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Filling Defect on ERCP: Biliary Cystadenoma, a Rare Tumor

Krishna Rayapudi Timothy Schmitt Mojtaba Olyaei

Kansas University Medical Center, Kansas City, Kans., USA

Key Words

Biliary tumor · Cyst · Biliary cyst

Abstract

Biliary cystadenomas are rare tumors of the bile ducts most commonly presenting as large right liver lobe lesions. These are usually slow-growing and mostly benign. They commonly present with abdominal pain. On physical exam an abdominal mass can be identified occasionally. Walls of biliary cystadenomas appear thicker than simple cysts, with soft tissue nodules and enhancing septations on CT or MRI. Radiographic images can vary with the amount of protein content in the fluid on CT or MRI. Due to the risk of malignant transformation, complete surgical resection is advised. Hereby, we describe a 37-year-old lady who presented to the outpatient clinic with bloating and abdominal discomfort with intermittent elevated liver enzymes and hyperbilirubinemia. Ultrasound of the liver and bile ducts followed by CT scan and magnetic resonance cholangiopancreatography confirmed the presence of biliary cystadenoma of the intra- and extrahepatic ducts. It was seen as a filling defect of the intra- and extrahepatic ducts (common hepatic duct) on endoscopic retrograde cholangiopancreatography. Involvement of the intra- and extrahepatic bile ducts simultaneously is a rare presentation of this tumor. She later on underwent exploratory laparotomy with extrahepatic bile duct resection, left hepatic lobe resection and reconstruction with hepaticojejunostomy. Pathology confirmed the presence of biliary cystadenoma with ovarian-like stroma. She had recovered uneventfully from the surgery when seen 2 weeks later in the clinic. Biliary cystadenoma is a rare, mostly benign neoplasm of the biliary tract that should be considered in the differential diagnosis of cystic lesions of the biliary tract.

Introduction

Biliary cystadenomas are rare tumors of the biliary tract. They are mostly benign with potential for malignant transformation. Biliary cystadenoma was initially described and published in 1887 and its first resection was performed in 1892 [1]. Several case reports and case series have described this condition later

on. It is estimated that there have been less than 200 cases reported worldwide [2]. The etiology of this condition is not known. Most cystadenomas arise within the intrahepatic bile ducts [3, 4]. Biliary cystadenoma involving the extra- and intrahepatic bile ducts simultaneously is less frequent. To our knowledge, there has been one published case [5] that describes a biliary cystadenoma involving the intrahepatic duct extending to the common bile duct. We aim to highlight here an instance of biliary cystadenoma involving the intra- and extrahepatic bile ducts, which is an uncommon presentation.

Biliary cystadenomas are slow-growing tumors. There is a female preponderance with mean age at presentation being 45 years [6]. Most common clinical presentation is with abdominal pain. In view of the potential for malignant transformation [7–9] to cystadenocarcinoma or sarcoma, complete surgical resection is advised per current recommendations. There is a high recurrence rate with incomplete resection [3, 10, 11]. Hereby, we present a patient with biliary cystadenoma involving both intra- and extrahepatic bile ducts that was resected completely with extrahepatic bile duct resection, left hepatic lobe resection and reconstruction with hepaticojejunostomy.

Case Report

A 37-year-old woman presented to the University Hospital Gastroenterology Clinic with intermittent abdominal bloating and discomfort for almost 20 months. Discomfort and bloating were not related to meals, defecation or change in position. Symptoms arose spontaneously and lasted several hours at a time. She recalled at least 1–2 episodes per month from the time symptoms started. She had not had any diarrhea, nausea, vomiting, fever or chills since the onset of symptoms. She recalled having elevated liver enzymes during testing at a health fair a year prior to presentation which showed aspartate transaminase (AST) 31 IU/l (range 10–30 IU/l), alanine transaminase (ALT) 40 IU/l (range 6–40 IU/l), alkaline phosphatase (ALP) 128 IU/l (range 33–115 IU/l) and total bilirubin 0.6 mg/dl. She went to her primary care doctor 3 months prior to presentation and was noted to have elevated liver enzymes and bilirubin (total bilirubin 3.2 mg/dl, direct bilirubin 1.9 mg/dl, AST 134 IU/l, ALT 387 IU/l, ALP 344 IU/l).

Ultrasound was done followed by a CT scan. Ultrasound showed a $2.9 \times 2.4 \times 2.9$ cm hypoechoic mass with calcification in the left hepatic lobe with areas of bile duct dilation greatest in the left hepatic lobe. CT scan (fig. 1) showed similar findings with a complex cyst in the inferior aspect of the left lobe of the liver with mild dilation of bile ducts of the left hepatic lobe. She was referred to a gastroenterology clinic 6 weeks prior to presentation where repeat testing showed that the liver enzymes and total bilirubin had normalized (total bilirubin 0.7 mg/dl, AST 18 IU/l, ALT 11 IU/l, ALP 71 IU/l). Magnetic resonance cholangiopancreatography (MRCP) was ordered and showed 2×2.5 cm cystic left hepatic lobe lesion with two thin internal septations which showed faint enhancement, with possible communication with the intrahepatic bile ducts. There was diffuse mild intrahepatic biliary dilation at the central left and right intrahepatic ducts. No extrahepatic bile duct dilation was noted. At the proximal common hepatic duct, a waist-like narrowing of the duct (focal absence of intraductal biliary signal) was noted. The possibility of a biliary cystadenoma versus Caroli disease versus hydatid cyst was raised. So, she was referred to the University Hospital Gastroenterology Clinic.

