Case Report

Intraductal papillary mucinous neoplasm of the biliary tract: A precursor lesion to cholangiocarcinoma

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ABSTRACT

Intraductal papillary mucinous neoplasm of the biliary tract (IPMN-B) is an increasingly recognized pathologic entity characterized by intraluminal papillary masses and increased mucin secretion, resulting in obstruction and dilation of the biliary tree. These lesions, rarely seen in clinical practice in the United States, are now considered to be important precursors for the development of cholangiocarcinoma. Therefore, it is critical that radiologists become familiar with the radiographic manifestations of IPMN-B in order to diagnosis these lesions at a time when surgical resection may be curative. Here we report a pathologically confirmed case of IPMN-B in a patient with chronic ulcerative colitis and subsequently discuss the main radiographic manifestations of this rare condition across multiple imaging modalities.

Introduction

Intraductal papillary mucinous neoplasm of the biliary tract (IPMN-B) is a rare but increasingly recognized pathologic entity characterized by intraluminal papillary masses in association with bile duct obstruction and dilation. A portion of these low-grade tumors secrete an abundance of mucin which can alter the normal flow of bile leading to diffuse intra- and extrahepatic biliary ductal dilation. Given the low incidence of these tumors in Western nations, particularly in the United States, they are infrequently encountered by radiologists in daily practice. However, because IPMN-B is now recognized as an important precursor lesion to cholangiocarcinoma, it is critical that radiologists to be familiar with the various radiographic presentations of these tumors in order to diagnose them at a time when surgical resection may be curative.

Despite increasing knowledge about this disease process, reports describing the radiographic manifestations of IPMN-B are scarce in existing literature. In this report, we describe the case of a patient who initially presented with elevated liver enzymes and was found to have IPMN-B, confirmed by pathology. We focus on the main radiographic manifestations of IPMN-B across multiple imaging modalities with the hope
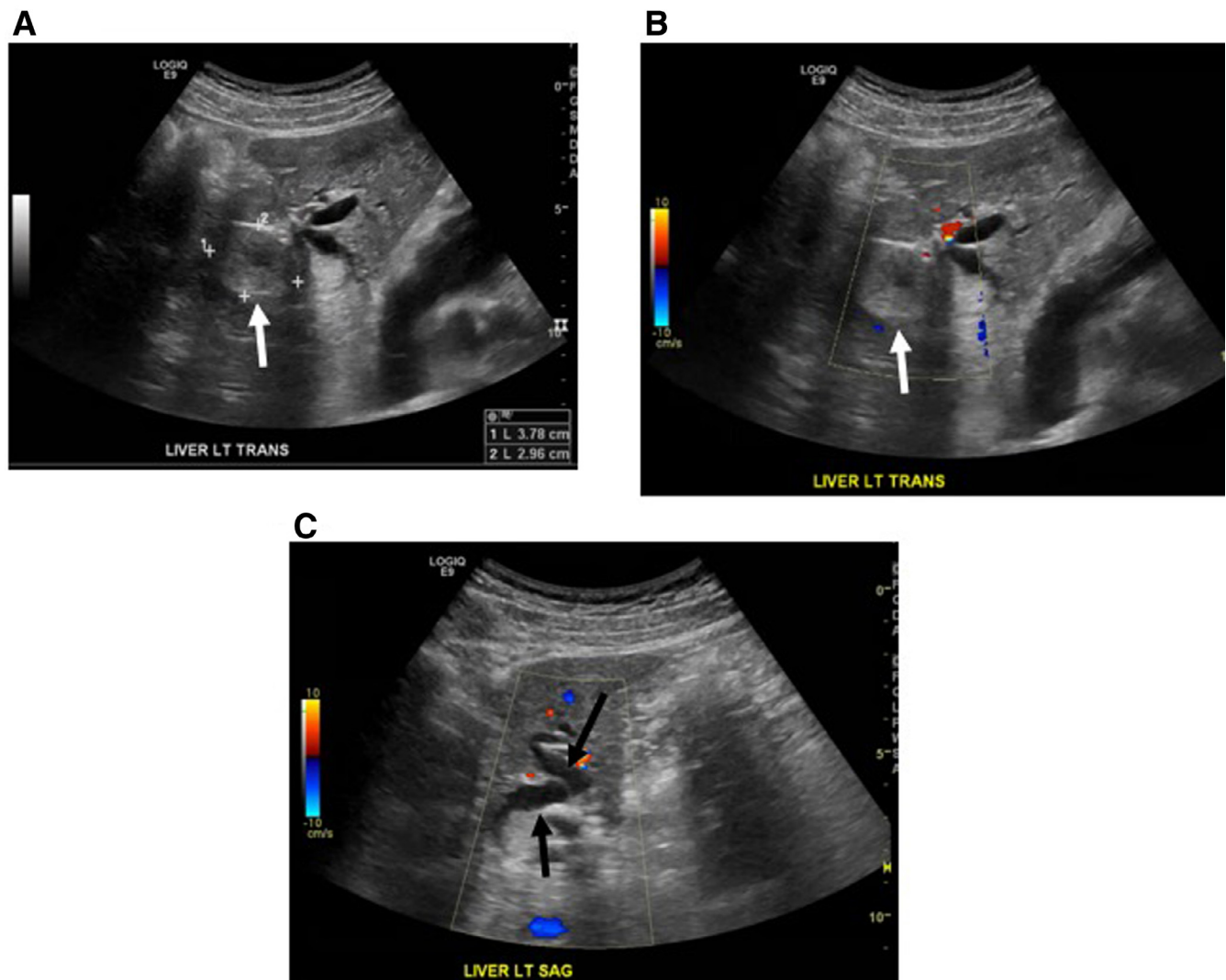
Fig. 1 – Transabdominal ultrasound in the transverse (A and B) and sagittal (C) planes shows a 3.8 x 3.0 cm heterogeneous hyperechoic mass (white arrow) centered in the extrahepatic bile duct resulting in severe biliary dilation of the right and left hepatic ducts (black arrow). There was no flow associated with the lesion on color Doppler (B). Notice the absence of flow within the bile ducts on the Doppler image (C) differentiating them from hepatic vessels.

