CASE REPORT

Rare event of biliary papillomatosis arising in a choledochal cyst

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SUMMARY

A 31-year-old man presented with features of recurrent cholangitis for 7 months. Examination revealed icterus and a palpable 10×8 cm lump in the right hypochondrium extending into the epigastrium. Total and direct bilirubin was raised (8.4, 6.7 mg/dL). Alkaline phosphatase (468 U/L) was raised but other liver enzymes were normal. Ultrasound of the abdomen showed dilated intrahepatic biliary radicals (IHBRs) and common hepatic duct (CHD) with a significant intrahepatic portion. Contrast-enhanced CT scan of the abdomen showed similar findings. MR cholangiopancreatography demonstrated diffusely dilated IHBRs and choledochal cyst involving the CHD. The common bile duct was mildly dilated without any filling defect. Tumour markers (carcinoembryonic antigen and cancer antigen 19-9) were normal. The patient underwent complete excision of the extrahepatic biliary system including choledochal cyst and Roux-en-Y hepaticojejunostomy. Opening up the bile duct showed very thick gelatinous material and multiple pedunculated papillary type structures arising from the wall of the choledochal cyst.

BACKGROUND

A choledochal cyst is a well-known premalignant condition involving the biliary system. The reported incidence of malignancy in a choledochal cyst is 2.5–26% and can involve the intrahepatic as well as extrahepatic biliary system and pancreas.¹ Biliary papillomatosis (BP) in a choledochal cyst is, however, an extremely rare event, reported only thrice so far to the best of our knowledge.^{2–4}

CASE PRESENTATION

A 31-year-old man presented with pain in his abdomen and fever for the past 2 days. He said he had, for the last 7 months, been taking treatment for jaundice without any resolution of symptoms and had also experienced five episodes of fever and pain which resolved with conservative management. He had a similar history of jaundice with several episodes of pain and fever 4 years prior which resolved with conservative management. Examination revealed icterus and a tender, palpable 10×8 cm lump in the right hypochondrium extending into the epigastrium. Ultrasound of the abdomen suggested a choledochal cyst. The patient was admitted and started on conservative management. The cholangitis resolved in a few days and the patient was discharged and re-called for further evaluation and management after 15 days.

INVESTIGATIONS

On admission, the haemoglobin of the patient was 12 g/dL and total count was 22 800/mm³. Liver function tests were deranged with total bilirubin 8.4 mg/dL and conjugated bilirubin 6.7 mg/dL. Alkaline phosphatase (ALP) was elevated (468 U/L); however, aspartate aminotransferase (AST) and alanine transaminase (ALT) levels were normal. Total protein was 6.9 g/dL and albumin was 2.6 g/dL. Chest X-ray was normal. Ultrasound of the abdomen showed presence of a hypoechoic lesion with internal echoes at porta hepatis suggesting a choledochal cyst. Before discharge, most parameters had returned to normal including a total count (7400/mm³) and ALP (178 U/L); bilirubin remained raised even after resolution of other symptoms.

The patient presented after 15 days for MR cholangiopancreatography. The MRI (figure 1A, B) showed a large 70.3×69.1 mm choledochal cyst with multiple signal voids within the lumen, involving the proximal part of CHD and displacing the well distended gallbladder with dilation of distal CBD, and mildly and diffusely dilated intrahepatic biliary radicals (IHBRs) suggestive of a type I choledochal cyst. The levels of carcinoembryonic antigen and cancer antigen 19-9 were within normal limits.

TREATMENT

The patient underwent complete excision of the extrahepatic biliary system including the choledochal cyst and Roux-en-Y hepaticojejunostomy. Operative findings included a distended gallbladder and a choledochal cyst involving the common hepatic duct extending into the liver (figure 2A, B). The common bile duct was also dilated but there was no distal obstruction. Opening up the bile duct surprised us with multiple pedunculated papillary type structures floating freely in thick gelatinous bile as well as arising from the wall of the choledochal cyst (figure 3A). However, right and left bile ducts were normal. A complete extrahepatic cholecystectomy (figure 3B) was carried out taking 2–3 mm of distal-most right and left bile ducts and two separate hepaticojejunostomies were performed. The immediate postoperative period exhibited a mild and transient increase in bilirubin and liver enzymes followed by a gradual return to normal values. The patient was discharged after 7 days of uneventful recovery period. At the time of discharge his liver functions were normal, as was the ultrasound scan of the abdomen showing no dilation of the IHBRs.

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Figure 1 (A, B) MR cholangiopancreatography image (A) and T2-weighted spectral attenuated inversion recovery (SPAIR) image (B) showing cystic dilation of the common hepatic duct extending into the liver. Irregular filling defects in the form of papillary projections noted in the intrahepatic cystic dilations.

