

Intrahepatic biliary papillomatosis: a rare case report and literature review

Abstract

Background: Biliary papillomatosis (BP) is a rare disease characterized by multiple papillary tumors of variable distribution, involving both the intra hepatic and extra hepatic biliary tract. Till now, its clinical features and outcome are still not well known and the diagnosis is often misdiagnosed for clinical rarity. **Case presentation:** We experienced a case of biliary papillomatosis of Intra hepatic biliary tract in a 52-year-old man who presented with right upper quadrant abdominal pain. Laboratory tests showed mild elevated bilirubin. Imaging examination (ultrasound, computed tomography and magnetic resonance cholangiopancreatography) demonstrated non-specific intra hepatic duct and common bile duct dilatation. Intraoperative Cholecholecscopy showed a dilated bile duct filled with papillary, friable tissue located in left intra hepatic ducts. Thereafter, the patient underwent left lateral lobectomy of liver and the T-tube was positioned. Histology demonstrated papillary lesion characterized by fibro vascular core with overlying mucin-producing columnar epithelial cells dysplasia. **Conclusion:** Intrahepatic biliary papillomatosis is an extremely rare disorder. Preoperative diagnosis of BP is somehow difficult and often misdiagnosed for its clinical rarity. Taken together, surgical resection is considered the optimal treatment for biliary papillomatosis and intraoperative cholangioscopy is a potential valuable auxiliary instrument for diagnosis and treatment of the disease.

Keywords: intrahepatic biliary papillomatosis, cholecholecscopy, biliary tract, surgery

Volume 1 Issue 2 - 2014

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Received: July 16, 2014 | Published: July 21, 2014

Abbreviations: BP, biliary papillomatosis; CK, cyto keratin; CT, computed tomography; ACT, alpha1-antichymotrypsin; TUS, transabdominal ultrasound; MRI, magnetic resonance imaging; ERC, endoscopic retrograde cholangiography; PET, positron emission tomography; EUS, endoscopic ultra sound

Introduction

Biliary papillomatosis (BP) is considered a rare condition of the biliary tract with a risk of malignant transformation and a high recurrence rate after operation due to the diffuse distribution of the disease. Clinical manifestations of BP are nonspecific, often misdiagnosed for clinical rarity. Recently, we experienced a case of BP of intra hepatic biliary tract in which Cholecholecscopy played an important role in the diagnosis of this disease.

Case presentation

A 56-year-old man was admitted to our hospital in April 2013 with a 2-year history of recurrent episodes of abdominal pain. He had a previous surgery history of cholecystectomy, common bile duct exploration and T tube drainage due to its own disease of cholelithiasis. Physical examination revealed definite tenderness in the right hypochondrium only. Laboratory tests detected a total bilirubin of 22.6 μ mol/L (normal range, 3.4-20.5 μ mol/L), direct bilirubin of 14.2 μ mol/L (normal range, 0.0-6.8 μ mol/L), ALT of 24IU/L (normal range <60 IU/L), AST of 19IU/L (normal range <60IU/L), ALP of 75 IU/L (normal range, 40-150IU/L), gamma GTP of 52IU/L (normal range, 4-87IU/L). Tumor markers (CEA, CA19-9, a-FP) were normal. Computed tomography (CT), abdominal ultrasound demonstrated intra hepatic duct dilatation localized to the left lobe with a markedly dilated common bile duct, and floccules in left intra hepatic duct. MRCP revealed dilated intra hepatic ducts and common bile duct, within multiple irregular filling defects inside the distal common bile duct. Intraoperative Cholecholecscopy demonstrated a dilated

(1.5cm diameter) bile duct filled with papillary, friable tissue located in left intra hepatic ducts. A decision was made to proceed with left lateral lobectomy of liver, which would have required a left hepatectomy (for which the patient had not given consent). A per cutaneous T-tube was left within the bile duct. Histopathological examination demonstrated papillary lesion characterized by fibro vascular core with overlying mucin-producing columnar epithelial cells dysplasia (Grade 2) (Figure 1). Immunohistochemical markers, cytokeratin (CK) 7 (+), CK 20 (-), CEA (-), Ki-67 (+) 20%, p53 (-), alpha-antichymotrypsin (ACT) (-). After 7 months of follow-up, there was no recurrence.

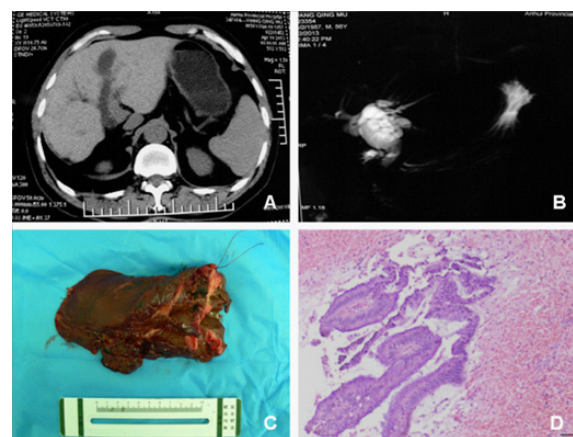


Figure 1 Imagings of the patient. (A) Computed tomography (CT) showed cyst-like dilatation of left lobe of bile duct. (B) Magnetic resonance cholangiopancreatography (MRCP) showed dilatate intra hepatic bile within multiple irregular filling defects inside the common bile duct. (C) Surgical specimen showed papillary fragile mass with gelatinous mucin-producing. Post-operative pathology demonstrated dysplasia of biliary epithelia, exerting as papillary (HE \times 100).