that readers will become more comfortable in making the diagnosis of this clinically important diagnosis.

Case

A 65-year-old male with a long-standing history of well-controlled ulcerative colitis was found to have elevated liver function tests and alkaline phosphatase levels on his routine blood work. The patient was asymptomatic and denied any abdominal pain, vomiting, diarrhea, or pruritus. Given elevated liver enzymes in the setting of a history of ulcerative colitis, there was initial concern for underlying primary sclerosing cholangitis and/or cholangiocarcinoma. An abdominal ultrasound was subsequently ordered which showed diffuse intrahepatic biliary ductal dilation upstream of an echogenic

mass along the common hepatic duct (Fig. 1). The common bile duct appeared thick walled but was normal in caliber.

Contrast-enhanced magnetic resonance imaging (MRI) of the abdomen subsequently performed showed marked dilation and enhancement (isoenhancing to liver) in the inferior segment of the common hepatic duct just superior to the cystic duct insertion (Figs. 2 and 3). Upstream to this was marked intrahepatic biliary ductal dilation with multiple areas of enhancing wall thickening as well as nodularity involving the right and left hepatic ducts. No evidence of periductal infiltration or vascular invasion was visualized. The common bile duct was unremarkable and measured 7 mm in maximum diameter. Given these findings, direct visualization of the mass was recommended for further evaluation.

