Pancreatic Cystic Lesions

Understanding the condition and treatment management options

by Dr Wong Jen San

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Pancreatic cystic lesions are being identified with increasing frequency. They range from inflammatory or benign types to precancerous or frankly malignant lesions. Most of these cysts are asymptomatic and are incidental findings due to the growing use of cross-sectional imaging.

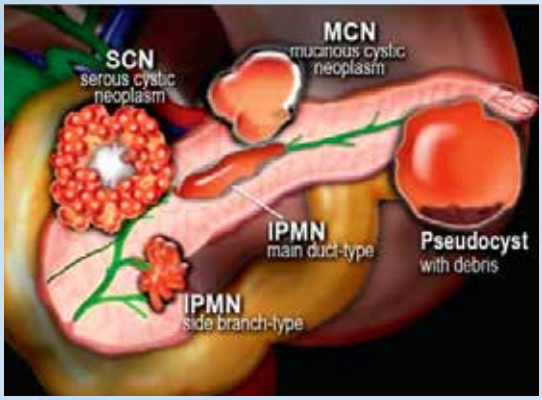

Figure 1. ***Classifications of pancreatic cystic lesions.***

Pancreatic cysts may be classified into inflammatory non-neoplastic pseudocysts or true pancreatic cystic neoplasms (PCNs) **[Figure 1].** Pseudocysts arise on a background of pancreatitis, alcohol abuse, stone disease or abdominal trauma. The lesion is unilocular and commonly contains non-enhancing dependent debris. These lesions are benign and managed based on their symptoms.

The most common PCNs are intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs) and serous cystadenomas (SCAs). SCAs are benign but IPMNs and MCNs have malignant potential. Other cystic pancreatic lesions make up fewer than 10% of cases and include solid pseudopapillary neoplasms (SPNs), cystic pancreatic neuroendocrine neoplasms (CPENs), cystic degeneration in solid neoplasms and cystic adenocarcinoma of the pancreas.

Patients with symptomatic PCNs may present with jaundice, chronic abdominal pain, and recurrent pancreatitis if obstruction is present. They may also have back pain, weight loss, diarrhoea, anorexia, nausea and vomiting.

Management

The clinical management of PCNs requires a reliable strategy to identify the small minority of cysts with early invasive cancer or high grade dysplasia and to predict those precancerous lesions that may develop them in the future. Hence, accurate characterisation of these cystic lesions is essential for further management, either surgical or conservative **[Table 1].**

Table 1. ***Management of commonly encountered cystic lesions of the pancreas.***

Lesion	Malignant Potential	Recommendation
Pseudocyst	None	Referral to gastroenterologist or pancreatic surgeon if lesion is symptomatic
Serious cystadenoma	Very low (malignant lesion is termed serous cystadenocarcinoma)	Serial imaging annually for 3 years; referral to surgeon if lesion is asymptomatic or larger than 4cm; for patients at poor surgical risk, endoscopic ultrasound (fine-needle aspiration to confirm diagnosis and rule out malignancy)
Mucinous cystic neoplasm	6% to 36% prevalence of invasive carcinoma (malignant lesion is termed mucinous cystadenocarcinoma)	Resection if patient's condition allows surgery
Side-branch	6% to 46% risk of development of high-grade dysplasia or malignancy	Resection - if lesion is symptomatic, larger than 30mm, or mural nodules or main duct dilatation larger than 6mm is present; if lesion is not resectable, imaging follow-up* is recommended; yearly follow-up imaging if lesion is smaller than 10mm, 6- to 12-month follow-up imaging if 10-20mm, 6-month follow-uo if > 20mm
Main-duct intraductal papillary mucinous neoplasm	57% to 92% risk of development of high-grade dysplasia or malignancy within 5 years; follow-up typically not conducted because the prevalence of carcinoma and carcinoma in situ at diagnosis is high	Resection if patient's condition allows surgery
Solid pseudopapillary neoplasm	Low malignant potential	Resection if patient's condition allows surgery
Cystic pancreatic neuroendocrine neoplasm	Variable malignant potential	Resection if patient's condition allows surgery

** Follow-up guidelines are based on Sendai criteria*

Imaging plays the initial role in the management of cystic lesions of the pancreas. Dedicated multi-detector CT (MDCT) of the pancreas or MRI pancreas with MRCP helps to characterise the cyst and identify suspicious features such as cyst size >3cm, enhancing or thickened walls, solid nodules, dilated pancreatic ducts >5mm, and enlarged lymph nodes. MRI with its superior soft-tissue and contrast resolution better demonstrates the cystic nature and the internal structure of the cyst and has the advantage of demonstrating the relationship of the cyst to the pancreatic duct as is seen in IPMN.

