CME Article

# Cystic pancreatic lesions: a pictorial review and management approach

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## ABSTRACT

**The majority of cystic pancreatic lesions are incidental findings, especially with the increasing use of advanced imaging modalities for non-related conditions. Most of these lesions were previously attributed to pseudocysts, although cystic neoplasms are now an important differential to be considered and excluded. This article aims to describe the types of cystic pancreatic lesions, demonstrate their imaging findings and discuss the management of these conditions.**


**Keywords: cystic pancreatic lesion, intraductal papillary mucinous tumour, mucinous cystic neoplasm, pseudocyst, serous cystadenoma**

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## INTRODUCTION

Most cystic pancreatic lesions occur as incidental findings. They are encountered with increasing frequency as more sensitive imaging modalities are performed for non-related conditions.[1-8] The four most common types are pancreatic pseudocyst, serous cystic pancreatic neoplasm, mucinous cystic neoplasm (MCN) and intraductal papillary mucinous tumour (IPMT).[4] The older literature attributes the majority of these lesions to pseudocysts.[5] However, with the widespread use of imaging for the screening of asymptomatic individuals, there has been an increase in the number of cystic pancreatic neoplasms.[5] While clinical findings may be helpful in diagnosing pseudocysts, the challenge lies in differentiating the remaining cystic lesions, which has implications on their management.

## CLASSIFICATION

### Inflammatory pseudocyst

Patients are likely to provide a history of acute or chronic pancreatitis. Pseudocysts are unilocular, have a thin wall (< 4 mm) and rarely have internal septations.[1] Known complications are that of a super-imposed infection or haemorrhage (Fig. 1). Associated findings in the pancreas may include ductal dilatation and intraductal calculi, as well as gland atrophy and parenchymal calcification with chronicity.[1]

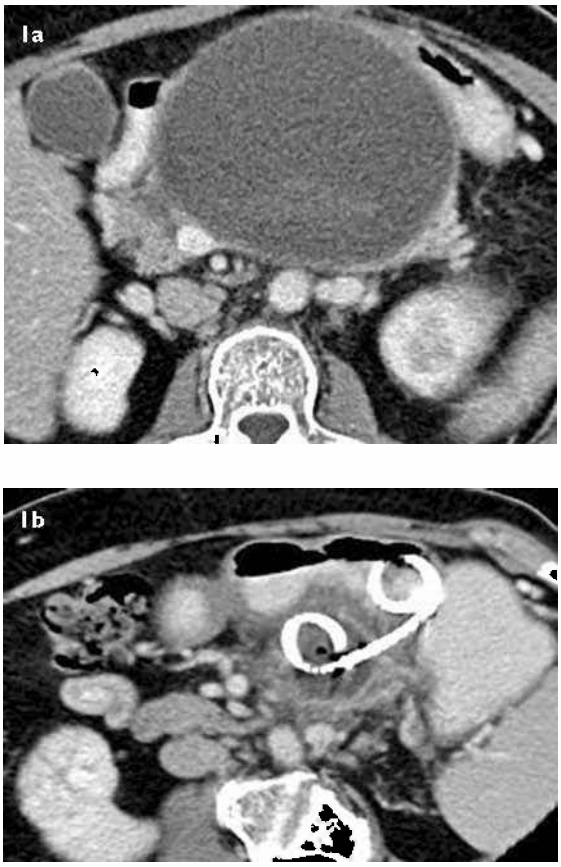
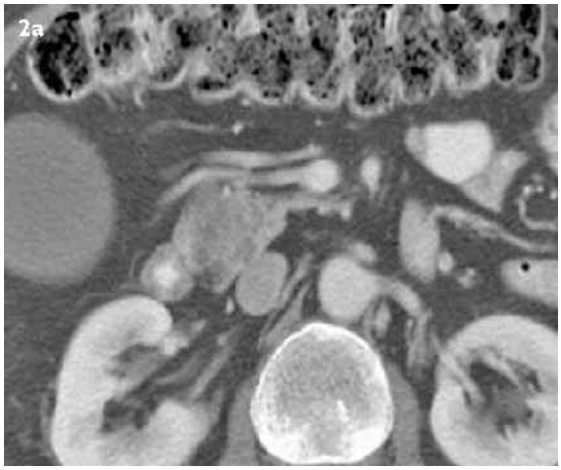


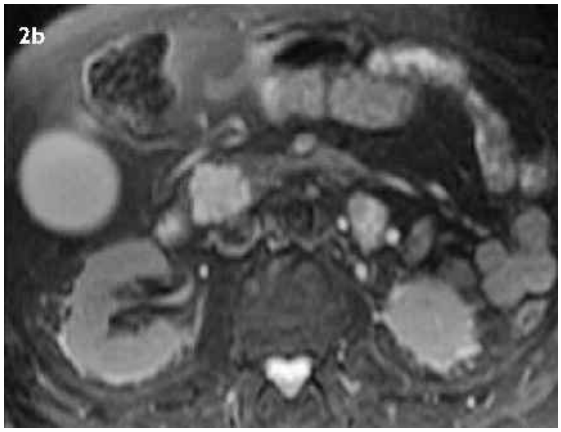

**Fig. 1** Pancreatic pseudocyst. (a) CT image shows a large cyst in the epigastrium with faint density within, likely from haemorrhage. (b) Follow-up CT image post-drainage shows decompression of the cyst and drain tube *in situ*.

