Intraductal papillary neoplasm of the bile duct

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ABSTRACT

Intraductal papillary neoplasm of the bile duct is characterized by intraductal papillary growth with fibrovascular cores that can grow anywhere along the biliary tree. Most cases have high-grade intraepithelial neoplasia or an associated invasive carcinoma. These tumors can spread superficially along the biliary tree and be multifocal, and preoperative biopsy cannot always reflect the maximum degree of atypia. Frozen section to assess the distal common bile duct margin is crucial to avoid the risk of recurrence. Theoretically, resection of the entire biliary tree by liver transplantation and pancreaticoduodenectomy is regarded as the only curative treatment.

KEYWORDS Bile duct tumor; intraductal papillary neoplasm of the bile duct

Intraductal papillary neoplasm of the bile duct (IPNB) is a variant of bile duct tumors that is recognized as a precursor lesion to invasive cholangiocarcinoma. There is a slight male predominance, and patients generally range from 50 to 70 years.¹ Clinical symptoms include intermittent abdominal pain, acute cholangitis, and jaundice.¹ IPNB has a tendency to spread superficially along the biliary tree and can be multifocal. Here, we describe a patient with IPNB, with a focus on pathological findings.

CASE DESCRIPTION

A 58-year-old man with a past medical history of ulcerative colitis and primary sclerosing cholangitis presented to our institution after biopsy of a hilar stricture at an outside institution showed adenocarcinoma. Magnetic resonance imaging of the abdomen showed mild prominence of the left hepatic biliary ducts. There was also a stable cystic lesion in the uncinate process of the pancreas. The patient was started on Mayo regimen transplant protocol and received neoadjuvant chemotherapy and brachytherapy. He eventually underwent hepatectomy with an allograft liver transplant; however, evaluation of the bile duct margin was not performed intraoperatively.

Following the procedure, the pathology department received perihepatic and periductal lymph nodes, the separately excised common bile duct margin, and the explanted

liver. Grossly, the native liver was remarkable for focal areas of bile duct dilatation measuring up to 1.1 cm. Microscopically, sections of the common bile duct showed an intraductal papillary neoplasm with low- and high-grade dysplasia (*Figures 1a and 1b*). The native liver showed focal periductal fibrosis, occasional fibro-obliterative lesions, cholestasis, and bridging fibrosis, consistent with sclerosing cholangitis (*Figure 1c*).

Due to the presence of high-grade dysplasia at the bile duct margin, the patient was taken back to the operating room. A frozen section of the bile duct stump showed at least low-grade dysplasia, and the decision to proceed with pancreaticoduodenectomy was made. Grossly, approximately 1 cm from the ampulla of Vater, the lumen of the bile duct was filled with a soft pink-tan papillary mass. The mass appeared to be confined to the bile duct and measured 2.5 cm in greatest dimension. Within the pancreatic head, there was a 0.8 cm in greatest dimension dilatation of the pancreatic duct. Microscopically, there was an intraductal papillary neoplasm with high-grade dysplasia involving the intrapancreatic duct with no evidence of invasive carcinoma (*Figure 1d*). All margins were negative.

DISCUSSION

Cholangiocarcinoma arises from one of two different precursor pathways. The more common precursor lesion is known as flat biliary dysplasia or biliary intraepithelial

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Figure 1. (a) Separately excised bile duct shows intraductal papillary neoplasm of the bile duct characterized by papillary growth with fibrovascular cores (inset) and micropapillae. (b) High-grade dysplasia is seen, characterized by nuclear enlargement and hyperchromasia, nuclear stratification, and loss of mucin cap. (c) The native liver shows primary sclerosing cholangitis characterized by concentric periductal fibrosis ("onion skin") and bridging fibrosis. (d) The pancreatic bile duct shows a papillary growth pattern with focal areas of high-grade dysplasia (inset).

neoplasia with progression from mild dysplasia to severe dysplasia/carcinoma in situ, similar to the progression of pancreatic intraepithelial neoplasia in pancreatic ductal adenocarcinoma.² The less common precursor lesion is known as intraductal papillary neoplasm.²

Intraductal papillary neoplasm is characterized by intraductal papillary growth with fibrovascular cores that can grow anywhere along the biliary tree. The World Health Organization classification separates IPNB into intraductal papillary neoplasm (IPN) with low- or intermediate-grade intraepithelial neoplasia, IPN with high-grade intraepithelial neoplasia, and IPN with an associated invasive carcinoma.³ Similar to intraductal papillary mucinous neoplasms of the pancreas, IPNBs are classified into four histologic subtypes: pancreaticobiliary, intestinal, gastric, and oncocytic.³ The most common subtype for all IPNBs is the pancreaticobiliary followed by the intestinal subtype, and these two subtypes are commonly associated with at least high-grade intraepithelial neoplasia.³ If these lesions progress to invasive adenocarcinoma, the tumor shows tubular or mucinous morphology.³

IPNBs are rare and comprise 9% to 38% of all bile duct tumors.³ Most cases of IPNB have high-grade intraepithelial neoplasia or an associated invasive carcinoma. In a study by Rocha et al, invasive carcinoma was seen in 29 of 39 cases (74%) of IPNB.⁴ There is wide geographic variation, and the disease is more commonly seen in Far Eastern countries due to endemic risk factors such as hepatolithiasis and clonorchiasis. IPNBs can be detected by ultrasonography, computed tomography, and magnetic resonance imaging and show bile duct dilatation and intraductal masses. Cholangioscopy can also show bile duct dilatation with mucin hypersecretion.

Appropriate surgical treatment is heavily dependent on preoperative assessment of tumor location, extension, depth of invasion, and lymph node metastasis. Surgical resection is considered for patients without distant metastasis and includes major hepatectomy with or without extrahepatic bile duct resection or pancreaticoduodenectomy.¹ Intraoperative frozen section should be performed at the bile duct stump to ensure a negative surgical margin, given the tendency of these tumors to spread superficially along the bile duct and their multifocal nature. The surgeon must keep in mind that different foci in multifocal IPNBs can also be at different stages, so a biopsy of one area may not reflect the stage of the entire tumor.¹ For cases with extensive superficial spreading or multifocal involvement, total hepatectomy with liver transplantation and pancreaticoduodenectomy is regarded as the only curative treatment.³ However, liver transplantation should not be performed for patients with advanced tumor invasion or positive lymph nodes.³

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