OUTCOME AND FOLLOW-UP

One week follow-up was on expected lines without any clinical jaundice or derangements of liver functions. Smears from bile showed a background of thick secretion, numerous inflammatory cells comprising of lymphocytes and macrophages and a few papillary structures without any distinct morphology. Histopathological examination of the gallbladder showed features of chronic cholecystitis. Sections from the wall of the common hepatic duct at some places showed papillary projections lined by benign appearing cuboidal to columnar cells supported by fibromuscular tissue (figure 4A). Sections from the freely floating papillary structures showed predominantly benign appearing columnar cells in a branching papillary pattern with fibrovascular core and presence of abundant intracellular and extracellular mucin (figure 4B). A single area showed pleomorphic cells with hyperchromatic nuclei arranged in a

Figure 2 (A, B) Intraoperative images of a large choledochal cyst with gall bladder (A) and completely mobilised extrahepatic biliary system and the cyst (B).

glandular pattern infiltrating the stroma. The margins of the resected choledochal cyst and bile ducts were negative. Stromal infiltration raised the concern of malignancy and an opinion was sought at a higher hepatobiliary institute. Since there was no invasion of the wall of the choledochal cyst or bile ducts and only a single focus of stromal infiltration was detected, that too of a freely floating papillary structure, there was a very low grade to non-existent malignant potential. The patient was told he did not require any further procedure and advised regular follow-up. Over the last 1 year, the patient has come for follow-up twice at an interval of 6 months and is doing well.

DISCUSSION

BP is an uncommon clinicopathological entity characterised by multiple papillary adenomas of the biliary epithelium. BP can involve any part of the biliary system including the gallbladder and pancreas producing large amounts of a thick jelly like substance leading to obstruction to bile flow and recurrent episodes of cholangitis.⁵ BP is considered to be a benign lesion; however, malignant transformation has been seen in as many as 35–41% cases which include dysplastic changes to carcinoma in situ and to invasive adenocarcinoma.^{6–8} Males are frequent sufferers

Figure 3 (A, B) Excised specimen (A). Endoscopic intraluminal view showing the papillary growth arising from the wall of the dilated common hepatic duct (B).

(male:female=2:1).⁸ Median age at diagnosis is 58 years.³ Imaging modalities may define the extent of the dilation of the biliary system as well as the filling defects or mass lesions.⁹

BP in a choledochal cyst is an extremely rare event and, to the best of our knowledge, reported thrice so far in the literature.²⁻⁴ Mutations in K-ras and p53 genes have been proposed as initiating events.²⁻⁴ Anomalous pancreatobiliary duct junctions may also add a malignant potential. Adenocarcinoma arising from BP in a choledochal cyst has been reported in 1 case.³ A classification has been proposed to define the malignant potential of BP: class 1 is BP with low-grade atypia, class 2 with high-grade atypia, class 3 with in situ carcinoma, class 4 with microscopic foci of stromal invasion and class 5 with invasion into hepatic parenchyma or bile duct wall.⁸ However, this classification may not hold true for BP arising in a choledochal cyst. Expression of mucin core proteins and mucin carbohydrate antigens further defines the malignant potential.⁸ Distant metastasis is rare.¹⁰⁻¹¹ Radical surgical procedures like bile duct excision, pancreaticoduodenectomy and hepatectomy have been described as the procedures of choice especially if invasive components are identified.³ Liver transplantation is an option in cases of diffuse biliary papillomatosis, but there is no consensus on what may be an optimal or most appropriate procedure for BP in a choledochal cyst, probably owing to rarity of occurrence and paucity of the literature. Local recurrence following these procedures is 14% and can involve the remaining biliary tree even after negative surgical margins.⁶⁻¹⁰ Five-year survival after curative resection is 81% while after palliative drainage it is 37 months.⁸

Figure 4 (A, B) Sections from the wall of common hepatic duct show papillary projections lined by benign appearing cuboidal and columnar cells (A). Sections from the growth show predominantly benign appearing columnar cells in a branching papillary pattern with fibrovascular core (B).

Learning points

- Biliary papillomatosis (BP) is an uncommon entity and BP in a choledochal cyst is extremely rare.
- Preoperative diagnosis of BP in a choledochal cyst may be relatively difficult due to the very thick and gelatinous nature of bile and biliary sludge, and a differentiation from papillary structures may not always be possible.
- The malignant potential of BP is low and treatment with a curative intent is possible in most cases.
- There are no established guidelines yet for BP in a choledochal cyst and therefore patients should be advised a careful follow-up.

Contributors VKS and KN were clinically associated with the patient and performed the surgery. BKS performed the radiology workup. All authors contributed equally in drafting the manuscript.

Competing interests None.

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