

Endoscopic ultrasound in the assessment of solid and cystic pancreatic lesions

Pancreatic masses can be solid or cystic, benign or malignant. Rapid and accurate diagnosis is essential for optimal management. Clinical presentation and radiological appearance are often inadequate for a definitive diagnosis. Endoscopic ultrasound allows more detailed assessment of the pancreas than traditional imaging techniques.

Focal lesions of the pancreas can be characterized as solid or cystic and incorporate non-neoplastic and neoplastic lesions. Neoplastic solid lesions include ductal adenocarcinoma, which represents 75–85% of solid lesions, and neuroendocrine tumours, lymphoma and metastases (Cem Balci and Semelka, 2001). Benign solid lesions are inflammatory in nature and usually caused by focal chronic pancreatitis although tuberculosis should be considered as a rare cause.

Pancreatic cystic lesions include benign, premalignant and malignant disease. Pseudocysts following pancreatitis make up the majority of cystic lesions of the pancreas. Cystic neoplasms represent only 10–15% of cystic pancreatic masses (Visser et al, 2004) and include serous cystadenoma, mucinous cystic neoplasms and intraductal papillary mucinous neoplasms. Mucinous cystic neoplasms and intraductal papillary mucinous neoplasms have malignant potential and should be considered for surgical resection, making accurate diagnosis essential.

Preoperative diagnosis and staging of pancreatic lesions can be difficult and requires a multimodality approach. Transabdominal ultrasound and computed tomography are the most common non-invasive first-line investigations but are unreliable when lesions are small (<3 cm). The sensitivity of transabdominal ultrasound decreases with smaller tumours; 95.8% > 3 cm, 81.7% for 1–3 cm and only 50% in tumours <1 cm (Bottger et al, 1998).

The performance of magnetic resonance imaging in diagnosing and staging pancreatic cancers remains similar to that of computed tomography (Săftoiu and Vilmann, 2009). The increased cost and image acquisition time and the limitations of magnetic resonance imaging detection of lung metastases favour computed tomography as the primary cross-sectional imaging modality for pancreatic lesions. Magnetic resonance

cholangiopancreatography is a non-invasive method of imaging the intra- and extrahepatic bile ducts and the pancreatic duct. It provides information on the level and scale of obstruction when no clear mass is seen on computed tomography (Peddu et al, 2009).

Endoscopic ultrasound has provided an important advance in the assessment of pancreatic lesions, giving a detailed morphological view of the pancreas and adjacent structures and allowing fine needle aspiration biopsy of pancreatic lesions and regional lymph nodes where appropriate. *Table 1* lists the main indications for endoscopic ultrasound and endoscopic ultrasound-fine needle aspiration of the pancreas.

Endoscopic ultrasound of the pancreas

The echoendoscopes used to perform endoscopic ultrasound have developed since their introduction 25 years ago, providing close proximity imaging of the upper and lower gastrointestinal tract and surrounding structures. Endoscopic ultrasound scopes provide high quality images with changeable frequencies between 7.5 and 20 MHz. Image resolution increases with higher frequencies at the expense of depth of penetration, useful when focussing on structures close to the bowel lumen. Images vary depending on the orientation of the transducer with respect to the endoscope.

Table 1. Indications for endoscopic ultrasound and endoscopic ultrasound-guided fine needle aspiration biopsy of the pancreas

Differential diagnosis of a solid mass within the pancreas
Differential diagnosis of a cystic lesion within the pancreas
Diagnosis of chronic pancreatitis
Histological confirmation of pancreatic adenocarcinoma
Preoperative staging of pancreatic adenocarcinoma
Investigation of the cause of a dilated common bile duct or pancreatic duct
Investigation of aetiology of acute pancreatitis
Investigation of microlithiasis or choledocholithiasis
Therapeutic pseudocyst drainage
Coeliac plexus block in pancreatic cancer and chronic pancreatitis

Dr Karen Mason is Specialist Registrar in Radiology in the Department of Radiology, **Mr Simon M Higgs** is Specialist Registrar in Upper Gastrointestinal Surgery and **Ms Sally A Norton** is Consultant General Surgeon in the Department of Surgery, University Hospitals Bristol NHS Foundation Trust, Bristol BS2 8HW

Correspondence to: Dr K Mason

A radial transducer provides a 360° image perpendicular to the long axis of the echoendoscope. A linear transducer provides a 120° view parallel to the long axis and allows visualization of biopsy needles introduced via the biopsy channel, enabling real-time endoscopic ultrasound-guided fine needle aspiration biopsy.

Endoscopic ultrasound-fine needle aspiration allows tissue acquisition for cytological diagnosis and analysis of cyst fluid enables detection of mucin, pancreatic enzymes and tumour markers, e.g. CEA. Endoscopic ultrasound is superior to transabdominal ultrasound and computed tomography in detecting pancreatic tumours >2 cm (Thirumurthi and Adler, 2006). Major complications may occur in 1–2% of patients and include haemorrhage, infection and pancreatitis (Hartwig et al, 2009). When performing fine needle aspiration biopsy of a pancreatic mass there is concern about the risk of seeding the peritoneal cavity or needle tract with malignant cells (Michl et al, 2006), particularly if a transperitoneal route via the stomach is used. It is hypothesized that the risk of needle tract seeding is lower for endoscopic ultrasound-fine needle aspiration biopsy, but this should still be considered, particularly in patients with potentially resectable tumours (Goldin and Bradner, 2007). The risks of endoscopic ultrasound-fine needle aspiration may outweigh the benefits and good communication between endosonographer and surgeon is essential.

Major vascular structures are easily identified with endoscopic ultrasound, and use of colour and power Doppler enables vascular flow to be confirmed. This is particularly useful when planning the approach for endoscopic ultrasound-fine needle aspiration of a lesion, as vessels within a possible biopsy tract can be accurately identified.

Endoscopic ultrasound examination takes approximately 30–45 minutes and is performed under conscious sedation. Patients are asked not to eat or drink for at least 6 hours before the examination and are allowed sips of water up to 2 hours before the examination.