### True cystic neoplasm of the pancreas

Approximately 90% of these encompass the serous and mucinous cystic neoplasms.[3] The remaining 10% include lesions such as solid pseudopapillary neoplasm, neuroendocrine tumour, acinar cystadenocarcinoma and lymphangioma.

Serous cystadenoma is commonly seen in women above 60 years of age.[1,3,9] It has a uniform distribution throughout the pancreas.[1] Usually composed of a cluster of microcysts (1–20 mm in size) and intervening septae, its appearance resembles a "honeycomb" (Figs. 2 & 3).[2] However, 20% of serous cystadenomas are macrocystic,



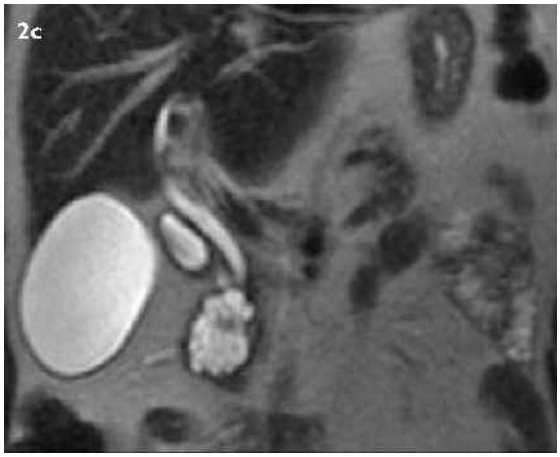
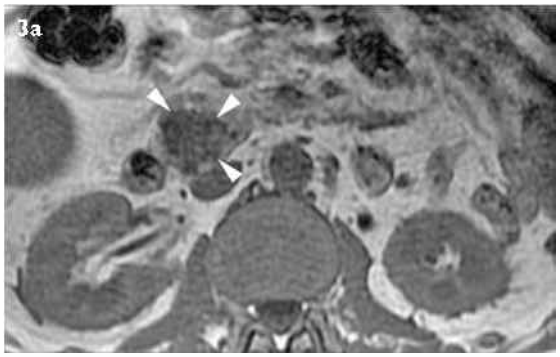




**Fig. 2** Serous cystadenoma in pancreatic head. (a) Axial CECT and (b) axial MR T2-W FSE images show a typical "honeycomb" appearance. (c) Coronal MR SSFSE image shows the central fibrous scar.



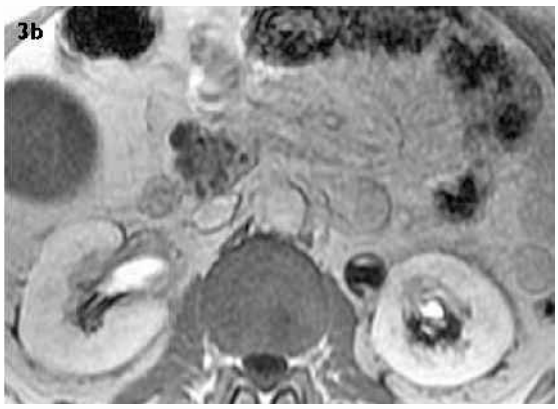




**Fig. 3** Serous cystadenoma in the pancreatic head (arrowheads). (a) Unenhanced and (b) post-contrast T1-W MR images show enhancement of the internal septae.

with some appearing solid,[1] while 20% of them show a calcified "central scar", which is a highly diagnostic feature (Fig. 4).[1,2] They have a glycogen-rich epithelial lining. Symptoms, if any, are usually related to a large size and pressure effect on the surrounding structures. The condition has a benign course, as the occurrence of serous cystadenocarcinoma is very rare, with about 20 cases reported to date.[3,8,9]

MCN represents a spectrum of neoplasms, from the benign mucinous cystadenoma to the frankly malignant cystadenocarcinoma. MCNs are found in women 40–50 years of age, and have a predisposition toward the pancreatic body or tail.[1,3,10] They are typically unilocular (Fig. 5), although some may comprise a few macrocysts,[1] usually measuring > 2 cm.[2] The contents of these lesions may be mucin, haemorrhage or debris.[2] No communication is demonstrated with the ductal system.[1] They are characterised by a mucin-secreting ovarian-type stroma, thus accounting for its almost exclusive occurrence in the female gender,[1,11] and a spectrum ranging from hyperplasia to invasive carcinoma, sometimes coexisting within the same tumour.[11] Malignant lesions tend to be large and may have thickened walls or septations,[1] as well as internal papillary excrescences.[2] Peripheral eggshell calcification is uncommon but specific and highly predictive of cancer (Fig. 6).[1]

