Three classic EUS imaging features of BD-IPMNs have been described: multiloculated lesions or bunch-of-grapes; finger-like; and clubbed features (Fig. 8.20) [51]. The first is the most common type and shows irregular contours and a "cyst-by-cyst" appearance rather that the "cyst-in-cyst" and multi-loculated appearance of a mucinous cystadenoma [53].

Solid Pseudopapillary Neoplasms

Solid pseudopapillary neoplasms of the pancreas SPNs can be either benign or low grade potential tumor of the pancreas [59, 60]. These tumors occur predominantly in women as shown by Buetow and colleagues in a study of 96 patients that recruited 56 patients with SPNs of the pancreas [61]. The study reported that more than 90 % of patients

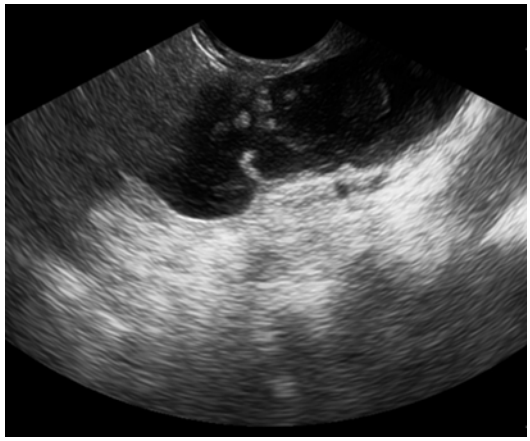

Fig. 8.20 This figure demonstrates a dilated side branch of the pancreatic duct at the body of the pancreas. These dilated side branches communicated with the main pancreatic duct. The final diagnosis was a side-branch intraductal papillary mucinous neoplasm of the pancreas (IPMN)

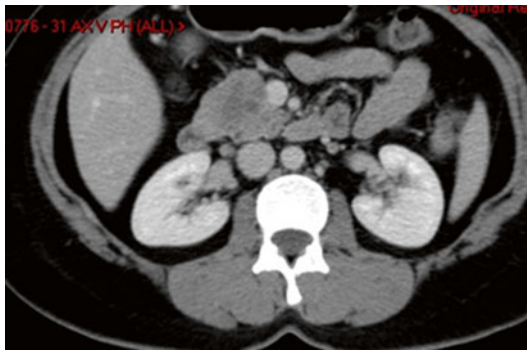

Fig. 8.21 An abdominal CT demonstrated a hypodense solid mass in the head of the pancreas. The mass measured approximately 3.1 cm × 3.9 cm × 4.1 cm. It was a heterogeneous enhancing mass. No vessel invasion was observed. No peri-lesional lymph node was observed

were female. The mean age of the patients was approximately 30 years [59, 60]. In general, the tumors were larger than 30 mm in diameter at the time of presentation. Radiographically, the tumor was an encapsulated mass with heterogeneous enhancement that included some cystic space and a solid component (Figs. 8.21, 8.22, 8.23, 8.24 and 8.25). EUS-FNA is an effective method to make a preoperative diagnosis of the SPNs [62].

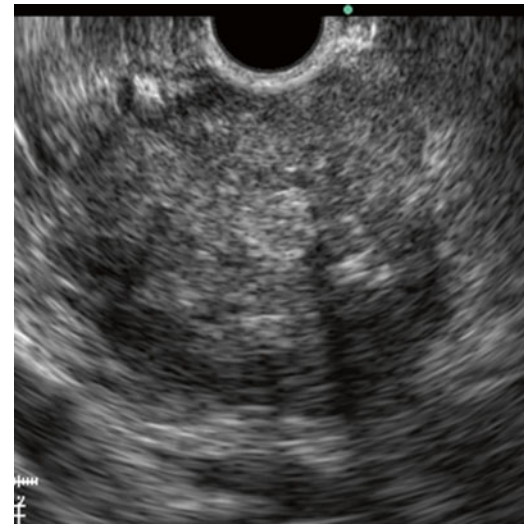

Fig. 8.22 An EUS examination demonstrated a well-defined, irregular border and a heterogeneous hypoechoic mass measuring 34 mm × 30 mm in diameter. A few tiny calcified spots were observed inside the mass