Normal endoscopic ultrasound appearances

Pancreatic examination begins in the third part of the duodenum (*Figure 1a*). Withdrawal of the echoendoscope reveals the pancreatic head, distal common bile duct and pancreatic duct (*Figure 1b* and *1c*). The pancreatic body and tail, coeliac axis and portal confluence are seen through the posterior wall of the stomach with the tip of the endoscope approximately 45–55 cm from the incisors (*Figure 1d*). The normal pancreas appears as a relatively hyperechoic homogenous structure but can be isoechoic with surrounding soft tissue. The ventral pancreas often appears more hypoechoic than the dorsal pancreas because of its lower fat content and can be mistaken for a pathological lesion.

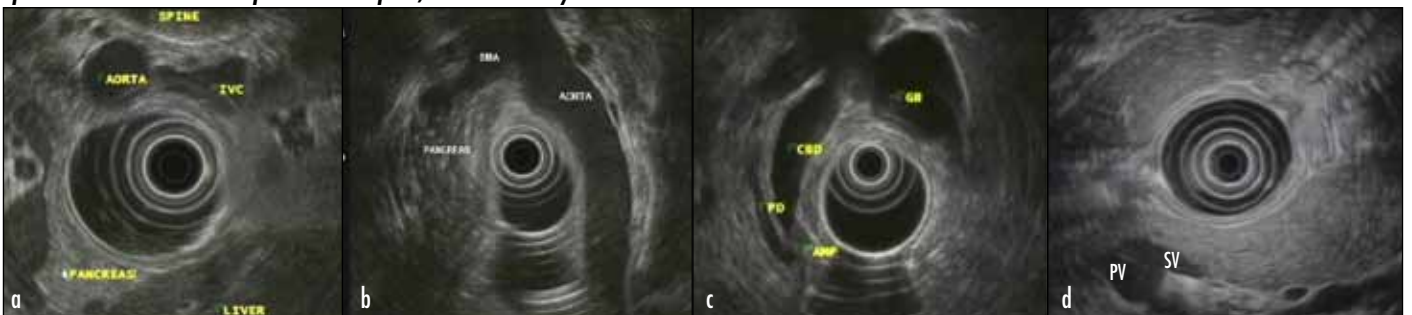
Solid lesions of the pancreas

Pancreatitis

Expansive fibrosis in chronic pancreatitis and the focal form of autoimmune pancreatitis can mimic malignancy, making differentiation from pancreatic adenocarcinoma difficult using standard imaging techniques. Features such as pancreatic fibrosis, atrophy, calcification and pancreatic duct dilatation do not exclude a diagnosis of malignancy and chronic pancreatitis can be associated with lymph node enlargement and vascular encasement causing further diagnostic dilemma. Chronic pancreatitis is also an independent risk factor for the development of pancreatic carcinoma with 4% developing cancer when followed up for 20 years (To'o et al, 2005).

Ardengh et al (2007) reported that precise differentiation between a pseudotumoural mass and carcinoma in the setting of chronic pancreatitis is not possible using endoscopic ultrasound morphology alone. The sensitivity of endoscopic ultrasound-fine needle aspiration biopsy for malignancy in parenchymal masses with features of chronic pancreatitis is 54–74% in contrast to 89% when the surrounding pancreatic tissue is normal (Seicean, 2010). Following a negative endoscopic ultrasound-fine needle aspiration when the suspicion for

Figure 1. Normal endoscopic ultrasound appearances. *a. 'Owls eye' view from deep in the second part of the duodenum (D2) demonstrates the spine at the top of the screen. The aorta is identified as a round anechoic structure and the inferior vena cava (IVC) is oval and easily compressed. b. The echoendoscope is withdrawn slowly from deep D2, demonstrating the aorta in long section. The superior mesenteric artery (SMA) is seen branching from the aorta. The hypoechoic ventral pancreas is seen between these two vessels. c. In the duodenum the common bile duct (CBD) is seen nearest to the echoendoscope. The normal pancreatic duct (PD) is thinner and lies between portal vein and CBD. d. The splenic vein (SV) enlarges to form the 'golf club'-shaped portal vein (PV) confluence. Following the splenic vein to the splenic hilum allows examination of the pancreatic body and tail. The pancreatic duct is identified between the splenic vein and echoendoscope. AMP = ampulla; LK = left kidney.*



malignancy is high, further endoscopic ultrasound-fine needle aspiration biopsy will confirm the diagnosis in a proportion of patients and should be considered.

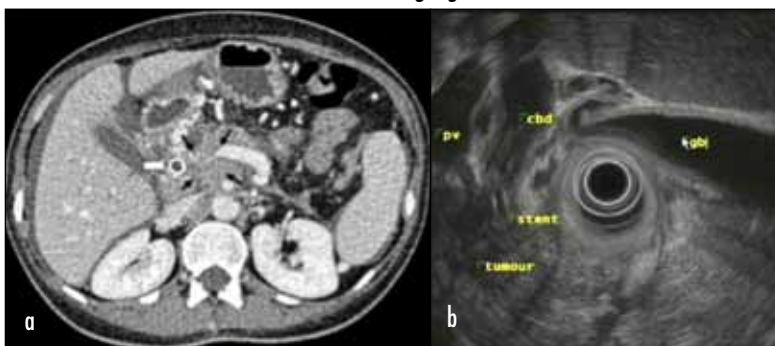
Pancreatic ductal adenocarcinoma

Pancreatic adenocarcinoma is one of the five major causes of cancer-related death in Europe and the USA and accounts for 75–85% of non-endocrine malignancies of the pancreas. Surgical resection is the only curative treatment option but is rarely possible because of distant metastasis or vascular involvement. Limited venous invasion is not an absolute contraindication to surgery so optimal preoperative imaging is paramount.

Transabdominal ultrasound is sensitive in detecting biliary tract dilatation but visualization of the pancreas parenchyma is poor especially in obese patients. Contrast enhanced computed tomography shows a low attenuation focal mass within the pancreas relative to the enhancing normal parenchyma (*Figure 2a*). It is important to remember that adenocarcinomas can be isoattenuating compared with normal pancreatic tissue (Prokesch et al, 2002).

