Spectrum and Classification of Cystic Neoplasms of the Pancreas

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KEYWORDS

• Cystic neoplasms of the pancreas • Mucinous cystic neoplasm
• Serous cystic neoplasm • Cystic pancreatic endocrine neoplasm
• Solid pseudopapillary neoplasm • Intraductal papillary mucinous neoplasm

KEY POINTS

- Cystic neoplasms of the pancreas are an increasingly recognized clinical entity, now in up to 10% of patients older than 70 years.
- Management of these lesions, particularly intraductal papillary mucinous neoplasm, remains controversial.
- Many of these neoplasms can be managed safely with surgical resection at high-volume pancreatic centers, whereas an increasing number of subgroups may be watched safely. Accurate diagnosis is paramount.
- The revised Sendai guidelines seem to provide a safe framework for management of mucinous cystic neoplasm and intraductal papillary mucinous neoplasm.
- Ongoing research will likely better stratify the underlying risk of invasive cancers in these patients.

INTRODUCTION

The incidental finding of pancreatic cysts creates significant concern for the clinician given the grave prognosis for patients with pancreatic ductal adenocarcinoma (PDAC). The increasing use of axial imaging has contributed to the surge in the diagnosis of pancreatic cystic lesions. In asymptomatic patients, up to 2.5% are found to have pancreatic cysts, a number that increases to 10% in patients older than 70 years.[1,2] Fortunately, more sophisticated understanding of these clinical entities

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has allowed for more nuanced management in recent years, which has obviated many unnecessary and morbid operations. However, despite our improved understanding of pancreatic cysts, there is still ongoing debate regarding management of these lesions. We aim to provide a guide to the diagnosis and management of cystic neoplasms of the pancreas (CNPs).

For cystic lesions of the pancreas, there is a spectrum from benign to malignant. Benign entities include pancreatic pseudocysts, infectious cystic lesions of the pancreas, congenital cysts, pancreatic duplication cysts, retention cysts, and lymphoepithelial cysts.[3,4] There are several rare nonepithelial neoplasms, including lymphangiomas, epidermoid cysts in an intrapancreatic spleen, cystic pancreatic hamartomas, and mesothelial cysts.[4] Of the epithelial neoplasms, the most common are mucinous cystic neoplasms (MCNs), serous cystic neoplasms (SCNs), cystic pancreatic endocrine neoplasms (CPENs), solid pseudopapillary neoplasms (SPNs), and intraductal papillary mucinous neoplasms (IPMNs). These 5 clinical entities are discussed in this review. Another notable cystic neoplasm is a PDAC with cystic degeneration, but this comprises less than 1% of resected specimens and is not discussed here.[5] Overall, the number of invasive cancers in this epithelial group of cystic neoplasms has significantly declined over the last 40 years, from 41% in the 1970s and 1980s to 12% in the 2000s, consistent with earlier diagnosis and treatment of incidentally discovered and presumably premalignant lesions.[5] It is predicted that this number will continue to decline as our diagnostic capabilities improve.[4]

MUCINOUS CYSTIC NEOPLASMS

Introduction

MCNs make up approximately 23% of the resected cystic tumors of the pancreas.[5] To make the diagnosis of an MCN, the cyst must contain ovarian-type stroma.[6,7] MCNs occur almost exclusively in women, as solitary lesions in the body or tail of the pancreas.[6,8–13] The median age of diagnosis is mid-to-late 40s.[6,8–13] Given the risk of invasive disease, current guidelines recommend resection for all patients with MCN who are fit enough to undergo an operation.[6]

Clinical Presentation

Many of the patients with an MCN are symptomatic at the time of presentation, with nonspecific abdominal pain as the most common symptom.[8–13] Other less-common symptoms include fatigue, weight loss, abdominal mass, and pancreatitis, and jaundice is exceedingly rare.[8–13] The remaining MCNs are found incidentally on imaging or on final pathology.[8–13] The mean size at resection in our series of 199 patients was 4.4 cm.[5]

Pathophysiology

The mechanism of MCN development remains under investigation. Recent reports implicate the KRAS pathway[14,15] and the canonical Wnt pathway.[16] Activation of the canonical Wnt pathway promotes development of the pathognomonic ovarianlike stroma in a mouse model of MCN.[16]

Pathology/Classification

The histologic hallmark of MCN is an inner epithelial layer, consisting of mucin-secreting cuboidal epithelium, and an outer layer of ovarianlike stroma.[6,7] The cysts often lack a connection to the duct.[10,11] There is a spectrum of disease from benign (mucinous cystadenoma) to malignant (mucinous cystadenocarcinoma), with invasive carcinoma present in 5% to 16% of MCNs.[8–13] Factors associated with a higher