An IPMT is an intraductal pancreatic tumour formed by papillary proliferation of mucin-producing cells, first described by Ohhasi in 1982. It has an equal gender distribution and an incidence in the sixth to seventh decades of life.[1,3] Unlike MCN, this usually occurs in the head or body of the pancreas.[1,4,11] Furthermore, it is distinguished from the latter by its communication

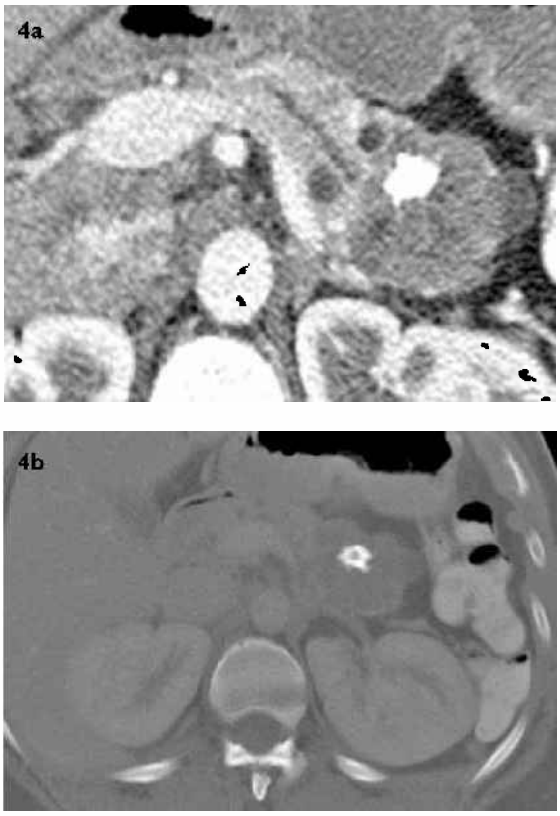



**Fig. 4** (a) Axial CECT image in the soft tissue window shows a serous cystadenoma in the pancreatic tail with classical central calcification, more conspicuous on the bone window. (b) Incidental finding of two more epithelial cysts adjacent to the aforementioned tumour.

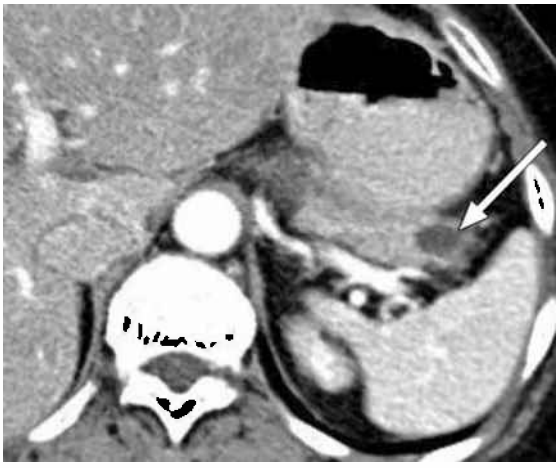


**Fig. 5** Axial CECT image shows a mucinous cystadenoma in the pancreatic tail (arrowhead).

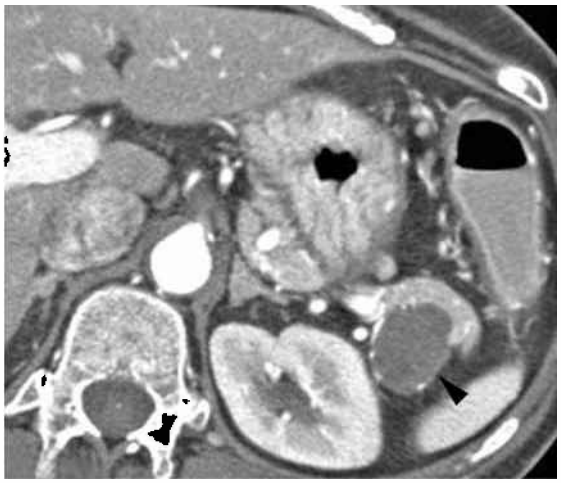


**Fig. 6** Axial CECT image shows a mucinous cystadenocarcinoma in the pancreatic tail (arrowhead) with rim-calcification, a predictor of malignancy.