With endoscopic ultrasound, pancreatic adenocarcinoma is usually seen as a hypoechoic mass with an irregular contour associated with an inhomogeneous echo pattern and dilatation of the proximal pancreatic duct and common bile duct (Yasuda et al, 1995). Distal pancreatic atrophy may also be seen. The high resolution of endoscopic ultrasound allows detection of focal lesions as small as 2–3 mm as well as demonstrating vascular invasion and local lymph node involvement. Blood vessel infiltration is indicated by loss of plane between tumour and vessel wall, vessel wall irregularity, tumour within vessel lumen and presence of collaterals (*Figure 2b*). Krishna et al (2009) showed endoscopic ultrasound and endoscopic ultrasound-fine needle aspiration biopsy to be accurate in the staging and diagnosis of pancreatic adenocarcinoma (sensitivity 96.6%, specificity 99%, negative predictive value 96.2%, positive predictive value 99.1%).

Figure 2. Pancreatic carcinoma in a patient presenting with obstructive jaundice. a. Axial computed tomography performed in the portal venous phase demonstrates a large low attenuation soft tissue mass within the pancreatic head (black arrows). The mass encases the coeliac axis and there is a small amount of ascites. A stent is seen in the common bile duct (white arrow). b. Radial endoscopic ultrasound demonstrates a 3.5 cm poorly-defined hypoechoic mass in the pancreatic head invading the portal vein (pv) and common bile duct (cbd) which contains a stent. gb=gallbladder.



The National Comprehensive Cancer Network (2009) guidelines recommend histological confirmation is sought before non-surgical treatment.

Neuroendocrine tumours

Pancreatic neuroendocrine tumours are rare, representing 1–2% of pancreatic neoplasms, with a peak incidence at 30–60 years of age (Frankel, 2006). Pancreatic neuroendocrine tumours include insulinomas, gastrinomas, glucagonomas and somatostatinomas and can either be functioning (producing hormonally active peptides) or non-functioning. They are slow-growing tumours with a more favourable prognosis than pancreatic adenocarcinoma, therefore accurate diagnosis and localization is important.

Functioning neuroendocrine tumours, such as insulinomas and gastrinomas, usually present because of the symptoms induced by the hormone they secrete. Insulinomas, the most common pancreatic neuroendocrine tumours, are usually benign and solitary and found anywhere in the pancreas. Gastrinomas are often malignant and multiple, typically found in the 'gastrinoma triangle', defined by the porta hepatis at the apex of the triangle with the second and third parts of the duodenum at its base.

Other functioning pancreatic neuroendocrine tumours such as glucagonomas and somatostatinomas are very rare. Glucagonomas are usually found in the body or tail of the pancreas and are often large at the time of presentation because of difficulty in recognizing the clinical syndrome (Rockall and Reznek, 2007). As a result metastases are common at presentation (most commonly hepatic). Somatostatinomas are large, slow-growing tumours often found in the pancreatic head.

Non-functioning neuroendocrine tumours either present as an incidental solid pancreatic mass identified on transabdominal ultrasound or computed tomography or as a result of mechanical symptoms caused by mass effect. They are often large at presentation and associated liver metastases are common. Typical characteristics include hypervascularity and calcification, which can be detected with thin-slice computed tomography (1.25–1.5 mm) in the arterial phase (*Figure 3a*). Kalra et al (2003) showed the most optimal magnetic resonance imaging sequences for detecting pancreatic neuroendocrine tumours were T2-weighted fast spin echo (hyperintense to pancreatic parenchyma) and fat suppressed T1-weighted spin echo and gradient echo (hypointense to pancreatic parenchyma).

Endoscopic ultrasound plays an important role in the preoperative assessment of pancreatic neuroendocrine tumours especially when small. Varadarajulu and Wallace (2004) found endoscopic ultrasound detects neuroendocrine tumours in the pancreas with high sensitivity (82%) and specificity (95%). They are generally hypoechoic, homogenous masses with distinct margins (*Figure 3b*) and demonstrate posterior acoustic enhancement

because of their hypervascularity. Gouya et al (2003) found that multiphase helical computed tomography with thin reformats has a sensitivity of 94% for detecting insulinomas which increases to 100% when combined with endoscopic ultrasound.

Endoscopic ultrasound can also demonstrate the relationship to other structures, facilitating laparoscopic enucleation or more extensive open surgery with either palliative or curative intent.

Octreotide scanning is a highly sensitive method of identifying pancreatic neuroendocrine tumours based on somatostatin receptors being present in 80–90% of pancreatic neuroendocrine tumours. It has a high sensitivity and specificity, allows imaging of the whole body and can predict sensitivity to somatostatin analogue treatment. Limitations include small tumours and those without somatostatin receptors (50% of insulinomas) (Alsohaibani et al, 2008).

Angiography and transhepatic portal venous sampling are rarely used in the diagnosis of pancreatic neuroendocrine tumours since the introduction of endoscopic ultrasound. A pancreatic neuroendocrine tumour causes a well-defined vascular blush in the capillary-early venous phase on angiography (the tumour enhances 45–60 seconds after injection of intravenous contrast). In contrast to endoscopic ultrasound small and hypovascular lesions are difficult to identify and false positives can be caused by a blush from bowel, a splenunculus or normal pancreas. Transhepatic portal venous sampling uses downstream venous sampling to identify high levels of hormone at a particular site, it does not allow direct visualization or accurate localization. Venous sampling can only identify hormonally active pancreatic neuroendocrine tumours and is unhelpful if there are multiple tumours (Reznek, 2006).

Endoscopic ultrasound is the most sensitive method for preoperative localization of pancreatic lesions (Oberg and Eriksson, 2005).

Primary pancreatic lymphoma

Primary pancreatic lymphoma is a rare form of extranodal lymphoma, typically Hodgkin's B-cell type, and accounts for <1% of extranodal lymphomas (<0.5% of pancreatic tumours). Although rare, it can mimic adenocarcinoma of the pancreas both clinically and radiologically (Boni et al, 2002). The prognosis for primary pancreatic lymphoma is significantly better than adenocarcinoma and accurate differentiation is important.