An endoscopic ultrasound and endoscopic retrograde cholangiopancreatography (ERCP) was performed and re-demonstrated a hyperechoic nonobstructing mass in the
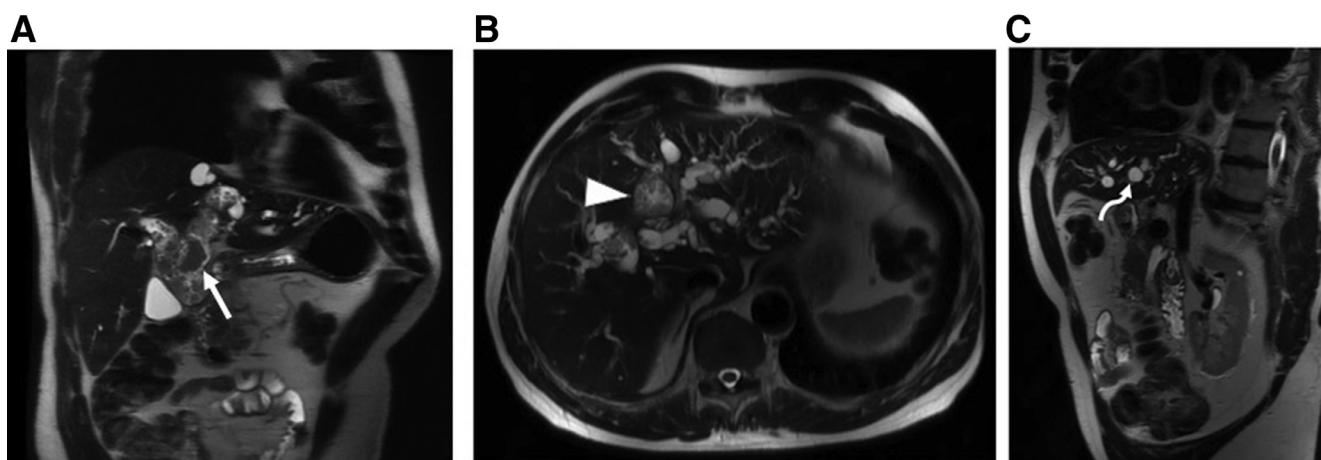
Fig. 2 – Coronal (A), axial (B), and sagittal (C) T2-weighted MR images show a large hypointense, fungating intraluminal mass (white arrow) centered in the proximal main hepatic duct which results in disproportionate, aneurysmal dilation of the involved segment of bile duct. The mass causes severe upstream intrahepatic duct biliary dilation (curved arrow). Numerous papillary projections are also seen arising from the intrahepatic bile duct walls, most prominent in the left main hepatic (arrowhead) duct also resulting in aneurysmal dilation of the involved duct. Note the walls of the bile ducts containing tumor appear congruent without frank discontinuity to suggest periductal infiltration. The cystic and common bile ducts (not shown) were free of tumor.
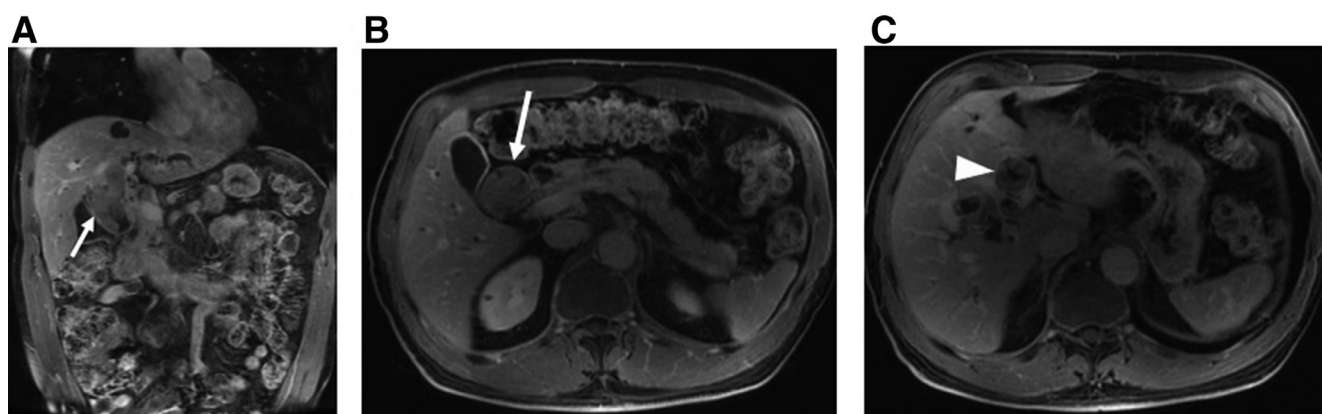

Fig. 3 – Coronal (A) and axial (B and C) postcontrast T1-weighted images reveal that the large intraluminal mass centered in the distal common hepatic duct (arrow) and the papillary projections in the intrahepatic ducts (arrowhead) are isoenhancing to the liver parenchyma in keeping with the diagnosis of IPMN-B. Again, notice the walls of the tumor-containing bile ducts appear congruent without frank discontinuity to suggest periductal infiltration.

proximal portion of the common hepatic duct with marked intrahepatic biliary ductal dilation (Fig. 4). By this time, the patient's alkaline phosphatase and liver function tests had normalized. No peribiliary tree lymphadenopathy was appreciated. Decision to undergo endoscopic biopsy was foregone due to concern for potential seeding of the tumor.