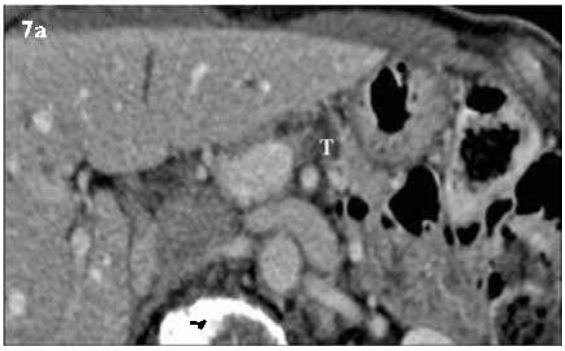
with the ductal system (Figs. 7–9)[1] and the lack of an ovarian-type stroma. The main-duct type (MDT-IPMT) and/or branch-duct type (BDT-IPMT) of IPMTs exist.[7,10] The characteristic findings on ultrasonography (US) or endoscopic ultrasonography (EUS) for MDT-IPMTs include segmental or diffuse dilatation of the main pancreatic duct (MPD), whereas BDT-IPMTs appear as "grape-like" clusters of dilated branch ducts, with a normal calibre of the MPD.[4,10] In addition, an enlarged and patulous papilla with mucin excretion from its orifice may be appreciated during endoscopy (Fig. 10).[1,4,10]

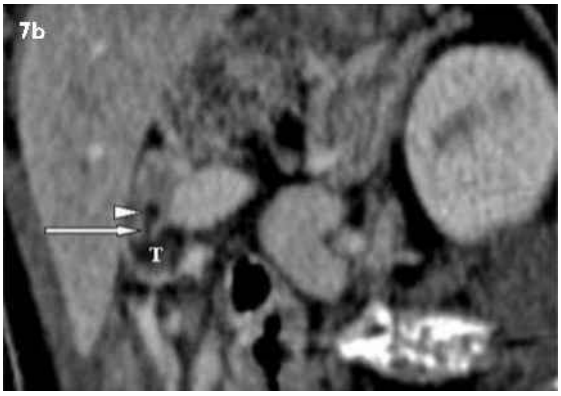
IPMTs are also classified according to the degree of epithelial dysplasia, ranging from adenoma, borderline tumour, carcinoma *in situ* and infiltrative carcinoma,[4,7,10] with a higher incidence of malignancy in MDT-IPMT.[1,7,10,11] Dilatation of the MPD > 10–15 mm in MDT-IPMT or in its side branches, and a tumour size > 3 cm (for BDT-IPMT) are considered by some authors to herald malignant change.[1,10,11] However, focal wall thickening > 3 mm and the presence of mural nodules (> 3 mm) appear to be more useful discriminators (Fig. 11).[10,11]

Other true cystic neoplasms of the pancreas include solid pseudopapillary (Frantz or Hamoudi) (Fig. 12) and neuroendocrine tumours. The former are found in children and women in their forties, usually of black or East Asian descent.[1,12] They have a predisposition for the pancreatic body and tail. Imaging findings reveal a large well-encapsulated mass with cystic as well as haemorrhagic degeneration, sometimes forming a fluid-debris level. Approximately one-third show calcification, which is peripheral.[12] These lesions have a low-grade potential for the development of cancer and a better prognosis than adenocarcinoma, even with a large tumour mass and metastases at presentation.[1] Neuroendocrine tumours (Fig. 13) have an equal gender predisposition, and occur in the fifth to sixth decade of life.[1] The majority of these tumours turn out to be non-functioning islet cell tumours.[13]

**Cystic degeneration in an otherwise solid pancreatic tumour**

Pancreatic adenocarcinoma is the commonest



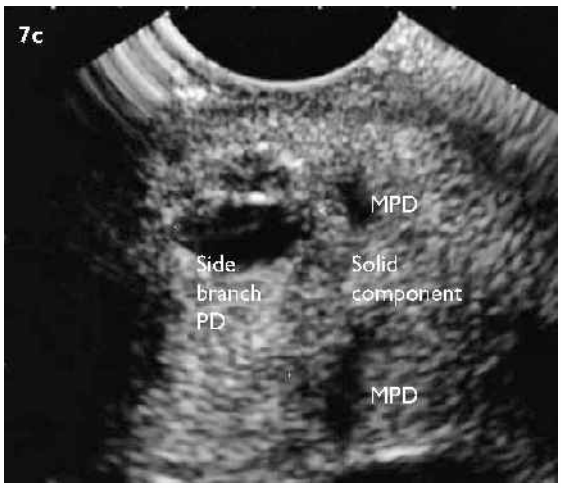
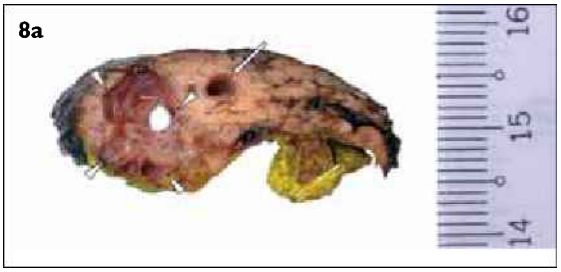




**Fig. 7** Side-branch intraductal papillary mucinous tumour. (a) Axial CT image at a level inferior to the main pancreatic duct (MPD) shows a cystic lesion (T). (b) Sagittal reformat and (c) endoscopic ultrasonography were necessary to demonstrate communication (arrow) with the MPD (arrowhead), otherwise not appreciated on the axial image.

primary pancreatic tumour, but it rarely undergoes cystic degeneration (Fig. 14).[9,12,13] Most secondary tumours involving the pancreas are also solid, with cystic metastases or cystic degeneration in a metastasis being exceedingly rare.[13] Imaging findings would be that of a mass with an associated fluid component.