Primary pancreatic lymphoma demonstrates two morphological patterns. The first is a bulky homogenous mass (often >8 cm) with extrapancreatic extension breaching anatomical boundaries; this can mimic the appearance of acute pancreatitis. The second is a localized, well-circumscribed tumoural form which can be misinterpreted as adenocarcinoma. It is rarely associated with dilatation of the main pancreatic duct (localized form), calcification and necrosis (Luo et al, 2009). There is often

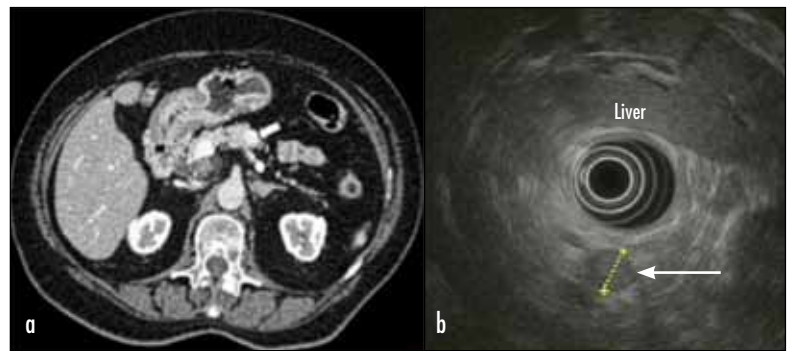


Figure 3. Neuroendocrine tumour: patient with previous pancreatitis under investigation for cyst within uncinate process of pancreas identified with transabdominal ultrasound. a. Axial computed tomography performed in the arterial phase also demonstrates a well-demarcated hypervascular lesion measuring 10 mm in the pancreatic body (arrow). b. Radial endoscopic ultrasound demonstrates a 10 mm hypoechoic lesion with distinct margins in the pancreatic body (arrow).

associated lymphadenopathy which, if seen below the level of the renal veins, makes a diagnosis of adenocarcinoma unlikely (Prayer et al, 1992). Computed tomography appearances may suggest a diagnosis of primary pancreatic lymphoma but are rarely conclusive.

Endoscopic ultrasound shows a bulky homogenous hypoechoic mass which does not demonstrate increased through transmission (Merkle et al, 2000) often associated with lymphadenopathy.

No single characteristic reliably distinguishes primary pancreatic lymphoma from pancreatic adenocarcinoma. Endoscopic ultrasound-fine needle aspiration or Trucut biopsy with flow cytometric analysis may achieve histological diagnosis (Battula et al, 2006).

Metastases

Pancreatic metastases are rare: in clinical series the frequency ranges from 2–5% of all pancreatic neoplasms (Tsitouridis et al, 2010). The majority of patients with pancreatic metastases have a past history of previous malignancy, most commonly kidney, lung, breast or melanoma.

On computed tomography most pancreatic metastases are low attenuation lesions. Contrast enhanced computed tomography and magnetic resonance imaging (Kalra et al, 2003) can demonstrate the hypervascularity often seen with renal and melanoma metastases. Endoscopic ultrasound-guided fine needle aspiration allows histological differentiation in the absence of a known primary (Figure 4).

Cystic lesions of the pancreas

Pancreatic pseudocyst

A pseudocyst is a localized collection of amylase-rich fluid located within or adjacent to the pancreas surrounded by a fibrous wall with no epithelial lining (Pitman and Deshpande, 2007) as a result of damage to the pancreatic parenchyma caused by acute or chronic pancreatitis. Pseudocysts classically develop 3–6 weeks



Figure 4. Pancreatic metastasis in a patient with a history of breast cancer who presented with jaundice requiring a common bile duct stent. Computed tomography demonstrated a bulky pancreatic head and pulmonary metastases. Radial endoscopic ultrasound demonstrates a poorly-defined lobulated mass in the pancreatic head which is hypoechoic. The mass appears to encase the portal vein (pv, small arrows). The pancreatic duct was normal. Large aorto-caval nodes measuring up to 15 mm in short axis. Endoscopic ultrasound fine needle aspiration biopsy identified malignant cells consistent with adenocarcinoma, likely of breast origin.

after a clear episode of acute pancreatitis but such a history is not always apparent.

Computed tomography usually demonstrates a rounded, well-defined, unilocular fluid collection with an extremely thin wall. A thick wall that demonstrates contrast enhancement should raise the suspicion of an infected pseudocyst (Kim et al, 2005) and correlation with the patient's clinical presentation and inflammatory markers is required. Septation is an unusual feature. Computed tomography may show other features of acute or chronic pancreatitis (Figure 5a).

Endoscopic ultrasound typically demonstrates a large hypoechoic cystic lesion within or adjacent to the pancreas. Internal bright echoes are often seen representing

inflammatory debris. Communication with the pancreatic duct may be demonstrated and an assessment of the biliary tree is useful to identify cholelithiasis and bile duct stones. Signs of chronic pancreatitis (parenchymal calcification, atrophy, fibrosis and ductal dilatation) are more easily diagnosed with endoscopic ultrasound (Figure 5b). Endoscopic ultrasound morphology alone does not have limitations and characterization of cyst fluid gives valuable additional information. Pseudocysts often contain turbid fluid with high amylase (>5000 U/litre), low CEA (<200 ng/ml) levels and low viscosity (Brugge, 2004) (Figure 5c).