Shortly after the endoscopic ultrasound and ERCP, the patient was taken to the operating room for a laparotomy. Intraoperative findings consisted of a large papillary tumor in the common hepatic duct with the largest gross specimen measuring 2.3 cm (of note, the final dimensions of the intraductal tumor could not be determined due to the sequential nature of the resection). There was no transmural involvement in the proximal common hepatic duct, consistent with findings on ultrasound and MRI. Intraoperative choledoscopy showed papillary content extending into the distal left biliary system. Therefore, a decision was made to perform a left hepatectomy, in addition to biliary duct resection and roux-en-Y bypass. Pathology reports from the intraoperative specimens were positive for intraductal papillary neoplasm (biliary type) with high-grade dysplasia superimposed on a background of chronic cholangitis. The patient had an uneventful recovery and was discharged from the hospital 5 days later. Follow-up computer tomography (CT) studies (not provided) were negative for any local recurrence or metastatic disease.
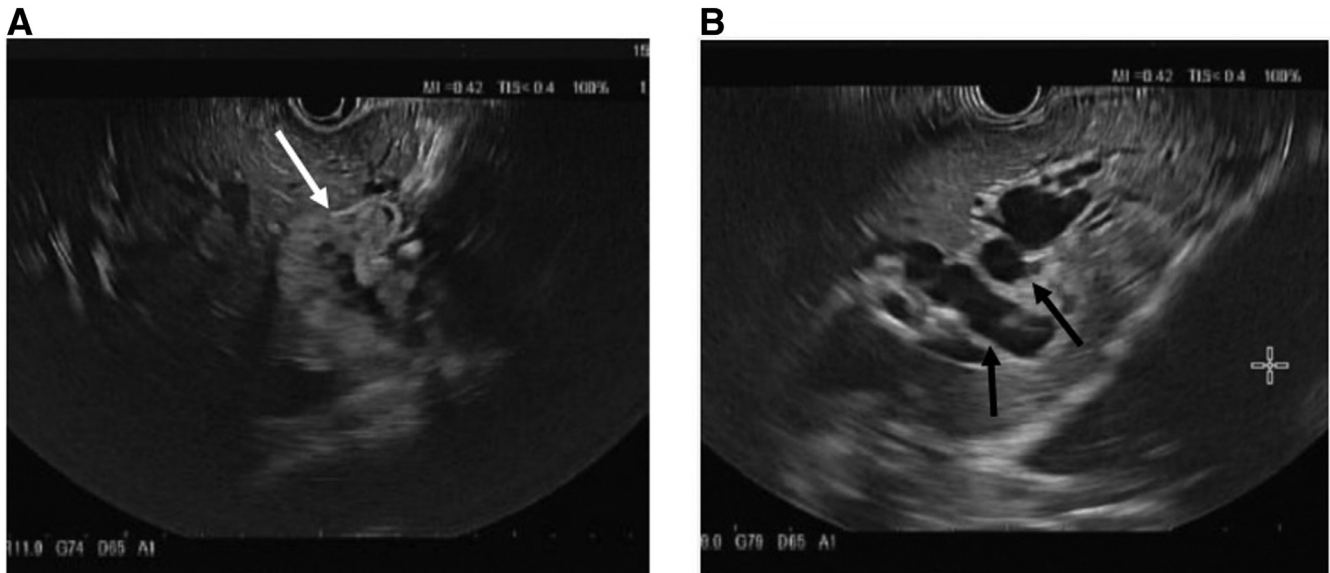
A

B

Fig. 4 – Endoscopic ultrasound shows a hyperechoic mass (white arrow) in image A centered in the extrahepatic duct resulting in severe intrahepatic duct dilation (black arrow).