**True epithelial cyst**

These include simple true cysts or cysts associated



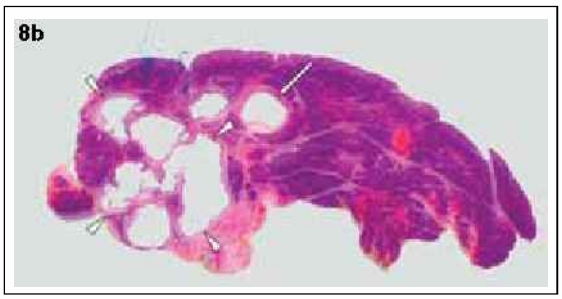




**Fig. 8** Side-branch intraductal papillary mucinous tumour. (a) Photograph of the gross specimen and (b) photomicrograph from Whipple resection show the main pancreatic duct (arrow) and dilated side-branch (arrowheads) (Haematoxylin & eosin, × 1).

with syndromes such as Von Hippel-Lindau (Fig. 15), polycystic diseases and cystic fibrosis, and are generally benign incidental findings.

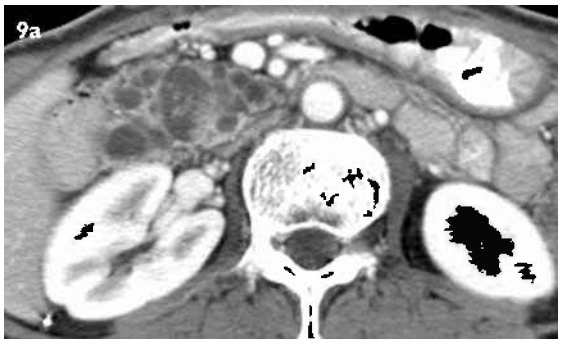
## IMAGING APPROACH AND MANAGEMENT

**Pancreatitis and pancreatic pseudocysts**

An important initial step is to differentiate a pancreatic pseudocyst from other cystic pancreatic neoplasia. Clinical symptoms and signs of pancreatitis should be sought. The imaging findings of a unilocular, thin-walled cyst without internal septation or a solid component are characteristic. If necessary, EUS and fine needle aspiration (FNA) of cyst contents may be performed to look for an elevated amylase level. Once diagnosed, treatment is directed at the underlying cause of pancreatitis. Drainage of the pseudocyst may also be attempted (Fig. 1b). Upon exclusion of a pseudocyst, the challenge lies in differentiating the various true cystic neoplasms, in particular, between a serous and a mucinous lesion. Cystic degeneration in a solid pancreatic tumour may be an added confounder.

**Serous and mucinous neoplasia and features of malignancy in these lesions**

Although the cystic lesion may be initially detected on US, multi-detector computed tomography with multiplanar reformats, magnetic resonance (MR) imaging and MR cholangiopancreatography should be performed in all cases.[1] The appearance of the lesion is important, whether it conforms to a cluster of microcysts with a



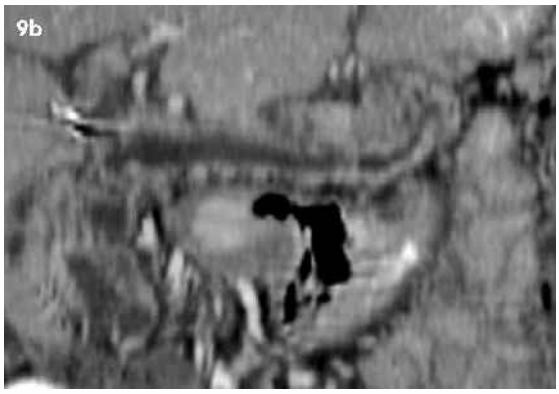




**Fig. 9** A patient with combined main and side-branch intraductal papillary mucinous tumour. (a) Axial CECT image shows a multicystic mass in uncinate process with associated solid component. (b) Curved-reformatted CT image shows contiguity with a grossly dilated main pancreatic duct.

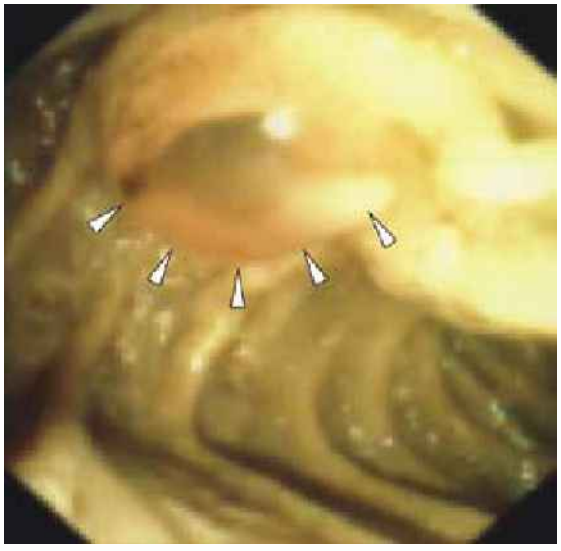


**Fig. 10** Endoscopic image shows an enlarged and patulous papilla with copious mucin excretion from the orifice (arrowheads).