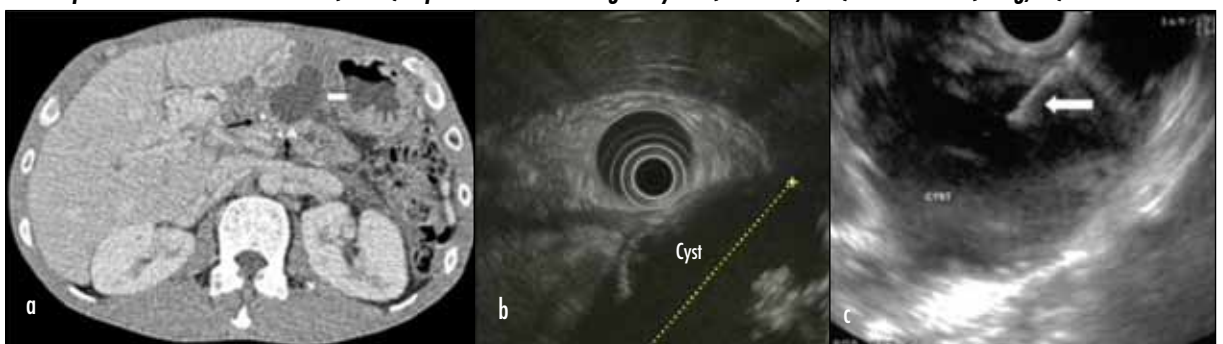
Serous cystadenoma

Serous cystadenoma is a cystic neoplasm of the pancreas, typically found in females >60 years of age and sometimes associated with von Hippel–Lindau disease. Although occasionally presenting with abdominal pain and weight loss, serous cystadenoma is more commonly an incidental finding on cross-sectional imaging. Surgical excision may be advised for larger (>4 cm) and symptomatic lesions. It is important to differentiate a benign serous cystadenoma from a mucinous cystadenoma which has malignant potential and requires excision.

Serous cystadenomas are well-demarcated lesions containing at least six small cysts separated by thin septae. The cysts range from 0.2–2.0 cm in diameter and the lesion itself is typically <2 cm but can measure up to 27 cm in maximum dimension (Bounds and Brugge, 2001). The septae may coalesce causing the appearance of a characteristic central scar, sometimes calcified (Curry et al, 2000).

On transabdominal ultrasound, serous cystadenomas can appear solid and echogenic because of the interfaces between multiple cysts. A finding of multiple small cysts measuring <3 mm within a cystic lesion suggests serous cystadenoma when imaged with computed tomography (92–96% accuracy) (Belsley et al, 2008) (Figure 6a). These cystic lesions can give the appearance of a solid mass on computed tomography because the microcystic structure is too small to be seen as 'oligocystic'.

Figure 5. Pancreatic pseudocyst. The patient had known chronic pancreatitis and presented with increasing epigastric pain. a. Axial computed tomography performed in the portal venous phase demonstrates pancreatic calcification (black arrows) and an adjacent cyst (white arrow). b. Radial endoscopic ultrasound demonstrates a large cyst within the pancreatic neck. The pancreatic head was heavily calcified. c. Linear endoscopic ultrasound and fine needle (arrow) aspiration revealed a high amylase (38 760 U/litre) and low CEA (24 ng/ml).



The classical endoscopic ultrasound appearance of serous cystadenoma is a 'honeycomb' or 'sponge-like' mass with posterior acoustic enhancement as a result of serous fluid within the cysts and a central scar (*Figure 6b*). Fluid obtained by endoscopic ultrasound-guided aspiration is usually thin and clear with cuboidal cells apparent on cytological assessment. CEA levels are rarely raised (<5 ng/ml) and amylase levels are usually low (Fasanella and McGrath, 2009). Unfortunately the small cystic cavities often yield insufficient material for CEA or amylase levels and cellularity is sparse. In a series performed by Belsley et al (2008) cytology only confirmed a diagnosis of serous cystadenoma in 21% of cases, but endoscopic ultrasound appearances suggested serous cystadenoma in 87.5% of cases. A multidisciplinary team approach to diagnosis using cytology, biochemistry and endoscopic ultrasound morphology is advised.

Serous cystadenoma may also present as a large unilocular cyst (macrocytic adenoma). This lacks the characteristic multilocular appearance of serous cystadenoma and is particularly difficult to differentiate from mucinous cystadenoma using cross-sectional imaging characteristics. Although usually unilocular on computed tomography, macrocytic cystadenomas are frequently multilocular when viewed with endoscopic ultrasound (O'Toole et al, 2004).

Mucinous cystic neoplasm

Mucinous cystic neoplasms are generally unilocular or thinly septated cystic lesions lined by tall columnar epithelium which produces mucin. Mucinous cystic neoplasms contain ovarian-type stroma occurring in females (aged 50–70 years). They demonstrate varying degrees of cellular atypia ranging from benign mucinous adenoma to invasive mucinous cystadenocarcinoma. Between 85 and 95% of lesions are found in the pancreatic body or tail (Edirimanne and Connor, 2008), often >2 cm in diameter and containing thick mucoid material.

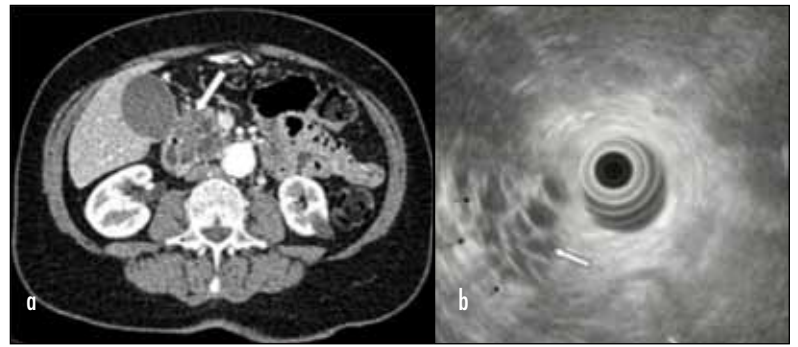
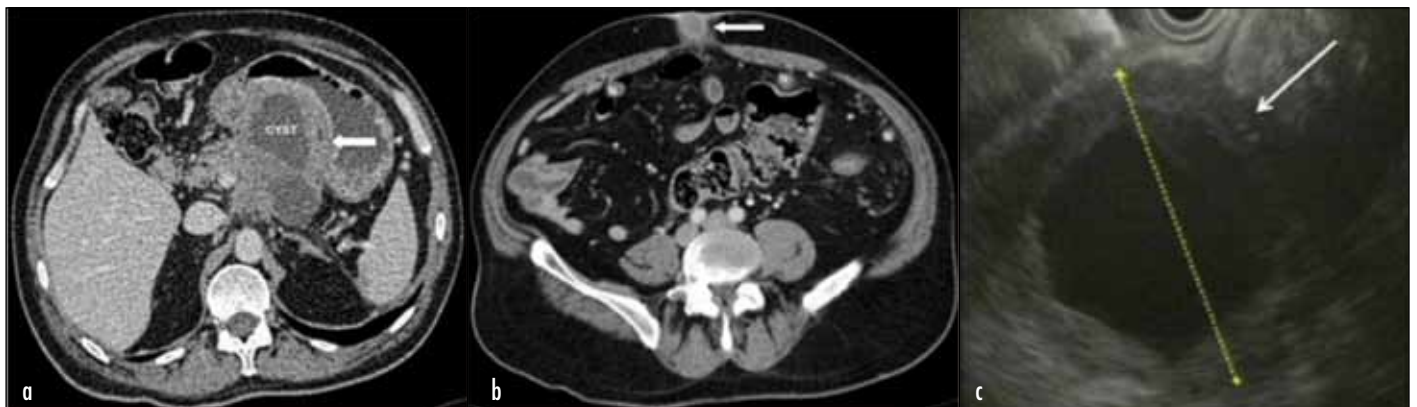


