

Hugh James Freeman, MD, FRCPC, FACP, Series Editor

## Intraductal papillary mucinous neoplasms and other pancreatic cystic lesions

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Author contribution: Freeman HJ contributed all to this paper.

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Received: February 18, 2008 Revised: March 20, 2008

### Abstract

Pancreatic cystic neoplasms are being increasingly recognized, even in the absence of symptoms, in large part, due to markedly improved imaging modalities such as magnetic resonance imaging (MRI)/magnetic resonance cholangio pancreatography (MRCP) and computer tomography (CT) scanning. During the past 2 decades, better imaging of these cystic lesions has resulted in definition of different types, including pancreatic intraductal papillary mucinous neoplasms (IPMN). While IPMN represent only a distinct minority of all pancreatic cancers, they appear to be a relatively frequent neoplastic form of pancreatic cystic neoplasm. Moreover, IPMN have a much better outcome and prognosis compared to pancreatic ductal adenocarcinomas. Therefore, recognition of this entity is exceedingly important for the clinician involved in diagnosis and further evaluation of a potentially curable form of pancreatic cancer.

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**Key words:** Pancreatic cancer; Pancreatic intraductal papillary mucinous neoplasms; Mucinous cystic neoplasm of pancreas; Serous cystadenoma; Pancreatic cystic lesions

**Peer reviewer:** Michael Steer, Professor, Department of Surgery, Tufts-Nemc, 860 Washington St, Boston, Ma 02111, United States

Freeman HJ. Intraductal papillary mucinous neoplasms and other pancreatic cystic lesions. *World J Gastroenterol* 2008; 14(19): 2977-2979 Available from URL: <http://www.wjgnet.com/1007-9327/14/2977.asp> DOI: <http://dx.doi.org/10.3748/wjg.14.2977>

### INTRODUCTION

Due to increasing precision of modern imaging modalities, particularly computer tomography (CT) scanning (with contrast enhancement) and magnetic resonance imaging (MRI)/magnetic resonance cholangio pancreatography (MRCP), pancreatic cystic lesions are commonly being detected. This has been reported in up to 25% of patients, particularly with increasing age<sup>[1,2]</sup>. From a pathological rather than imaging perspective, however, a cyst is formally defined as a fluid-filled and closed cavity with an epithelial lining. In the pancreas (as opposed to liver and spleen), cyst-like lesions have special significance as different neoplasms in the pancreas are true cysts, or alternatively, may appear cystic either from dilation of a tumor obstructed or stenosed pancreatic duct or from necrotic changes and degeneration within a solid neoplastic lesion, possibly from rapid tumor growth that outstrips its blood supply.

Most commonly, a pancreatic cystic lesion defined by imaging represents a pseudocyst, usually due to alcoholic pancreatitis. Pseudocysts are distributed evenly throughout the pancreas and have no evident risk of malignancy. In a pseudocyst, no epithelial lining is present. As such, the pathological criteria for a true cyst (despite its cystic imaging appearance) are not satisfied. Most other true cysts (with the exception of congenital pancreatic cysts) are neoplastic and, therefore, these represent a potentially significant clinical finding<sup>[3,4]</sup>. A number of different neoplastic cystic lesions in the pancreas have been identified and labeled as capitalized abbreviations (Table 1)<sup>[4]</sup>. As prognosis for each type of cystic neoplasm may differ, precise definition of any imaged cystic lesion, even if asymptomatic or incidentally detected, is crucial<sup>[5]</sup>.

### NEOPLASTIC PANCREATIC CYSTIC LESIONS

Most neoplastic cystic lesions of the pancreas occur in young or middle-aged females [serous cystadenoma (SCA), mucinous cystic neoplasia (MCN), and solid pseudo-papillary neoplasia (SPN)], however, intraductal papillary mucinous neoplasms (IPMN) are most often detected in elderly males (more so than females)<sup>[4]</sup>. Most cystic neoplasms are evenly distributed throughout the pancreas, however, the pancreatic head and uncinata process are

Table 1 Types of pancreatic cystic neoplasms

Types of pancreatic cystic neoplasms
Serous cystadenoma, or SCA
Mucinous cystic neoplasm, or MCN
Intraductal papillary mucinous neoplasm, or IPMN
Solid pseudopapillary neoplasm (with degeneration), or SPN
Cystic necrosis (endocrine tumor, ductal adenocarcinoma)

most common sites for IPMN while the body and tail are most common sites for MCN<sup>[4]</sup>. For most cystic types, malignant potential appears to be low, except for MCN and rapidly growing pancreatic ductal adenocarcinomas or even more rare endocrine neoplasms<sup>[4]</sup>. In contrast, most IPMN are slow growing and have low malignant potential, with a much better prognosis, especially if compared to pancreatic ductal adenocarcinoma<sup>[4]</sup>. Thus, their recognition is significant because an opportunity may be present at the time of recognition to resect surgically this type of pancreatic cystic neoplasm.

## INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

IPMN appears to be quite a unique type of neoplasm, representing a broad spectrum of mucin-producing lesions of the exocrine pancreas classified as benign adenomas to invasive carcinoma. IPMN appear to arise from the epithelium of the main duct or its branches, often with variable duct dilation and IPMN are also believed by some to follow the so-called “adenoma-carcinoma” sequence. Neoplastic cells are most often papillary, although flat epithelium may also be defined.

IPMN of pancreas represents up to one-third of all pancreatic cystic neoplasms, but only about 1% of all pancreatic cancers<sup>[3,6]</sup>. Of particular note, IPMN also represents about 25% of all surgically resected pancreatic neoplasms, again likely emphasizing the critical significance of early recognition<sup>[6]</sup>. IPMN was first described by Ohhashi and colleagues in 1982 followed by a notation by the same group of a very prolonged survival (over a quarter century) of a case of IPMN<sup>[7]</sup>. The first series of North American patients were described only in 1990<sup>[8]</sup>. Since then, interest in this neoplasm appears to have increased exponentially as reflected in the annual number of publications in Medline from 1994 to 2006 related to IPMN noted elsewhere<sup>[6]</sup>. Interestingly, IPMN has also been documented to be multifocal and there is a higher occurrence rate of synchronous extrapancreatic malignancies (compared to pancreatic ductal adenocarcinoma)<sup>[9]</sup>. Finally, independent synchronous or metachronous pancreatic ductal adenocarcinomas<sup>[10]</sup> as well as endocrine tumors<sup>[11]</sup> with IPMN have also been described.

Based on anatomic involvement of the pancreatic duct, IPMN of the pancreas may predominantly involve the main pancreatic duct (“main duct type”), secondary ducts (“branch duct type”) or both (“mixed type”). Branch duct type IPMN are usually smaller, less papillary and

tend to occur in the periphery of the pancreatic head or in the distal pancreas. Malignant transformations occur less often in the branch duct type. Evidence suggests that asymptomatic branch duct IPMN less than 3 cm in size without mural nodules, thickened septa or high grade dysplasia have a relatively benign biological behavior and should be considered optimal candidates for surgical treatment<sup>[6]</sup>.

Diagnosis may be enhanced by MRCP combined with dynamic imaging since this improves localization, staging and, most important, the potential for surgical resectability. A contrast-enhanced CT scan may also yield added information regarding invasion, but also the relationship of the lesion to contiguous organs and vessels. Finally, endoscopic visualization of a patulous or so-called “fish-eye” papilla of Vater, especially at the time of ERCP may be helpful, if not pathognomonic. ERCP also permits an opportunity for added sampling of ductal content for cytology. Endoscopic ultrasonograph (EUS) may also provide added imaging information and permit fine needle aspiration biopsy although some concerns have been raised regarding the risk of seeding and dissemination of malignant cells<sup>[4]</sup>. Positron emission tomographic scanning may be helpful but its role needs to be better defined. Finally, serological studies including CA 19-9 and CEA may serve some value but it is limited since these are reported to be elevated in less than 20% of IPMN<sup>[4]</sup>. For pre-operative evaluation, all of these investigations may provide useful information, but are most important if surgical resection is being contemplated. Unfortunately, some patients are older with other concomitant health issues. In these, surgical treatment and resection may not lead to a significant positive long-term result and, as in these patients, even a more judicious approach to invasive evaluative investigations may be reasonable. If surgical excision is complete, recurrence may still occur, usually at a distant site, but this rate of recurrence is limited, and the overall 5-year survival rate has been reported to exceed 80% for noninvasive IPMN and approximately 50% for malignant invasive IPMN. Thus, accurate evaluation of IPMN is exceedingly important as a recent analysis<sup>[4]</sup> has suggested that this is one of the few surgically curable pancreatic neoplasms.

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