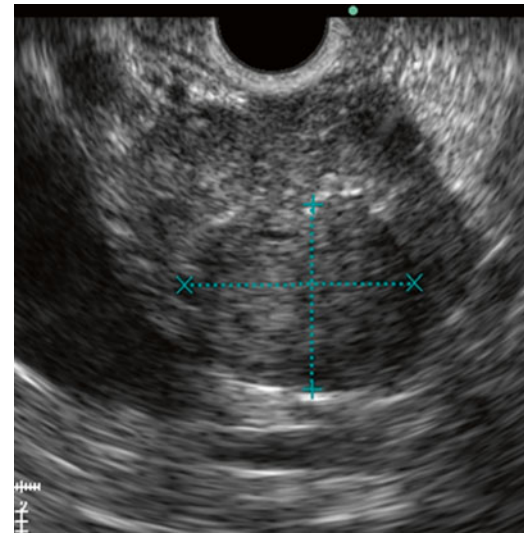

Fig. 8.23 There was a hypoechoic area measuring approximately 20 mm × 17 mm inside the mass. Endosonographically, it showed a well-defined border, it was encapsulated, and hypoechoic solid lesions showed an irregular margin. A deep hypoechoic area was observed inside the mass, likely the beginning of cystic degeneration of the mass. This area was not detected in a CT scan, reflecting the superiority of EUS over CT. No vessel invasion was observed. No lymph node was observed

Fig. 8.24 Gross surgical biopsy of the mass

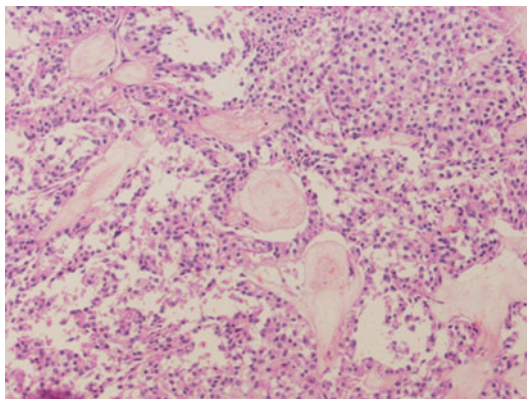

Fig. 8.25 Surgical histopathological examination following a Whipple procedure showed a circumscribed mass composed of solid sheets of uniform bland-looking cells admixed with delicate blood vessels that are surrounded by myxoid material. These findings were consistent with a solid pseudopapillary neoplasm of the pancreas

EUS-Guided Needle-Based Confocal Laser Endomicroscopy

Confocal laser endomicroscopy (CLE) is an endoscope-integrated or probe-based miniprobe that can provide real-time magnified endoscopic images at the cellular level. It has been applied for making real-time diagnoses of gastrointestinal tract mucosal lesions. Results from a recent meta-analysis were impressive [63]. Subsequently, the probe-based CLE has progressed into the submillimeter needle-based CLE (nCLE), which may be

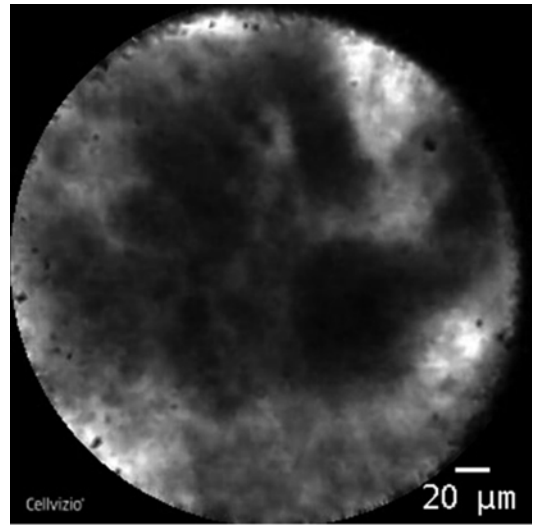

Fig. 8.26 Dark clumps of cells were demonstrated by EUS-guided needle-based confocal laser endomicroscopy of a solid pancreatic lesion with a final diagnosis of pancreatic adenocarcinoma

inserted into a 19-G EUS-FNA needle. Since this development, EUS-guided needle-based confocal laser endomicroscopy (EUS-nCLE) has been applied for the evaluation of both cystic and solid pancreatic lesions.