Figure 6. Serous cystadenoma. Incidental finding of pancreatic cystic lesion identified on magnetic resonance imaging scan for investigation of endometrial polyps. a. Axial computed tomography performed in the portal venous phase demonstrates a 4.5 cm mass in the pancreatic head containing multiple cystic spaces of < 2 cm (arrow). b. Radial endoscopic ultrasound demonstrates a 'honeycomb'-like cyst in the pancreatic head (white arrow) with posterior acoustic enhancement (black arrows) characteristic of serous cystadenoma.

Computed tomography features of mucinous cystic neoplasms include enhancing septa and solid intramural nodules (*Figures 7a and 7b*). A characteristic feature is peripheral calcification, seen in 10–25% of these lesions (Buetow et al, 1998) and allowing differentiation from other cystic lesions. An important feature of a mucinous cystic neoplasm is that it does not communicate with the pancreatic duct.

Endoscopic ultrasound provides detailed assessment of internal architecture. The presence of intramural nodules, thickened septations and/or a solid component strongly raises the suspicion of malignancy (*Figure 7c*). Unfortunately these appearances are rarely enough for definitive diagnosis and cyst fluid analysis may be required if risk of tumour seeding is warranted. Endoscopic ultrasound-guided aspiration often demonstrates low amylase, high CEA (>200 ng/ml), high CA 19-9 (>50 000 U/ml) and high fluid viscosity (Rafique et al, 2007).

Figure 7. Metastatic mucinous cystadenocarcinoma in a patient who presented with epigastric pain. Transabdominal ultrasound identified a cystic lesion in the epigastrium. a. Axial computed tomography scan performed in the portal venous phase demonstrates a complex lesion involving the pancreatic body and tail with both solid (arrow) and cystic components. b. Note was made of a periumbilical cystic structure (arrow) and peritoneal nodules (N). c. Radial endoscopic ultrasound demonstrates a 32 mm thick-walled (arrow) pancreatic cyst with a solid component. Endoscopic ultrasound-guided aspiration revealed a high CEA (4390 ng/ml) and low amylase. Biopsy of the periumbilical nodule was performed which further confirmed the diagnosis.



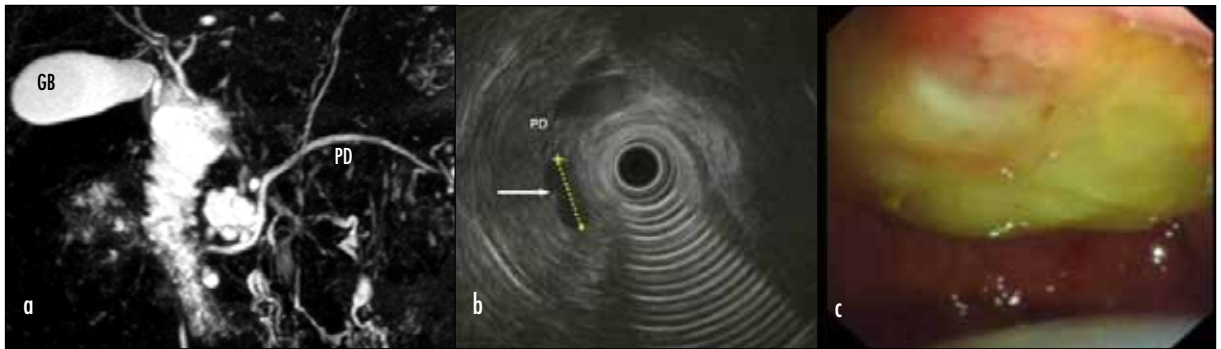


Figure 8. Intraductal papillary mucinous neoplasm. Incidental finding of a pancreatic cyst on computed tomography performed for investigation of small bowel obstruction. a. Coronal magnetic resonance imaging maximum intensity projection image demonstrated a multiloculated cystic structure (arrow) within the uncinate process of the pancreas which appeared to communicate with the main pancreatic duct (PD). b. Radial endoscopic ultrasound demonstrated a cystic structure (arrow) within the uncinate. c. The endoscopic view demonstrated a gaping papilla extruding mucin. GB = gallbladder.

All mucinous cystic neoplasms have malignant potential and surgical resection is recommended in those patients considered fit for surgery (Tanaka et al, 2006).

Intraductal papillary mucinous neoplasm

Intraductal papillary mucinous neoplasm is an intraductal mucin-producing tumour composed of tall mucin-producing epithelium. Intraductal papillary mucinous neoplasms are not lined by ovarian stroma in contrast to mucinous cystic neoplasms and are most commonly found in the pancreatic head arising from the main pancreatic duct, a side branch or both (Adsay et al, 2002). Intraductal papillary mucinous neoplasm has an increased frequency in men >60 years (Acar and Tatli, 2010). Like mucinous cystic neoplasms, intraductal papillary mucinous neoplasms can be divided into

subtypes according to amount of cellular atypia varying from benign adenoma to invasive malignancy; all have malignant potential.