Studies have suggested PET-CT to have better sensitivity and specificity in distinguishing benign from malignant PCNs. However, the limitations of PET-CT are higher cost, false-negative results for borderline tumours, and false positive results in post-biopsy and pancreatitis areas.

Endoscopic ultrasound (EUS) is an excellent imaging technique to detect suspicious features in the cystic lesions with the added benefit of being able to sample the cyst fluid. The use of EUS and fine needle aspiration (FNA), with the analysis of cyst fluid cytology, carcinoembryonic antigen (CEA) and amylase levels, has assisted greatly in the diagnosis of these lesions. Cyst fluid CEA is useful for the diagnosis of mucinous cystic lesions (MCN and IPMN). Meanwhile, the presence of amylase in cyst fluid indicates a communication with the pancreatic duct. Hence, SCAs and MCNs have low amylase levels while IPMNs and pseudocysts have high amylase levels. However, the disadvantages of EUS are that it is invasive and operator-dependent.

Serous cystadenomas (SCAs)

Serous cystadenomas are essentially benign tumours that are most common in women in the sixth to seventh decade of life. They are mostly found in the body or tail of the pancreas and have a lobulated surface. They appear as microcystic or honey-combed cysts with a central stellate scar. The cysts are lined by a glycogen-rich cuboidal epithelium with clear cytoplasm, do not produce mucin, and do not communicate with the pancreatic duct.

Malignant transformation is extremely rare and management is mainly expectant. Surgical resection is offered for symptomatic lesions or when there is uncertainty about the true nature of the lesion.

Mucinous cystic neoplasms (MCNs)

Mucinous cystadenomas are commonly premalignant or malignant. They occur almost exclusively in women with a peak incidence in the fifth decade and are usually found in the distal pancreas. MCNs are lined by mucin-secreting columnar epithelial

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cells and are macrocystic with thick walls and thin septae. Peripheral calcifications are seen in 25% of them which allows one to make a specific diagnosis. MCN may resemble IPMN but, unlike IPMN, they have ovarian stroma, lack communication with the pancreatic duct and are always single lesions. Findings associated with malignant transformation include cyst size >4cm, cyst wall irregularity and thickening, septal thickening, intramural nodules, wall calcifications and pancreatic duct (PD) dilation.

Surgical resection is recommended for all fit patients due to the risk of malignancy. Observation may be considered in elderly patients with lesions <3cm and no intramural nodules.

Intraductal papillary mucinous neoplasms (IPMNs)

IPMNs are cystic lesions lined by intraductal dysplastic epithelium which secrete excessive mucin causing cystic dilation of the PDs. They are distinguished from MCNs due to the ductal involvement. IPMNs can be divided into main-duct IPMN (MD-IPMN), branch-duct IPMN (BD-IPMN) or mixed IPMN. IPMNs usually occur in the seventh decade of life and are more frequently seen in males. They are mostly found in the pancreatic head, but 20-40% of BD-IPMNs have multifocal disease. MD-IPMNs appear as diffuse dilatation of the main pancreatic duct whereas BD-IPMN resemble a 'bunch of grapes' connected to the main pancreatic duct BD-IPMNs are more indolent compared to MD-IPMNs. The frequency of malignancy in BD-IPMNs is 18-25%, whereas the frequency in MD-IPMNs is 40-60%. As such, all MD-IPMNs and mixed IPMNs should be resected. As for BD-IPMNs, the Fukuoka Guidelines of 2012 aid in their management by characterizing the cyst characteristics into 'high-risk stigmata' or 'worrisome features'. Patients with any of the high-risk stigmata (obstructive jaundice in a patient with cystic lesion of the head of the pancreas, enhancing solid component within cyst, main pancreatic duct >10mm in size) should undergo surgical resection.

If there are no high-risk stigmata but there are worrisome features (pancreatitis, cyst >3 cm, thickened/enhancing cyst walls, main duct size 5-9mm, non-enhancing mural nodule, abrupt change in caliber of pancreatic duct with distal pancreatic atrophy), these patients should undergo further evaluation with EUS to evaluate for concerning features such as definite mural nodule, evidence of main duct involvement, or cytology which is suspicious or positive for malignancy. If any of these are present, surgical resection should be offered. If they are absent, follow-up surveillance is determined by cyst size.

Conclusion

Improvements in imaging and endoscopic techniques have enabled more accurate diagnosis of pancreatic cystic lesions. This is essential to distinguish benign from malignant lesions, while also determining the potential for malignant transformation. A multidisciplinary approach involving radiologists, gastroenterologists, and surgeons is needed to ensure the most appropriate management for each patient. MG

References:

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