Discussion

Cholangiocarcinoma is an aggressive malignancy with a poor prognosis that is frequently diagnosed late in the disease course. While cholangiocarcinoma often arises spontaneously without an identifiable precursor lesion, there are two premalignant lesions of cholangiocarcinoma: biliary intraepithelial neoplasia and IPMN-B. Radiology studies cannot detect biliary intraepithelial neoplasia as it is an atypical growth of the biliary epithelium which is identified histologically. However, the subtypes of IPMN-B have distinct radiologic features that can be diagnosed using multiple imaging modalities [1]. Therefore, it is important for a radiologist to be familiar with the various imaging characteristics of this uncommon disease process in order to detect these lesions early enough for surgical resection to be potentially curative and before transformation to invasive cholangiocarcinoma can occur.

Over the past few decades, IPMN-B has been increasingly recognized as a distinct subtype of biliary neoplasm. The 2010 World Health Organization describes these rare tumors as papillary or villous neoplasms covering fibrovascular stalks within bile ducts [2]. The papillary masses invariably lead to obstruction and dilation of the intrahepatic and/or extrahepatic biliary ductal systems resulting in characteristic imaging findings.

The incidence of IPMN-B and incidence of the transformation of IPMN-B into cholangiocarcinoma are currently unknown; however, it is recognized to be far higher in Eastern countries such as Japan and Korea compared to Western nations [3,4]. The higher incidence in these Asian countries is reportedly related to endemic hepatolithiasis and clonorchiasis infections, 2 of the main risk factors for the development of IPMN-B [5]. Additional risk factors include primary sclerosing cholangitis, choledochal cysts, and gardner syndrome [6]. In stark contrast to cholangiocarcinoma, IPMN-B is a low-grade neoplasm that is typically limited to the bile duct mucosa with favorable long-term prognosis after surgical resection [7]. Patients typically present in their 60-70s with recurrent upper abdominal pain, biliary colic, jaundice, and fevers [8]. The symptomatology is thought to be related to recurrent biliary duct obstruction from excessive mucin production or tumor-induced stenosis [9].

Diagnosing IPMN-B can be challenging and will typically require a multi-imaging modality approach. In patients presenting obstructive jaundice, ultrasound will typically be the first imaging modality ordered due its low cost, widespread availability, and lack of ionizing radiation. Ultrasound will typically show the nonspecific finding of biliary ductal dilation. If a tumor is visualized, it will classically be characterized as a nonshadowing, well-defined echogenic intraluminal mass with preservation of the bile duct walls, compatible with the low-grade nature of these lesions [10]. If no visible intraductal mass is seen but there is irregular contouring of the bile ducts, then the presence of sessile papillary tumors adherent to the walls may be inferred. Associated findings may include cholelithiasis or choledocholithiasis [11]. Due to the nonspecific nature of these findings, additional cross-sectional imaging with CT, MRI, or magnetic resonance cholangiopancreatography (MRCP) will be required for better characterization of the findings.

The literature classically describes four distinct radiologic manifestations of IPMN-B on CT and MRI which will be subsequently discussed (Table 1). The first radiographic manifestation of IPMN-B is an intraductal fungating mass (classically in the left hepatic lobe) with aneurysmal, cystic dilation of the bile ducts both upstream and downstream to the tumor, which is a unique feature of IPMN-B. Upstream dilation of the bile ducts can result from either obstruction by the tumor itself or from tumor-induced stenosis [12]. In either case, there will typically be disproportionate dilation of the segmental bile duct containing the tumor. Dilation downstream to the

Table 1 – Pathologic and radiographic features of the four types of IPMN-B presentations.