The imaging appearance of intraductal papillary mucinous neoplasms varies according to type, i.e. main duct intraductal papillary mucinous neoplasm, branch duct intraductal papillary mucinous neoplasm or mixed. Typical features include a cystic lesion containing mucus located in the uncinate process, with a ‘grape-like’ locular appearance. Demonstration of communication with the pancreatic duct on magnetic resonance imaging favours intraductal papillary mucinous neoplasm as mucinous cystic neoplasms do not communicate with the duct (Lim et al, 2001) (Figure 8a).

The initial discovery of an intraductal papillary mucinous neoplasm is often made with cross-sectional imaging. Thin-cut computed tomography can demonstrate the cystic lesion and detect enhancing mural nodules. A main duct >10 mm and mural nodules are features associated with malignancy.

Endoscopic ultrasound provides high resolution imaging and allows endoscopic ultrasound-fine needle aspiration of mural nodules, thickened walls or septae and aspiration of cyst contents (Figure 8b). The endoscopic view provided by endoscopic ultrasound may show a gaping papilla extruding mucin (Figure 8c) – a characteristic sign. Cytological evidence of mucin producing epithelium in the absence of ovarian type stroma supports the diagnosis of an intraductal papillary mucinous neoplasm. Cyst aspirate often demonstrates low amylase, high CEA and high viscosity. Assessment of cyst mucin and CEA are complementary, with the best profile obtained when both markers are determined along with cytology (Morris-Stiff et al, 2010).

Conclusions

The diagnosis of pancreatic lesions requires a multimodality approach. Endoscopic ultrasound with or without fine needle aspiration provides vital additional information and plays an integral role in the staging of pan-

KEY POINTS

- With the increasing use and sensitivity of cross-sectional imaging modalities incidental detection of pancreatic lesions is becoming more common.
- Lesions can be characterized as solid or cystic and incorporate non-neoplastic and neoplastic disease.
- Benign and malignant lesions share several common imaging features and differentiation is often challenging.
- In the presence of chronic pancreatitis the ability of endoscopic ultrasound to distinguish between inflammatory mass and malignant lesion is limited.
- Mucinous cystic neoplasms and intraductal papillary mucinous neoplasms are potentially malignant and surgical resection should be considered.
- Preoperative diagnosis and staging of pancreatic lesions can be difficult and requires a multimodality approach.
- Endoscopic ultrasound with or without fine needle aspiration biopsy provides vital additional information and plays an integral role in the staging of pancreatic malignancy.
- When used in combination endoscopic ultrasound morphology and fine needle aspiration cytology or cyst fluid analysis is an accurate tool in determining the nature of solid and cystic pancreatic lesions.

creatic malignancy. When used in combination endoscopic ultrasound morphology, fine needle aspiration cytology and cyst fluid analysis are useful tools in determining the nature of pancreatic lesions. Accurate diagnosis and staging are essential to guide appropriate patient management. **BJHM**

Conflict of interest: none.

