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CASE REPORT | BILIARY

Balloon Extraction of an Intraductal Tubulopapillary Neoplasm of the Bile Duct During Endoscopic Retrograde Cholangiopancreatography

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ABSTRACT

Intraductal tubulopapillary neoplasm (ITPN) of the bile duct is a rare type of intraductal neoplasm of the bile duct that has mainly been described in the literature in case reports and small case series. Only within the past decade has ITPN of the bile duct been identified as its own entity and have definitive diagnostic criteria been established. Given its rarity, there is no standard of care for treatment. Here, we describe a case report of biliary ITPN diagnosed in a unique manner.

INTRODUCTION

Intraductal tubulopapillary neoplasm (ITPN) of the bile duct (biliary ITPN) is a rare intraductal neoplasm of the bile duct.[1] Biliary ITPN was first described in 2010 as a single case report of a bile duct tumor with histologic findings and immunohistochemical staining similar to pancreatic ITPN, a location where it is a more well-established entity.[2,3] Unlike biliary intraepithelial neoplasia (BilIN) and intraductal papillary neoplasms of the bile duct (IPNB), biliary ITPN is nonmucinous and is not a known precursor of cholangiocarcinoma.[3]

CASE REPORT

An 83-year-old woman with type 2 diabetes, hypertension, hyperlipidemia, and a seizure disorder presented to the hospital with melena. She admitted to using ibuprofen twice daily for a while. Her admission laboratory tests revealed hypoalbuminemia (2.4 g/dL), hyperbilirubinemia (2.8 mg/dL), and elevated aspartate transaminase (88 U/L) and alkaline phosphatase (224 U/L). Review of her medical record revealed a computed tomography scan from 2 years before demonstrating a cirrhotic liver. Abdominal ultrasound confirmed a cirrhotic liver; however, the common bile duct (CBD) was also dilated to 19 mm with left-sided intrahepatic biliary dilation. Upper endoscopy revealed a clean-based pyloric channel ulcer; evaluation of her biliary tree was therefore delayed to prevent iatrogenic injury. Abdominal magnetic resonance imaging was obtained and revealed abnormal signal in the mid to upper CBD extending into the bilateral hepatic ducts.

Endoscopic ultrasound later demonstrated CBD dilation to 17 mm with intraluminal congealed sludge or soft-tissue mass (Figure 1). Endoscopic retrograde cholangiopancreatography demonstrated a dilated biliary tree with extensive filling defects. After sphincterotomy, the CBD was swept with an extraction balloon resulting in the removal of several large, black stones. A repeat cholangiogram suggested a stricture in the proximal CBD. Choledochoscopy revealed several additional stone particles at the stricture, and lithotripsy was performed. Another balloon sweep removed several additional large stone particles and blood clots. Interestingly, a large piece of soft tissue was also extracted and was sent for histology (Figure 2). A fully-covered metal stent and a double pigtail plastic stent were placed.

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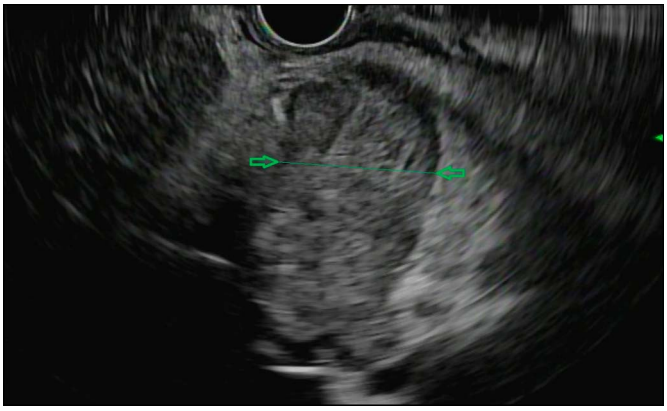

Figure 1. Endoscopic ultrasound image demonstrating common bile duct dilation to 17 mm with intraluminal soft-tissue mass and biliary sludge.

Histology demonstrated a compact tubular and papillary growth pattern with fine vascular capillary containing cores lined by neoplastic biliary epithelial cells with mild-to-moderate nuclear atypia; overall, it was consistent with a biliary ITPN (Figure 3). Medical Oncology stated that there was no role for chemotherapy citing the indolent nature of the malignancy and her poor performance status. Surgical Oncology deemed resection to be high risk because of poor functional status and Child Pugh class B cirrhosis. Before discharge, workup revealed positive antimitochondrial antibody (titer 1:80) and antinuclear antibody (titer 1:640) concerning for primary biliary cholangitis, but of unclear significance to her malignancy. Outpatient follow-up was planned; however, she opted to pursue hospice care. She ultimately died in the comfort of her own home 6 weeks after discharge.