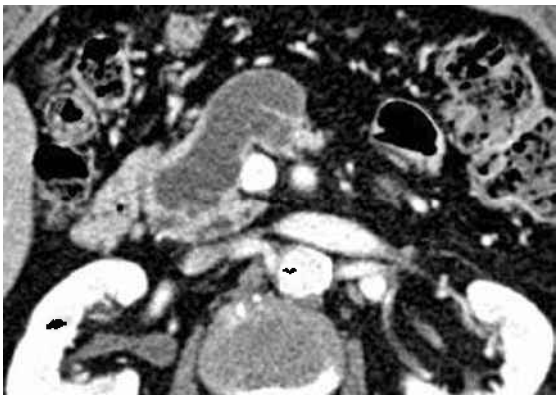


**Fig. 11** Axial CECT image of a main-duct intraductal papillary mucinous tumour shows a dilated main pancreatic duct with mural nodule within, suspicious for malignant change.

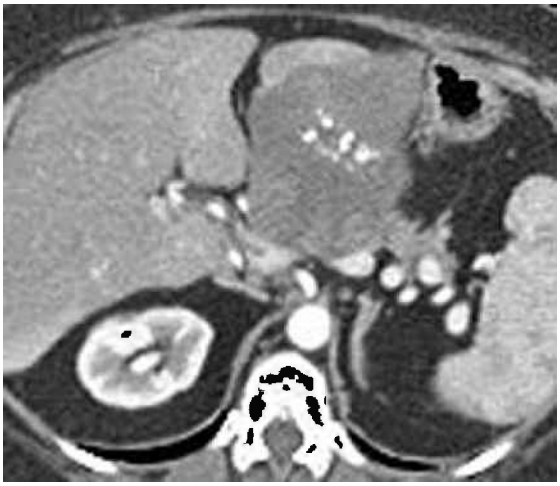


**Fig. 12** Axial CECT image shows a solid pseudopapillary tumour with punctuate central, rather than peripheral calcifications.

possible calcified central scar (i.e. serous cystadenoma) or several macrocysts (i.e. mucinous cystadenoma). Imaging features, such as thickened walls or septae, papillary excrescences and calcification in the latter, would be suspicious for malignant change. IPMTs classically communicate with the pancreatic ductal system. However, failure to demonstrate communication with the MPD does not exclude an IPMT. The imaging predictors of malignancy include the presence of thick walls, mural nodules and an MPD > 10–15 mm in diameter. Clinical predictors of malignant change include age > 70 years, weight loss and jaundice.[3,6-8] The incidence of malignancy or potential malignancy in mucinous lesions increases from 73% to 90% in symptomatic individuals.[3] A trial utilising positron emission tomography to separate malignant from benign lesions has revealed no significant difference in their standardised uptake values.[14]

**Role of endoscopic ultrasonography**

EUS has a higher sensitivity and accuracy, compared to US or CT, in the differential diagnoses of cystic pancreatic lesions and to better stage IPMT.[1,4,10,15] EUS-guided FNA of cystic fluid for cytology is generally performed, but the false negative rate is high due to the paucity of cells in most cysts or dilution as a result of communication with the pancreatic ducts.[2] The