- Acar M, Tatli S (2010) Cystic tumors of the pancreas: a radiological perspective. *Diagn Interv Radiol* DOI 10.4261/1305-3825.DIR.3254-09.1
- Adsay NV, Conlon KC, Zee SY et al (2002) Intraductal papillary-mucinous neoplasms of the pancreas: an analysis of in-situ and invasive carcinomas in 28 patients. *Cancer* **94**(1): 62–7
- Alsohaibani F, Bigam D, Kneteman N, James Shapiro AM, Sandha GS (2008) The impact of preoperative endoscopic ultrasound on the surgical management of pancreatic neuroendocrine tumours. *Can J Gastroenterol* **22**(10): 817–20
- Ardengh JC, Lopes CV, Campos AD, Pereira de Lima LF, Venco F, Modena JLP (2007) Endoscopic ultrasound and fine needle aspiration in chronic pancreatitis: differential diagnosis between pseudotumoral masses and pancreatic cancer. *J Pancreas (Online)* **8**(4): 413–21
- Battula N, Srinivasan P, Prachalias A, Rela M, Heaton N (2006) Primary pancreatic lymphoma: diagnostic and therapeutic dilemma. *Pancreas* **33**(2): 192–4
- Belsley NA, Pitman MB, Lauwers GY, Brugge WR, Deshpande V (2008) Serous cystadenoma of the pancreas. Limitations and pitfalls of endoscopic-ultrasound-guided-fine-needle aspiration biopsy. *Cancer Cytopathol* **114**(2): 102–10
- Boni L, Benevento A, Dionigi G, Cabrini L, Dionigi R (2002) Primary pancreatic lymphoma. *Surg Endosc* **16**: 1105–10
- Bottger T, Boddin J, Duber C, Heintz A, Kuchle R, Junginger T (1998) Diagnosing and staging of pancreatic carcinoma. What is necessary? *Oncology* **55**: 122–9
- Bounds BC, Brugge WR (2001) EUS diagnosis of cystic lesions of the pancreas. *Int J Gastrointest Cancer* **30**: 27–31
- Brugge WR (2004) Evaluation of pancreatic cystic lesions with EUS. *Gastrointest Endosc* **59**: 698–707
- Buetow PC, Rao P, Thompson LD (1998) Mucinous cystic neoplasms of the pancreas: radiologic-pathologic correlation. *Radiographics* **18**: 433–49
- Cem Balci N, Semelka RC (2001) Radiologic diagnosis and staging of pancreatic ductal adenocarcinoma. Radiologic diagnosis and staging of pancreatic ductal adenocarcinoma. *Eur Radiol* **38**: 105–12
- Curry CA, Eng J, Horton KM, Urban B, Siegelman S, Kuszyk BS, Fishman EK (2000) CT of primary cystic pancreatic neoplasms: can CT be used for patient triage and treatment? *AJR Am J Roentgenol* **175**: 99–103
- Edirimanne S, Connor SJ (2008) Incidental pancreatic cystic lesions. *World J Surg* **32**: 2028–37
- Fasanella KE, McGrath K (2009) Cystic lesions and intraductal neoplasms of the pancreas. *Best Pract Res Clin Gastroenterol* **23**: 35–48
- Frankel WL (2006) Update on pancreatic endocrine tumours. *Arch Pathol Lab Med* **130**: 963–6
- Goldin GB, Bradner MW (2007) Assessment of pancreatic neoplasms: review of biopsy techniques. *J Gastrointest Surg* **11**: 783–90
- Gouya H, Vignaux O, Augui J et al (2003) CT, endoscopic sonography, and a combined protocol for preoperative evaluation of pancreatic insulinomas. *AJR* **181**: 987–92
- Hartwig W, Schneider L, Diener MK, Bergman F, Buchler MW, Werner J (2009) Preoperative tissue diagnosis for tumours of the pancreas. *Br J Surg* **96**: 5–20
- Kalra MK, Maher MM, Mueller PR, Saini S (2003) State-of-the-art imaging of pancreatic neoplasms. *BJR* **76**: 857–65
- Kim YH, Saini S, Sahani D, Hahn PF, Mueller PR, Auh YH (2005) Imaging diagnosis of cystic pancreatic lesions: pseudocyst versus nonpseudocyst. *Radiographics* **25**: 671–85
- Krishna NB, LaBundy JL, Saripalli S, Safdar R, Agarwal B (2009) Diagnostic value of EUS-FNA in patients suspected of having pancreatic cancer with a focal lesion on CT scan/MRI but without obstructive jaundice. *Pancreas* **38**: 625–30
- Lim JH, Lee G, Oh YL (2001) Radiologic spectrum of intraductal papillary mucinous tumour of the pancreas. *Radiographics* **21**: 323–37
- Luo G, Jin C, Fu D, Long J, Yang F, Ni Q (2009) Primary pancreatic lymphoma. *Tumori* **95**: 156–9
- Merkle EM, Bender GN, Brambs HJ (2000) Imaging findings in pancreatic lymphoma. *AJR* **174**: 671–5
- Michl P, Pauls F, Gress TM (2006) Evidence-based diagnosis and staging of pancreatic cancer. *Best Pract Res Clin Gastroenterol* **20**: 227–51
- Morris-Stiff G, Lentz G, Chalikhonda S et al (2010) Pancreatic cyst aspiration analysis for cystic neoplasms: mucin or carcinoembryonic antigen—which is better? *Surgery* **148**(4): 638–45
- National Comprehensive Cancer Network (2009) *Clinical practice guidelines in oncology: Pancreatic adenocarcinoma*. www.nccn.org/professionals/physicians_gls/PDF/pancreatic.pdf (accessed 28 January 2011)
- O'Toole D, Palazzo L, Hammel P et al (2004) Macrocystic pancreatic cystadenoma: the role of EUS and cyst fluid analysis in distinguishing mucinous and serous lesions. *Gastrointest Endosc* **59**(7): 823–9
- Oberg K, Eriksson B (2005) Endocrine tumours of the pancreas. *Best Pract Res Clin Gastroenterol* **19**(5): 753–81
- Peddu P, Quaglia A, Kane PA, Karani JB (2009) Role of imaging in the management of pancreatic mass. *Crit Rev Oncol Hematol* **70**: 12023
- Pitman MB, Deshpande V (2007) Endoscopic ultrasound-guided fine needle aspiration cytology of the pancreas: a morphological and multimodal approach to the diagnosis of solid and cystic mass lesions. *Cytopathology* **18**: 331–47
- Prayer L, Schurawitzki H, Mallek R, Mostbeck G (1992) CT in pancreatic involvement of non-Hodgkin lymphoma. *Acta Radiol* **33**: 123–7
- Prokesch RW, Chow LC, Beaulieu CF (2002) Isoattenuating pancreatic adenocarcinoma at multi-detector row CT: secondary signs. *Radiol* **224**: 764–8
- Rafique A, Freeman S, Carrol N (2007) A clinical algorithm for the assessment of pancreatic lesions: utilization of 16- and 64-section multidetector CT and endoscopic ultrasound. *Clin Rad* **62**: 1142–53
- Reznek RH (2006) CT/MRI of neuroendocrine tumours. *Cancer Imaging* **31**(6): 163–77
- Rockall AG, Reznek RH (2007) Imaging of neuroendocrine tumours (CT/MR/US). *Best Pract Res Clin Endocrinol Metab* **21**(1): 43–68
- Săftoiu A, Vilman P (2009) Role of endoscopic ultrasound in the diagnosis and staging of pancreatic cancer. *J Clin Ultrasound* **37**(1): 1–17
- Seicean A (2010) Endoscopic ultrasound in chronic pancreatitis: Where are we now? *World J Gastroenterol* **16**(34): 4253–63
- Tanaka M, Chari S, Adsay V et al (2006) International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatol* **6**(1-2): 234–46
- Thirumurthi S, Adler DG (2006) Pancreatic adenocarcinoma. *Hosp Physician* **Aug**: 39–49
- To'o KJ, Raman SS, Yu NC et al (2005) Pancreatic and peripancreatic diseases mimicking primary pancreatic neoplasia. *Radiographics* **25**(4): 949–65
- Tsitouridis I, Diamantopoulou A, Michaelides M, Arvanity M, Papaioannou S (2010) Pancreatic metastases: CT and MRI findings. *Diagn Interv Radiol* **16**: 45–51
- Varadarajulu S, Wallace MB (2004) Applications of endoscopic ultrasonography in pancreatic cancer: neuroendocrine tumors. *Cancer Control* **11**(1): 15–22
- Visser BC, Muthusamy VR, Mulvihill SJ, Coakley F (2004) Diagnostic imaging of cystic pancreatic neoplasms. *Surg Oncol* **13**: 27–39
- Yasuda K, Mukai H, Nakajima M (1995) Endoscopic ultrasonography diagnosis of pancreatic cancer. *Gastrointest Endosc Clin N Am* **5**: 699–712