Introduction

Pancreatic cysts are frequently identified on ultrasonography during a health check-up and these cysts are often identified incidentally during investigations of unrelated diseases. Non-neoplastic pancreatic pseudocysts were previously believed to be the most common pancreatic cysts. However, with the increase in the sensitivity of imaging, small neoplastic cysts, especially branch duct-type intraductal papillary mucinous neoplasms (BD-IPMNs) are frequently being detected, and these cysts are likely far more common than pseudocysts. Therefore, the international consensus guidelines for the management of cystic mucinous neoplasms were formulated in Sendai in 2006 and updated in Fukuoka in 2012.¹

Differential diagnosis for pancreatic cysts

Pancreatic cystic lesions include various diseases. In general, they can be categorized into non-neoplastic (e.g., pseudocysts) and neoplastic cystic lesions. Neoplastic cystic lesions can be subcategorized into mucin-producing cystic neoplasms, serous cystic neoplasms, and other cystic neoplasms. Mucin-producing cystic neoplasms include mucinous cystic neoplasms (MCNs) and IPMNs. The other cystic neoplasms include solid-pseudopapillary neoplasms (SPNs), dermoid cysts, epidermoid cysts, lymphoepithelial cysts, cystic neuro-endocrine tumors, and other such lesions.

According to the international consensus guidelines,¹ IPMNs can be classified into the following 3 types based on imaging studies and/or their histology: main duct type (MD-IPMN), BD-IPMN, and mixed type. MD-IPMNs are characterized by segmental or diffuse dilation of the main pancreatic duct (MPD) to >5 mm without other causes of obstruction. Pancreatic cysts >5 mm in diameter that communicate with the MPD are considered as BD-IPMNs. Mixed type IPMNs meet the criteria for both MD-IPMN and BD-IPMN.

BD-IPMNs, MCNs, SCNs, and pseudocysts are common pancreatic cysts, and each cystic lesion has typical clinical and imaging features.
Basic treatment strategy for neoplastic pancreatic cysts

1. Indications for surgical resection

SCNs are almost always benign serous cystadenomas, and they are generally slow-growing and asymptomatic. Therefore, if their diagnosis is confirmed, they need to be only observed periodically.

MCNs show low prevalence of invasive carcinoma (<15%), and no malignancy is generally noted in MCNs of <4 cm without mural nodules. Therefore, observation may be considered in elderly frail patients. However, most patients are relatively young, there is a risk of progression to invasive MCNs, and the pancreatic body and tail are common locations. Additionally, the natural history of MCNs is still unknown and non-operative management requires years of follow-up with high resolution imaging that is associated with high costs. Therefore, surgical resection is recommended for all surgically fit patients.

In patients with MD-IPMNs, surgical resection is strongly recommended in all surgically fit patients considering the high incidence of malignant/invasive lesions. However, in patients with BD-IPMNs, indications for resection are more conservative. In resected BD-IPMNs, the mean frequency of malignancy is 25.5% (range, 6.3-46.5%) and the mean frequency of invasive cancer is 17.7% (range, 1.4-36.7%). Thus, resection of BD-IPMNs warrants consideration. However, these lesions mostly occur in elderly patients and the annual malignancy rate is only 2-3%. Therefore, examining “high-risk stigmata (of malignancy)” and “worrisome features” have been proposed.

2. “High-risk stigmata” and “worrisome features” in BD-IPMNs

“High-risk stigmata” includes obstructive jaundice in a patient with cystic lesion of the head of the pancreas, enhancing solid component within cyst, and MPD ≥10 mm in size. “Worrisome features” on imaging include cyst of ≥3 cm, thickened enhanced cyst walls, MPD size of 5-9 mm, non-enhanced mural nodules, abrupt change in the MPD caliber with distal pancreatic atrophy, and lymphadenopathy.

All cysts with “high-risk stigmata” should be resected. If no “worrisome features” are present, further initial work-up is not recommended, although surveillance is required. A BD-IPMN >3 cm in diameter is a weaker indicator of malignancy than the presence of mural nodules and positive cytology; therefore, a BD-IPMN >3 cm in diameter without “high-risk stigmata” can be observed without immediate resection, particularly in elderly patients. Patients with a rapidly growing BD-IPMN and those who develop “worrisome features” should be strongly considered for resection.

Role of endoscopic examinations in the management of BD-IPMN

1. ERCP

In the diagnosis of BD-IPMNs using imaging, multidetector-row-CT (MD-CT) and MRCP are currently believed to be the most useful primary methods for defining the morphology, location, multiplicity, and communication with the MPD. Reliable distinguishing features of BD-IPMNs including multiplicity and visualization of a connection with the MPD, can be evaluated, and therefore, BD-IPMNs can be distinguished from other cysts using MRCP in most of cases. In these cases, routine ERCP for obtaining a pancreatogram is not
recommended. A connection between a BD-IPMN and the MPD is not always observed in MD-CT and MRCP, and in cases in which MRCP fails to show a connection, a precise pancreatogram with direct injection of contrast medium may be required. Additionally, a dilated papilla with mucin extrusion and/or a mural nodule visualized using ERCP definitely confirms the diagnosis of IPMN.

2. Cytology and further analysis of pancreatic juice

Pancreatic juice can be obtained during ERCP or after the placement of a naso-pancreatic drainage tube. Some reports have described variable results for pancreatic juice cytology of BD-IPMNs. A large series showed the significant role of CEA levels >30 ng/mL in the diagnosis of malignant BD-IPMNs. However, routine ERCP for pancreatic juice sampling is not recommended owing to its limited efficacy, and it should only be used in selective cases.

3. Intraductal ultrasonography and peroral pancreatoscopy

Intraductal ultrasonography (IDUS) and peroral pancreatoscopy (POPS) can be used to obtain additional information on the surgical margin in challenging cases.

4. EUS

All cysts with “worrisome features” should be evaluated using EUS to further stratify the risk of the lesion. Patients with cysts >3 cm in diameter and no “worrisome features,” particularly elderly patients, can be considered for EUS to verify the absence of thickened walls or mural nodules. Additionally, EUS can be used for detecting mural nodules and invasion, and is considered the most effective method for delineating malignant characteristics.

5. EUS-FNA

Analyses of CEA and amylase levels as well as cytology of the cyst contents obtained using EUS-FNA may be useful for the differential diagnosis of cysts. However, it is important to highlight that Japanese investigators do not recommend fluid analysis of cysts for the diagnosis of mucinous-like cystic lesions, and they believe that a cyst of any size with “worrisome features” should not be aspirated, because aspiration may cause leakage of the cyst contents, possibly leading to peritoneal dissemination.

References

