

## Concomitant pancreatic adenocarcinoma in a patient with branch-duct intraductal papillary mucinous neoplasm

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**Key words:** Pancreatic adenocarcinoma; Intraductal papillary mucinous neoplasm; Endoscopic ultrasound; Surveillance

**Core tip:** Patients with intraductal papillary mucinous neoplasm are not only at risk for malignant degeneration within the cyst, but some reports have indicated an increased risk for the development of pancreatic adenocarcinoma separate from the cyst. The current international guidelines emphasize surveillance of the cyst but this case report highlights the importance for endosonographers to carefully evaluate parenchyma not involved with the cyst to identify small pancreatic adenocarcinomas.

### Abstract

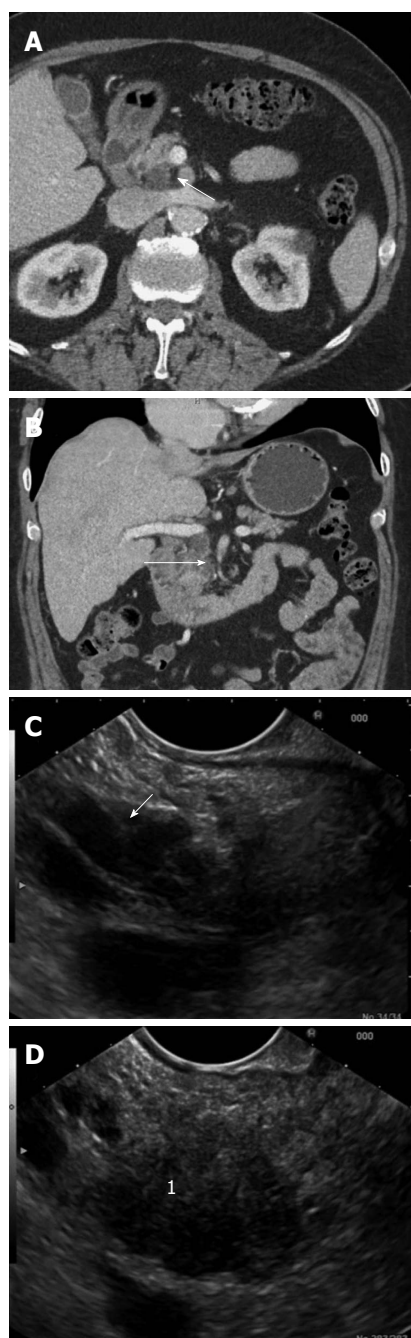
Branch duct intraductal papillary mucinous neoplasms (BD-IPMN) are pre-malignant pancreatic cystic lesions which carry a small risk of malignant transformation within the cyst. Guidelines exist with respect to surveillance of the cysts using computed tomography, magnetic resonance imaging, and/or endoscopic ultrasound (EUS). There are reports that patients with IPMNs are at increased risk of developing pancreatic adenocarcinoma, which arises in an area separate to the IPMNs. We present two cases of pancreatic adenocarcinoma arising within the parenchyma, distinct from the IPMN-associated cyst, identified with EUS. This case report highlights that patients with BD-IPMN are at increased risk for pancreatic adenocarcinoma separate from the cyst and also the importance for endosonographers to carefully survey the rest of the pancreatic parenchyma separate from the cyst in order to identify small pancreatic adenocarcino-

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### INTRODUCTION

Incidental pancreatic cysts are detected frequently due to the widespread availability and use of cross-sectional imaging. Over the past decade, 2.6% of patients undergoing multidetector computed tomography (CT) scans and up to 13.5% of patients undergoing magnetic resonance imaging (MRI) were found to have incidentally detected pancreatic cysts<sup>[1,2]</sup>.

Intraductal papillary mucinous neoplasm (IPMN) account for almost 50% of surgically resected cystic pancreatic neoplasms<sup>[3]</sup> and can progress from benign



**Figure 1** Abdominal imaging and endoscopic ultrasound of a patient 1 undergoing routine surveillance for a pancreatic cyst. (A) and (B) demonstrate the cystic lesion in the head/uncinate process of the pancreas as seen on computed tomography scan (arrow); and seen on endoscopic ultrasound (C). Image (D) shows a mass<sup>1</sup> within the head of the pancreas which was separate to the cyst.

neoplastic epithelium to invasive carcinoma through increasing severity of dysplasia. The risk of malignant transformation is dependent on whether or not there is involvement of the main pancreatic duct. Main, or mixed duct IPMN is associated with a risk of high-grade dysplasia or invasive adenocarcinoma of 44% to 62% in surgical series<sup>[4]</sup>. In contrast, only 16% to 25% of surgically resected branch-duct IPMN contain either high-grade dysplasia or invasive adenocarcinoma<sup>[4]</sup>.

We present two cases of patients with BD-IPMN who had no high-risk or worrisome features within their cysts but were found to have a pancreatic adenocarcinoma unrelated to a cyst while undergoing routine surveillance with EUS.