Discussion

Biliary papillomatosis (BP), first reported by Chappet in 1894, is a rare disease characterized by multiple papillary adenomas of variable distribution and extent in the intra hepatic and/ or extra hepatic biliary tree.^{1,2} Intrahepatic biliary papillomatosis is extremely rare, and it is absence of specific clinical manifestations. Hoang and Bluemke³ reported that the disease involves the extra hepatic ducts alone in 58% of cases, both extra- and intra-hepatic ducts in 33% and intra hepatic ducts alone in 9%. It is a low-grade neoplasm with high malignant potential and should be regarded as a premalignant lesion. Recent literature suggests BP has a rate of malignant transformation between 41% and 83%.^{4,5} Mutations in K-ras and p53 genes have been proposed as initiating events. BP can be classified into mucin or non-mucin secreting according to cholangioscopic views. In terms of the mucin-secreting type of BP, the inspissated mucus produced by the tumors leads to chronic insufficient obstruction of the bile duct, which finally results in diffuse dilatation of whole biliary tree with a segment or a lobe cyst-like bile duct dilatation where the tumors are located.⁴ In this case, based on intraoperative choledochoscopic exploration of common bile duct (large amount amorphous mucus without definite neoplasm), we found that the smooth surface of right-sided intra hepatic bile duct wall has shown no neoplasm, and 1cm x 1.5cm diameter papillary neoplasm located in left intra hepatic duct, from which dark green and gelatinous liquid out flowed. Therefore mucin-secretion type of intra hepatic biliary papillomatosis was preliminary consideration during operation.

BP is often clinically challenging to diagnosis before surgery. Conventional trans abdominal ultrasound (TUS), computed tomography (CT), magnetic resonance imaging (MRI), endoscopic retrograde Cholangiography (ERC) and positron emission tomography (PET) have a low specificity to differentiate benign from malignant tumors.^{6,7} Transabdominal US and CT often demonstrate non-specific bile duct dilatation, but the ability to visualize small tumors within the ducts is limited. MRCP shows irregular filling defects, complete or incomplete obstruction of the bile duct, and proximal biliary dilatation. The appearances of BP on ERCP are similar to those of MRCP. Moreover, ERCP may also show excessive mucus within the common bile duct and duodenum. Nevertheless, due to the obstruction and mucin secretion, the dilated bile ducts may not completely fill with contrast material. Thus, small papillomas may not be observed. Besides, the availability of ERCP is restricted by the complications such as cholangitis and pancreatitis.⁷⁻¹¹ Therefore, in order to improve the preoperative diagnosis of BP, the introduction of new diagnostic imaging techniques is of importance. Endoscopic ultrasound (EUS) is used for BP as well, because it can discover the duct wall or adjacent vessels invasion as well as metastasis to regional lymph nodes.¹² Elastography is a newly developed dynamic technique that can provide an estimation of tissue stiffness, which is likely to be helpful to differ between malignant and benign lesions infiltrating the bile duct wall but this has to be proven in further studies.⁷ Despite improvements in diagnostic techniques, cholangioscopic would be considered the best diagnostic instrument, because it allows direct visualization of the bile duct mucosa and subtle mucosal lesions, which is crucial for choosing the appropriate surgical treatment.^{1,4}

Surgical resection is considered the optimal treatment for biliary papillomatosis. Lee et al.² reported that patient received a curative surgical treatment has a 5-year survival rate of up to 81%. Meanwhile, the mean survival is 37 months after palliative drainage. However, local resection often remains incomplete due to high risk of recurrence in view of positive resection margins or recurrence on the remnant

bile duct because of the multifocality of the disease. For patients with diffuse or recurrent BP, pancreaticoduodenectomy can be curative. Nevertheless, in terms of patients with invasive cholangiocarcinoma or positive lymph node, liver transplantation is not very effective.⁴ Since both endoscopic and percutaneous biopsies failed to establish the diagnosis of malignancy or the degree of invasion, the size of the tumor can be overestimated, especially in type of mucin-producing tumor. So, the preoperative assessment of BP seems to be more difficult. Thus, initial partial resection before liver transplantation may help to eliminate advanced tumor invasion and/or positive lymph nodes on definitive analysis of the specimen. This strategy selects cases with superficial foci of malignancy without positive lymph nodes in whom liver transplantation would be reasonable.¹³ In addition, other treatment options have been described in treatment with BP. Gunven et al.¹⁴ first applied Intra luminal brachytherapy with Iridium-192 and the patient survived for 6 years without recurrence. Jazrawi et al.¹⁵ utilized intra ductal argon plasma coagulation for the management of BP and achieved a certain impact, but residual tumor was still found, and recurrence happened.

Conclusion

Radical surgical resection and/ or liver transplantation can be considered as definitive approach.^{4,13,16,17} Intraoperative cholangioscopy is beneficial for a radical successful surgical resection. Nevertheless, due to the relatively small cases at present, large sample support of evidence-based medicine is still lack. In future, the pathogenesis, evolution, diagnosis and treatment of BP need to be further evaluated.

Conflicts of Interest

The author declares that there is no conflicts of interest.

Acknowledgements

None.

Funding

None.

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