	Pathologic characteristics	Bile duct dilation	Mucin	Tumor	Differential diagnosis
Type 1	- Intraductal fungating mass - Excessive mucin production	-Dilation of the entire biliary tree, both proximal and distal to the mass	Linear filling defects on ERCP/MRCP	Intraductal fungating tumor with disproportionate dilation of the segmental bile duct containing tumor	Recurrent pyogenic cholangitis with bile duct stones
Type 2	- Intraductal fungating mass - No mucin production	- Dilation of the biliary tree upstream to the tumor only	None	Intraductal fungating tumor with disproportionate dilation of the segmental bile duct containing tumor	Intrahepatic cholangiocarcinoma, hepatocellular carcinoma with biliary duct invasion, intraductal metastasis, and hepatolithiasis
Type 3	- Multiple Intraductal fungating masses - Variable mucin production	- Aneurysmal dilation upstream to the tumor - Downstream dilation dependent on mucin production	Linear filling defects on ERCP/MRCP if mucin production present.	Multiple intraductal fungating masses resulting aneurysmal dilation of the bile duct	Caroli disease, mucinous cystadenoma/cystadenocarcinoma, and hepatic cysts
Type 4	- Superficial, spreading tumor not visible radiographically - Excessive mucin production	-Dilation of the entire biliary tree without disproportionate or focal dilation	Linear filling defects on ERCP/MRCP	No visible tumor	Ampullary adenoma/carcinoma, pancreatic adenocarcinoma, and choledocholithiasis

tumor occurs when excessive mucin production obstructs the hepatopancreatic ampulla which leads to diffuse dilation of the intra- and extrahepatic biliary ductal systems [13]. When these distinctive features are detected on imaging, the radiologist can be confident in making the diagnosis of IPMN-B.

The second variant of IPMN-B is an intraluminal fungating mass resulting in only upstream dilation due to the absence of mucin production. The mass is typically iso-enhancing to hepatic parenchyma on contrast-enhanced CT and MRI [9]. Due to the absence of fibrous tissue, these tumors typically lack enhancement on delayed imaging, which is an important discriminating feature compared to cholangiocarcinoma because it may otherwise look very similar. Differential considerations for this subset of IPMN-B will typically include cholangiocarcinoma, hepatocellular carcinoma with bile duct invasion, intraductal metastasis, and hepatolithiasis (high attenuating focus on a unenhanced CT or lack of enhancement on contrast-enhanced imaging.)

Third, bile ducts containing tumor may show focal, aneurysmal dilation of the involved duct resulting in a cystic, mass-like appearance on imaging. In this variant of IPMN-B, distal bile duct dilation may be seen if excessive mucin is produced. It has been reported that aneurysmal dilation of any branch of the bile duct system should be considered a characteristic feature of IPMN-B [9]. However, other entities presenting as cystic-like masses in the liver including localized Caroli disease, cystadenoma, and cystadenocarcinoma may look similar to IPMN-B and can be considered in the differential.

The last radiographic manifestation of IPMN-B is diffuse dilation of both the intra- and extrahepatic bile ducts due to excessive mucin production resulting in obstruction of the

ampulla of Vater without evidence of an intraluminal mass on imaging [14]. In cases where the tumor spreads superficially along the bile ducts, an intraductal mass may not be visible. Mucin, which is unable to be appreciated on CT due to similar attenuation characteristics to bile, is best appreciated on MRCP as linear, hypointense lines in dilated bile ducts. Excessive mucin-producing IPMN-B has been reported in the literature as causing fistulous connections with nearby structures (such as bowel) or can rupture, leading to pseudomyxoma peritonei [9].

Patients diagnosed with IPMN-B and who are considered surgical candidates will likely undergo surgical resection as definitive treatment [15]. If there is extensive superficial spreading of the tumor along the biliary tree, liver transplant and pancreaticoduodenectomy may be performed. Prognosis after resection is favorable, with the 5-year survival rate approaching 80%, considerably higher than that of cholangiocarcinoma [16]. Unfortunately, recurrence is not unusual after surgical resection. Therefore, patients with IPMN-B will continue to need long-term follow-up imaging.

Conclusion

IPMN-B is an uncommon precursor lesion to cholangiocarcinoma which is rarely encountered in everyday radiology practices in the United States. Pathologically, they are characterized as frond-like intraductal tumors that may or may not secrete large amounts of mucin, which invariably leads to obstruction and dilation of the biliary tree. Although the

findings on various imaging modalities are variable depending on the pathologic subtype of the tumor, if the following characteristics are identified, then the diagnosis of IPMN-B can be confidently made: generalized dilation of the bile ducts with areas of more focal, aneurysmal-like dilation in a segment of the biliary tree and excessive mucin in the bile ducts (best appreciated on MRCP or ERCP as linear filling defects).

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2019.01.023.

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