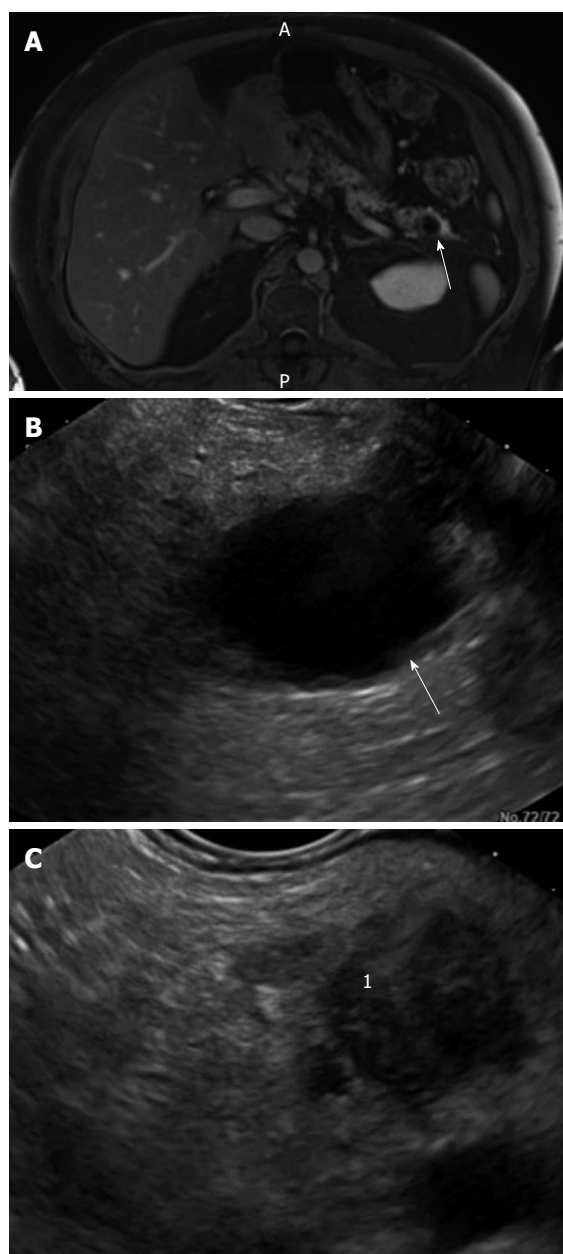
## CASE REPORT

### Case 1

A 67-year-old man with a history of resected prostate cancer and no significant family history underwent an abdominal CT scan for surveillance of his prostate cancer. An incidental 1.4 cm cyst in the uncinate process of the pancreas was found. EUS with fine needle aspiration (EUS-FNA) was performed at an outside hospital. The findings were consistent with a branch duct IPMN (BD-IPMN), with no worrisome features. He underwent surveillance with a pancreatic protocol CT scan six months later, which revealed a 2 cm cystic lesion in the uncinate process (Figures 1A, B) with multiple smaller cysts in the body, none of which had any worrisome or high-risk features. Six months later the patient was seen in our multidisciplinary pancreatic cyst clinic; he underwent a routine EUS and was found to have a 2.2 cm cyst (Figure 1C). In addition, a 2.6 cm × 1.9 cm mass was identified within the head of the pancreas, separate from the cyst (Figure 1D). EUS-FNA of the lesion was performed, which confirmed an adenocarcinoma on cytopathology. The patient underwent a pancreaticoduodenectomy and was found to have a moderately differentiated adenocarcinoma, with invasion through the muscularis propria and into the submucosa of the small intestine, with 1 of 34 lymph nodes involved by metastatic adenocarcinoma. In addition, an IPMN with low to intermediate grade dysplasia was found.

### Case 2

A 55-year-old man had an incidental finding of a 3 cm × 3 cm multi-lobulated cyst in the uncinate process and a 2 cm × 2 cm cyst in the distal tail of the pancreas, when he underwent an abdominal CT scan for evaluation of flank pain. He was found to have markedly atypical cells worrisome for malignancy in the cyst in the uncinate process, and underwent a pylorus-preserving pancreaticoduodenectomy. The pathology demonstrated an IPMN with high-grade dysplasia with no evidence of involvement of the surgical resection margin. He underwent routine transabdominal surveillance of the remnant pancreas with a combination of CT and MR imaging at 6-monthly intervals. Five years after initial detection, the lesion in the tail was noted to have increased minimally in size to 2.4 cm on a MRI scan. In addition, multiple sub-centimeter cystic lesions were present throughout the remnant body and tail (Figure 2A), none of which contained any suspicious features. The patient underwent a routine EUS which demonstrating a 2.9 cm cystic lesion in the tail of the pancreas (Figure 2B), with additional smaller cysts in the body and tail of the pancreas



**Figure 2** Abdominal imaging and endoscopic ultrasound of the pancreatic remnant in patient 2 who was status post pancreaticoduodenectomy for intraductal papillary mucinous neoplasm. A: Magnetic resonance imaging of the remnant pancreas performed 6 mo before the endoscopic ultrasound (EUS). The arrow demonstrates the cyst in the tail of the pancreas; B: EUS image of the cyst in the tail of the pancreas (arrow) corresponding to the MRI image seen in (A); C: Demonstrates an ill-defined hypoechoic area<sup>1</sup> in the body of the pancreas.

none of which contained any worrisome features. However in the body of the pancreas, separate to any cyst, a 1.4 cm mass was visualized (Figure 2C). EUS-FNA was performed, and cytopathology confirmed a pancreatic adenocarcinoma. The patient underwent a staging CT scan, which found multiple spiculated nodules in the lung, which were confirmed as metastatic pancreatic adenocarcinoma on biopsy.