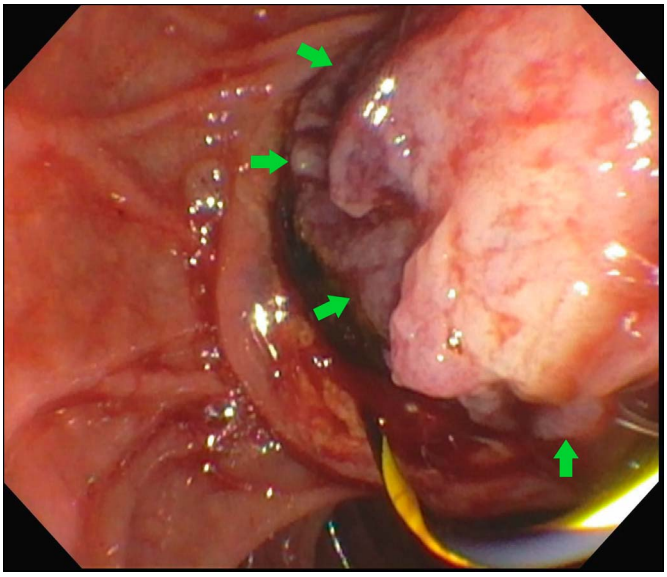

Figure 2. Endoscopic retrograde cholangiopancreatography demonstrating the soft-tissue mass extruding through the papilla after balloon sweep of the common bile duct. The mass is delineated by the arrows.

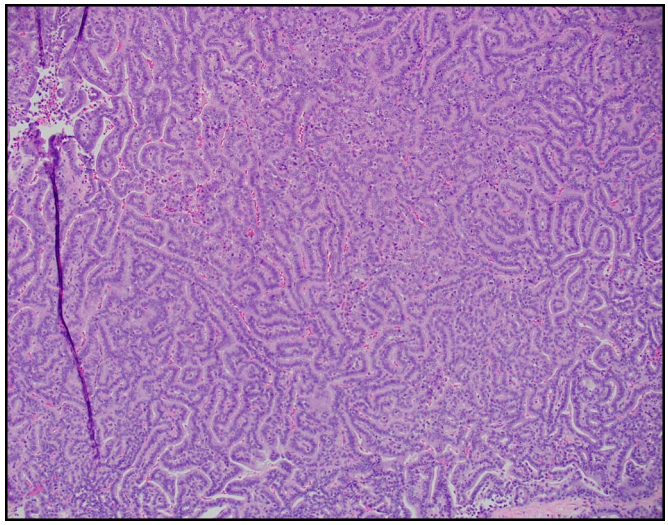

Figure 3. Histologic image demonstrating a compact tubular and papillary growth pattern with fine vascular capillary containing cores lined by neoplastic biliary epithelial cells with mild-to-moderate nuclear atypia.

DISCUSSION

Biliary ITPN is a rare intraductal neoplasm described mainly in case reports, and its rarity is evidenced by the 2 largest review articles that only identify 30 total cases.[1,3] It was first described as a case report of a bile duct tumor with histologic findings and immunohistochemical staining similar to pancreatic ITPN, a better established entity that differs from intraductal papillary mucinous neoplasms because of the predominantly tubular architecture of the tumor cells and the absence of mucin overproduction.[1,2] Diagnostic criteria for biliary ITPN are based on those for pancreatic ITPN: (i) a dysplastic, (ii) exophytic neoplasm, and (iii) growing within the bile duct system that is (a) $\geq$70% nonmucinous tubular units and (b) $\leq$30% papillary growth.[1]

Biliary ITPNs are most commonly diagnosed in the seventh decade of life and have a slight female predominance. They are most often within the intrahepatic bile ducts but may be extrahepatic. They more commonly present with invasive adenocarcinoma, and liver infiltration is possible.[1,3] Presenting symptoms are variable but most commonly include jaundice, abdominal pain, and weight loss.[1,3] The classic appearance on magnetic resonance imaging is intraductal soft tissue with contrast enhancement, peribiliary liver parenchyma enhancement, and mild dilation of the upstream bile duct.