In the case of pancreatic lesions, EUS-nCLE has been evaluated in a feasibility trial that recruited patients with 16 cystic and 2 solid pancreatic lesions [64]. The trial reported a complication of acute pancreatitis in 2 of the 16 patients with pancreatic cysts. Subsequently, EUS-nCLE was used in 66 patients with pancreatic cysts in a multicenter study, known as the In vivo nCLE Study in the Pancreas with Endosonography of Cystic Tumors (INSPECT). The sensitivity and specificity rates of the finding of epithelial villous structure for the diagnosis of cystic pancreatic neoplasms using an nCLE miniprobe were 59 % and 100 %, respectively [65]. Characteristic nCLE signs for serous cystadenoma and IPMN were a superficial vascular network and finger-like projections, respectively [65, 66].

For solid pancreatic lesions, at the time of writing, to the best of our knowledge, there have only been two trials that have systematically reported on results of EUS-nCLE for solid pancreatic lesions. The first was a multicenter trial,

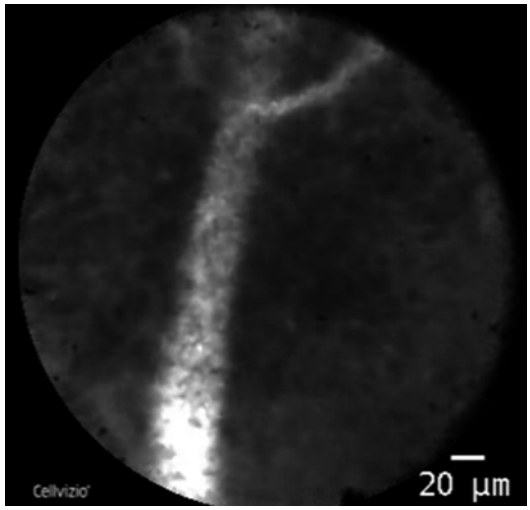

Fig. 8.27 A dilated vessel larger than 20 µm was demonstrated by EUS-guided needle-based confocal laser endomicroscopy of a solid pancreatic lesion with a final diagnosis of pancreatic adenocarcinoma

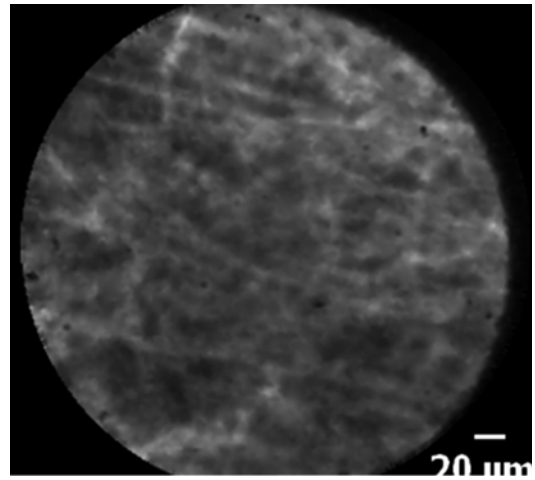

Fig. 8.28 A fine reticular network was demonstrated by EUS-guided needle-based confocal laser endomicroscopy of a solid pancreatic lesion with a final diagnosis of mass-forming chronic pancreatitis

the Clinical Evaluation of Needle-Based Confocal LASER Endomicroscopy (nCLE) for the Diagnosis of Pancreatic Masses (Contact Study), which thus far has been reported only in abstract form. In this retrospective study, nCLE images were reviewed by experts who knew the clinical information and diagnosis of all lesions. The criteria for malignant lesions, dark-cell aggregates with pseudo-glandular aspects and straight hyperdense elements, were described. [66] The second study, the Endoscopic Ultrasound Guided Needle Confocal Laser Endomicroscopy to Distinguish Between Benign and Malignant Lesions in Solid Pancreatic Masses (ENES Study), is a prospective blind study from our group that evaluated the efficacy of EUS-nCLE for solid pancreatic lesions. Preliminary results from the ENES study concluded that the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate were 100 %, 66.7 %, 90.9%, 100 %, and 92.3 %, respectively. From this study, the criteria of EUS-nCLE for malignant lesions included dark clumping with or without dilated vessels (>20 µm) (Figs. 8.26 and 8.27). For benign lesions, the criteria included a fibrous band, small black-cell movement, and normal acini (Fig. 8.28) [67]. Interestingly, of 33 patients from the three available studies listed above, no procedure-related complications have thus far been reported.

EUS-nCLE for both solid and cystic pancreatic lesions appears to be a promising technique for providing real-time histology. However, with data available from only a few studies, it is still too early to draw conclusions regarding its efficacy in actual clinical practice. More studies are required to clarify several unclear questions, such as interobserver variations, standard criteria, and correlations with histopathology, among others.

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