**Table 1** High-risk and worrisome criteria

High-risk stigmata	Worrisome features
Jaundice secondary to a pancreatic cyst	Acute pancreatitis
Enhancing solid component	Cyst $\geq 3$ cm
Main pancreatic duct $\geq 10$ mm	Thickened or enhancing cyst walls on cross-sectional imaging
	Main pancreatic duct 5-9 mm
	Non-enhancing mural nodule
	Abrupt change in the caliber of the main pancreatic duct with distal pancreatic atrophy

## DISCUSSION

Patients with IPMN are known to be at increased risk of developing pancreatic ductal adenocarcinoma, the majority of which arise from an IPMN related cyst. Patients with IPMN are followed using the International Consensus Criteria guidelines, which recommend surveillance of patients with BD-IPMN and no worrisome features at 3-6 mo intervals alternating with MRI and EUS for cysts  $> 2$  cm and for patients with smaller cysts, CT and/or MRI are recommended every one to three years depending on the cyst size<sup>[4]</sup>. Both the EUS literature<sup>[5,6]</sup>, and these guidelines, stress the importance of looking for high-risk or worrisome features in the IPMN related cysts (Table 1). However, there have been a number of retrospective studies reporting cases of patients with IPMN developing adenocarcinoma in areas unrelated to pancreatic cysts with incidences of between 4% to 11%<sup>[7-14]</sup>. In a single prospective study, which followed 89 patients with IPMN over a 17 years period, 4 developed concomitant pancreatic adenocarcinoma<sup>[15]</sup>.

The current guidelines recommend that BD-IPMN measuring  $< 2$  cm are followed with MRI or CT, with EUS being used for larger cysts or those with worrisome features<sup>[4]</sup>. However, very few studies have compared the sensitivity and specificity of these three imaging modalities. One prospective, multicenter study by Canto *et al*<sup>[16]</sup>, compared CT, MRI and EUS in high-risk patients, and found that EUS was the most sensitive test for identifying cysts. Several studies have shown that EUS is superior to CT for identifying small solid pancreatic neoplasms, but there are no studies to date examining its role in detecting concomitant pancreatic adenocarcinoma in patients with IPMN. In this series, both patients underwent high quality imaging with either CT or MRI with a mass only detected on EUS. A recent study by He *et al*<sup>[17]</sup>, found that up to 17% of patients who underwent resection of IPMN, will develop lesions in the remnant pancreas which fulfill the criteria for surgical resection. It may be that high risk groups such as this may benefit from increased use of EUS. Large, prospective studies are necessary to compare these three imaging modalities and determine their optimum combination and timing.



In conclusion, patients with IPMN are at risk of developing concomitant pancreatic adenocarcinoma. Small concomitant pancreatic adenocarcinomas may not be seen on CT or MRI. Endosonographers should examine not only the cysts, but also the entire pancreatic parenchyma carefully.

## COMMENTS

### Case characteristics

Two patients undergoing surveillance for branch duct intraductal papillary mucinous neoplasm are found to have concomitant adenocarcinoma (*i.e.*, separate from the cystic lesion) found on endoscopic ultrasound.

### Clinical diagnosis

Pancreatic adenocarcinoma separate and distinct from branch duct intraductal papillary mucinous neoplasm (BD-IPMN) was detected in two patients undergoing surveillance by endoscopic ultrasound (EUS).

### Differential diagnosis

In both cases, the adenocarcinoma was an incidental finding that was not detected on cross sectional imaging; the differential for a solid-appearing lesion in the pancreas includes pancreatic neuroendocrine tumor, lymphoma, and metastases.

### Imaging diagnosis

Both patients were undergoing surveillance of BD-IPMN with cross-sectional imaging as recommended by the international consensus guidelines and included either computed tomography (CT), magnetic resonance imaging (MRI), and/or EUS.

### Pathological diagnosis

Through EUS-guided fine needle aspiration, a cytopathologic diagnosis confirmed pancreatic adenocarcinoma.

### Treatment

In the first case, the patient underwent surgical resection in the form of a pancreaticoduodenectomy; the second patient presented with lung metastases and was treated with palliative chemotherapy.

### Term explanation

Concomitant pancreatic adenocarcinoma is the term used to describe a lesion that is unrelated to the cystic lesion.

### Experiences and lessons

These two cases are meant to emphasize the need for endosonographers to survey the pancreatic parenchyma not involved with cyst in the evaluation of patients with BD-IPMN.

### Peer review

In the two cases, endoscopic ultrasound were preferable to CT and MRI in surveillance of pancreatic adenocarcinoma from BD-IPMN. However, it is still hard for us to choose which cyst to take a FNA if EUS finds some cysts which are < 2 cm with no worrisome features in clinical practice.

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