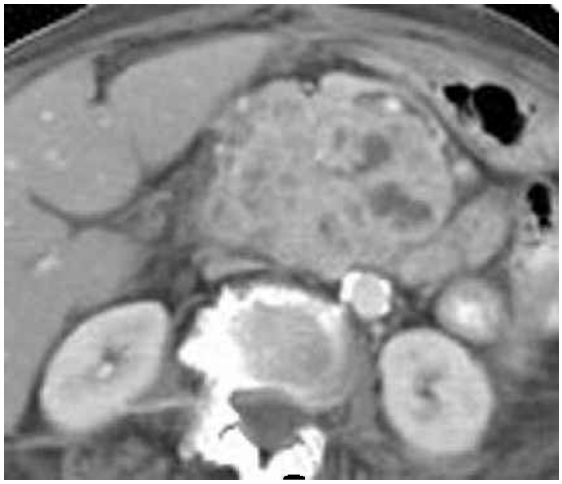


**Fig. 13** Axial CECT image shows a neuroendocrine tumour in the pancreatic body.

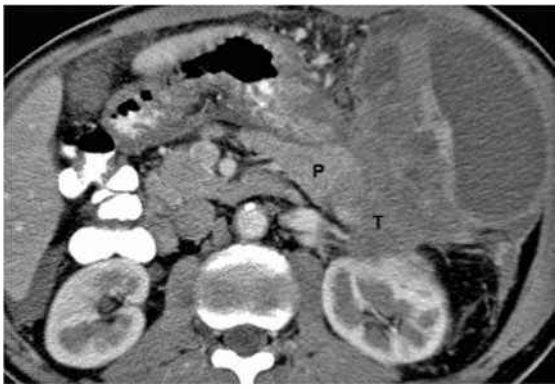



**Fig. 14** Axial CECT image shows cystic degeneration of adenocarcinoma (T) arising from the pancreatic tail (P). Note the ill-defined margin at the anterior left kidney as well as the free fluid in the peri-hepatic and peri-splenic spaces, suspicious for cyst rupture.

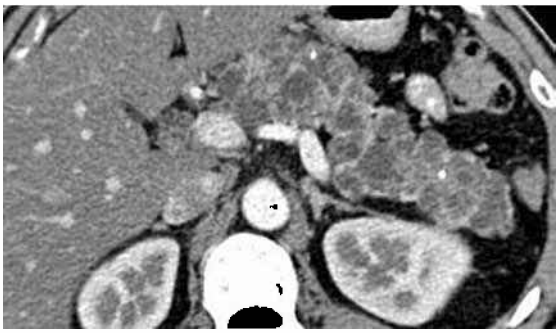


**Fig. 15** Axial CECT image of a patient with Von Hippel-Lindau syndrome with multiple cysts in the pancreas.

cellular yield may be increased by targeted FNA of the cyst wall or any solid component (e.g. mural nodule), if present. Occasionally, FNA of a non-pancreatic cyst (e.g. mesenteric duplication cyst) may lead to a false-positive result.[2] Biochemical analysis of the cyst fluid is often more useful than cytological analysis. The biochemical tests often include tests for the presence of mucin and amylase as well as tumour markers, especially carcinoembryonic antigen (CEA).[2,5] Mucin-rich fluid is found with mucinous, but not serous neoplasms. The additional finding of amylase in cyst fluid suggests communication with the pancreatic ductal system, and thus a positive result in IPMTs.[1] The best test for differentiating serous from mucinous neoplasms, with an accuracy of 79%, is an elevated CEA level ≥ 192 ng/ml in the latter,[1,3,5,8,15] as concluded by the Cooperative Pancreatic Cyst Study.[3]

However, EUS-FNA is not recommended in resectable cases[1] when a cystic lesion suspicious for malignancy is located in the pancreatic body or tail, in view of the risk of needle-tract seeding.[2,6] It is less of an issue if the lesion is located in the pancreatic head because a Whipple operation, if indicated, would remove the needle tract en bloc.

**Surgical management of cystic pancreatic lesions**

International consensus guidelines allow for close follow-up for an incidentally discovered, small (≤ 3 cm) cystic tumour with no suspicious imaging features in an asymptomatic individual, as there is only a 3.3% risk of occult malignancy in this lesion, which is almost parallel to the mortality rate from pancreatic resection.[8,15] However, surgery is recommended for a cystic lesion > 3 cm, in association with a solid component in a good pre-morbid symptomatic patient, or if the lesion is confirmed to be mucinous in nature,[1,15] as these are considered to be pre-malignant.[3] Annual or biannual imaging may be performed, and resection is suggested in surgically fit candidates who develop symptoms, or if the cyst shows a progressive increase in size.[3,6,15] MCN, which is predominantly in the pancreatic tail, usually requires a distal pancreatectomy and a possible splenectomy.[1]

In view of the high incidence of malignancy in MDT-IPMT, surgical intervention is advised.[11] IPMTs, having a predisposition for the pancreatic head, entail a Whipple procedure.[1] As these tumours grow longitudinally along the ducts rather than radially into the parenchyma, intraoperative frozen section is advised to confirm a negative surgical margin in order to prevent recurrence.[1,10] Up to 19% of IPMTs require total pancreatectomy. Surgery is also recommended for BDT-IPMTs that show malignant features.[11] Otherwise, the development of BDT-IPMTs is slow, and follow-up may be adequate in lesions < 2.5 cm that have a thin wall and normal MPD,[10] as well as in the elderly, in patients with high surgical risk and in those who would otherwise require total pancreatectomy for multiple lesions.[11]

Although the occurrence of malignancy in serous cystadenoma has rarely been reported, it is generally safe to monitor it non-operatively.[3] Surgery can be considered for those with symptoms (e.g. pressure effect).[5] If resection is attempted, the type of surgery will depend on its location, given that it has a uniform distribution in the pancreas when compared to mucinous neoplasms. Whipple procedure is recommended for a proximal lesion and middle/distal pancreatectomy for a more distal lesion.[1]

Enucleation has been reported for smaller and benign cystic lesions without surrounding inflammation or local invasion. Its advantages include a shorter operative time with less blood loss and the preservation of pancreatic parenchyma, particularly for a lesion at the uncinate, head, neck and body.[16] Pancreatic fistulas occur in one-third of cases, with most resolving non-operatively.[17] This technique has been refined with the use of intraoperative US and post-enucleation closure of the pancreatic defect.[16] Solid pseudopapillary[12] and neuroendocrine[18] tumours also warrant surgical resection as these have high cure rates. Treatment for cystic degeneration within a pancreatic adenocarcinoma or metastasis is dependent on the stage of the disease.