Given these presenting findings, cholangiocarcinoma is the main diagnosis of exclusion. The differential diagnosis also includes, IPNB—the biliary equivalent of pancreatic intraductal papillary mucinous neoplasms.[5] IPNB seem like a biliary ITPN on imaging and present similarly. In fact, an earlier case series of intraductal neoplasms of the intrahepatic bile duct described biliary ITPN as a subcategory of "IPNB with tubular structure."[6] However, there are 2 important distinctions between these

entities. Histologically, IPNB are characterized by papillary proliferation, whereas biliary ITPNs are predominantly tubular.[1] The second is mucin gene expression where MUC5AC, and therefore mucin overproduction, is absent in biliary ITPN, whereas it is expressed in 78% of IPNB.[3] Biliary ITPNs also lack MUC2 expression and KRAS mutations and have low rates of TP53 overexpression.[3,4]

Given the genetic profile and histologic features, it has been proposed that biliary ITPNs originate from peribiliary glands, rather than the surface epithelium.[7] Peribiliary glands are minute structures located along the biliary tree that assist in several physiological functions and are the location of biliary tree stem/progenitor cells. Peribiliary glands are also believed to play a role in primary sclerosing cholangitis and immunoglobulin G4-related sclerosing cholangitis.[8]

Importantly, biliary ITPNs are not known to be a precursor of cholangiocarcinoma; unlike IPNB that develops through the adenoma-carcinoma sequence and is an established precursor of cholangiocarcinoma.[3,9] Supporting this is the favorable 5-year survival which, despite the high incidence of invasive carcinoma, has been reported at approximately 90% compared with 60% with IPNB.[1] BilIN, a third intraductal neoplasm, is another precursor lesion to cholangiocarcinoma and has known associations with primary sclerosing cholangitis, choledochal cysts, and hepatolithiasis.[5] However, BilIN is a microscopic lesion, easily differentiating it from biliary ITPN and IPNB.[7]

In contrast to the other intraductal neoplasms where certain risk factors are known, none are established for biliary ITPN. Given the rarity, there is no standard of care for treatment of biliary ITPN. Surgical resection of pancreatic ITPN has demonstrated favorable results, and this may be extrapolated to biliary ITPN.[10,11] Biliary ITPN should be included on the initial differential diagnosis of solid intraductal biliary tree lesions.

DISCLOSURES

Author contributions: MJ Sullivan wrote the manuscript, revised the manuscript for intellectual content, approved the final manuscript, and is the article guarantor. J. Grau provided the pathology images, revised the manuscript for intellectual content, and approved the final manuscript. S. Shah provided the endoscopy images, revised the manuscript for intellectual content, and approved the final manuscript.

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Informed consent could not be obtained from the family of the deceased patient despite several attempts. All identifying information has been removed from this case report to protect patient privacy.

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REFERENCES

1. Nakagawa T, Arisaka Y, Ajiki T, et al. Intraductal tubulopapillary neoplasm of the bile duct: A case report and review of the published work. *Hepatol Res* 2016;46:713–8.
2. Park HE, Jang KT, Heo JS, et al. A potential case of intraductal tubulopapillary neoplasms of the bile duct. *Pathol Int* 2010;60:630–5.
3. Schlitter AM, Jang KT, Kloppel G, et al. Intraductal tubulopapillary neoplasms of the bile ducts: Clinicopathologic, immunohistochemical, and molecular analysis of 20 cases. *Mod Pathol* 2015;28:1249–64.
4. Wu CH, Yeh YC, Tsuei YC, et al. Comparative radiological pathological study of biliary intraductal tubulopapillary neoplasm and biliary intraductal papillary mucinous neoplasm. *Abdom Radiol* 2017;42:2460–9.
5. Zen Y, Adsay NV, Bardadin K, et al. Biliary intraepithelial neoplasia: An international interobserver agreement study and proposal for diagnostic criteria. *Mod Pathol* 2007;20:701–9.
6. Naito Y, Kusano H, Nakashima O, et al. Intraductal neoplasm of the intrahepatic bile duct: Clinicopathological study of 24 cases. *World J Gastroenterol* 2012;18(28):3673–80.
7. Zen Y, Amarapukar AD, Portmann BC. Intraductal tubulopapillary neoplasm of the bile duct: Potential origin from peribiliary cysts. *Hum Pathol* 2012;43:440–5.
8. Matsubara T, Kozaka K, Matsui O, et al. Peribiliary glands: Development, dysfunction, related conditions, and imaging findings. *Abdom Radiol (NY)* 2020;45:416–36
9. Fuente I, Gonzalez M, de Santibanes M, et al. Intraductal papillary neoplasm of the bile duct (IPNB): Case report and literature review of a challenging disease to diagnose. *J Gastrointest Cancer* 2019;50(3):578–82.
10. Fritz S, Kuper-Steffen R, Feilhauer K, et al. Intraductal tubular papillary neoplasm (ITPN), a novel entity of pancreatic epithelial neoplasms and precursor of cancer: A case report and review of the literature. *Int J Surg Case Rep* 2019;55:187–91.
11. Kuscher S, Steinle H, Soleiman A, et al. Intraductal tubulopapillary neoplasm (ITPN) of the pancreas associated with an invasive component: A case report with review of the literature. *World J Surg Oncol* 2017;15:203.