## FOLLOW-UP AND PROGNOSIS

Although surgery is a definitive procedure, it is noteworthy that pancreatic resection carries a morbidity rate as high as 58%, as quoted in the literature.[3,8,15] These morbidities include complications of fistula formation, pancreatic exocrine insufficiency and susceptibility to infections, if splenectomy is also performed. Some of these complications may require a lengthy hospital stay. The mortality rate in a surgically fit candidate is under 5%. Follow-up imaging is justified in the setting of IPMT, given that there is a 7% recurrence rate in the pancreatic remnant.[7] The prognosis after the resection of MCN (without trans-mural invasion) is nearly 100%.[1] For IPMT without invasive features, the five- and ten-year survival rates are 100%,[7] while the rates are over 50% for those with invasive carcinoma. These fare much better in comparison with pancreatic adenocarcinomas and pancreatic secondaries, which have poorer prognoses.[2,7]

## CONCLUSION

As cystic pancreatic lesions are being detected with increasing frequency, the challenge lies in making an accurate diagnosis so as to guide appropriate management. We have highlighted the imaging findings and the clinical approach with regard to the treatment of these lesions. Of importance is the ability to distinguish pancreatic pseudocysts and serous cystadenomas from the rest of the lesions, as these may be conservatively managed, thus avoiding unnecessary resection and concomitant morbidity/mortality, and to differentiate mucinous neoplasia from pancreatic adenocarcinomas, as the former has a better prognosis.

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# SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
## Multiple Choice Questions (Code SMJ 201008B)

| | True | False |
|---|---|---|
| **Question 1.** The following is the differential diagnosis/diagnoses of cystic neoplasms of the pancreas: | | |
| (a) Serous cystadenoma. | ☐ | ☐ |
| (b) Solid pseudopapillary tumour of the pancreas. | ☐ | ☐ |
| (c) Can present as vomiting and abdominal pain. | ☐ | ☐ |
| (d) Pancreatic lymphoma. | ☐ | ☐ |
| **Question 2.** Regarding cystic lesions of the pancreas: | | |
| (a) Serous cystic neoplasms are usually benign. | ☐ | ☐ |
| (b) Serous cystic neoplasms usually communicate with the main pancreatic duct. | ☐ | ☐ |
| (c) Intraductal papillary mucinous tumours (IPMTs) can be reliably differentiated from pseudocysts by demonstration of communication with the main pancreatic duct. | ☐ | ☐ |
| (d) Cystic degeneration of adenocarcinoma is a common occurrence. | ☐ | ☐ |
| **Question 3.** Regarding true cystic pancreatic neoplasms: | | |
| (a) All IPMTs are associated with a dilated main pancreatic duct. | ☐ | ☐ |
| (b) Both main-duct type (MDT-IPMT) and branch-duct type (BDT-IPMT) intraductal papillary mucinous tumours never co-exist. | ☐ | ☐ |
| (c) Mucinous cystic neoplasms are almost always benign. | ☐ | ☐ |
| (d) Solid pseudopapillary tumours are associated with better prognosis than adenocarcinoma of the pancreas. | ☐ | ☐ |
| **Question 4.** Regarding IPMTs: | | |
| (a) They are more commonly found in the tail of the pancreas. | ☐ | ☐ |
| (b) Ovarian-type stroma is characteristic of these lesions. | ☐ | ☐ |
| (c) They may have a "cluster of grape" like appearance on endoscopic ultrasonography. | ☐ | ☐ |
| (d) A diameter of the main pancreatic duct > 15 mm is suspicious for malignant change in an IPMT. | ☐ | ☐ |
| **Question 5.** In a favourable pre-morbid patient, surgery is indicated for: | | |
| (a) 1-cm cystic tumour of the pancreas with no mural nodules. | ☐ | ☐ |
| (b) 5-cm cystic tumour with solid mural components. | ☐ | ☐ |
| (c) Suspected MDT-IPMT. | ☐ | ☐ |
| (d) 2-cm simple epithelial cyst of the pancreas. | ☐ | ☐ |

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**Doctor's particulars:**

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

**SUBMISSION INSTRUCTIONS:**
(1) Log on at the SMJ website: http://www.sma.org.sg/cme/smj and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

**RESULTS:**
(1) Answers will be published in the SMJ October 2010 issue. (2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 22 October 2010. (3) All online submissions will receive an automatic email acknowledgment. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

**Deadline for submission: (August 2010 SMJ 3B CME programme): 12 noon, 15 October 2010.**