The patient had no history of intravenous drug use or tattoos or body piercing, no history of excessive alcohol use or obesity, no history of unprotected sex or sex with multiple sexual partners and no history of working with toxic chemicals. She had no prior history of surgery or medical illness. She had no known allergies. She was not using any medications. There was no significant family history of biliary or liver disease.

Her blood pressure was 126/78 mm Hg, heart rate 74/min, respiratory rate 14/min, temperature 98.6° Fahrenheit and oxygen saturation 99% while breathing ambient air. Physical exam

demonstrated mild tenderness in the left upper quadrant on deep palpation without any palpable mass, hernia or scars. The rest of the physical exam was within normal limits. Repeat labs done at the clinic at presentation showed total bilirubin 0.3 mg/dl, AST 16 IU/l, ALT 11 IU/l, ALP 37 IU/l, hemoglobin 13.1 g/dl, white cell count 7,100/mm³ (neutrophils 60.8%, lymphocytes 31.4%, monocytes 6.3%, eosinophils 1.2%, basophils 0.3%), INR 1.0, albumin 4.5 g/dl, CA19-9 10 U/ml (normal <37 U/ml). She was instructed to present for follow-up in 3 months and obtain repeat labs if she developed any intercurrent symptoms.

Two months after clinic visit, repeat lab studies showed elevated total bilirubin and liver enzymes (total bilirubin 4.5 mg/dl, direct bilirubin 2 mg/dl, AST 146 IU/l, ALT 361 IU/l, ALP 166 IU/l). This was accompanied by intermittent episodes of itching that started in the abdominal area and back and spread to the wrists, hands and feet. She was treated with a 14-day course of ciprofloxacin (500 mg twice daily) suspecting cholangitis along with ursodiol (500 mg twice daily) with relief of her itching and jaundice. Three months after clinic visit, lab studies showed normal bilirubin and liver enzyme levels (total bilirubin 0.4 mg/dl, AST 18 IU/l, ALT 15 IU/l, ALP 57 IU/l). Six months after clinic visit, lab studies showed repeat elevation of liver enzymes and total bilirubin (total bilirubin 4.0 mg/dl, AST 152 IU/l, ALT 280 IU/l, ALP 180 IU/l) which normalized on testing 2 weeks later. She received a repeat dose of ciprofloxacin 500 mg p.o. twice daily for 14 days and ursodiol 500 mg p.o. twice daily. She had no relief of her pruritus although her jaundice resolved.

Liver function test fluctuations continued for 15–18 months from initial presentation but were not accompanied by other lab abnormalities. Cholestyramine did not help relieve the pruritus either, so endoscopic retrograde cholangiopancreatography (ERCP) was planned. This was done 18 months from her initial presentation to the clinic. She did not have elevation of CA19-9 when checked periodically during her clinical course. ERCP showed dilation of the right and left hepatic ducts and a 3–4 cm oblong filling defect in the common hepatic duct extending into the left hepatic duct ([fig. 2](#)). The defect did not appear to fill up on ERCP. Biopsy and brushings of the lesion were done. Balloon sweep during ERCP demonstrated slight movement of the filling defect. A biliary sphincterotomy was done during the procedure with removal of sludge and debris. A 10 Fr 5 cm plastic double pigtail stent was placed into the left hepatic duct across the filling defect during ERCP. Cytological analysis of brushings obtained from the lesion showed no evidence of malignancy. Pathological analysis of the biopsies showed normal bile duct mucosa. ERCP was complicated by pancreatitis necessitating hospital admission for 3 days from which she recovered uneventfully.

Three weeks after ERCP an exploratory laparotomy was done with extrahepatic bile duct resection, left hepatic lobectomy and reconstruction of the right hepatic duct with a Roux-en-Y hepaticojejunostomy with cholecystectomy. Pathology showed cystic dilation of the common hepatic and left hepatic duct with no evidence of malignancy. It also showed chronic inflammation of the extrahepatic bile ducts and focal pericholangitis in the liver. The gallbladder was normal on the excised specimen. Histological exam showed mucinous lining of the cystic lesion with ovarian-like stroma suggestive of biliary cystadenoma with no evidence of malignancy ([fig. 3](#)).

The patient was seen 2 weeks after surgery in the clinic. She was able to eat normally and had minimal pain resulting from surgery. She was scheduled for a repeat MRCP in 1 year's time.

Discussion

Biliary cystadenomas are made up of communicating chambers of varying sizes usually containing clear fluid. The chambers are lined by columnar epithelium resembling biliary epithelium with cytoplasmic mucin. The mesenchymal tissue within resembles ovarian stroma. Epithelium can have varying degrees of dysplasia with high-grade or invasive carcinoma suggesting transformation to cystadenocarcinoma. They are predominantly intrahepatic in origin and rarely seen in extrahepatic bile ducts or gallbladder [6]. Patients, more commonly middle-aged females, generally present with vague abdominal symptoms sometimes associated with liver enzyme elevation or hyperbilirubinemia. Jaundice can develop due to transient obstruction of biliary flow or

due to direct external compression of the biliary tree. CA19-9 and carcinoembryonic antigen (CEA) may be elevated [12]. CT scan and MRI (MRCP) may be used to make the diagnosis and present as loculated, septated lesions. On CT scan, the intraluminal content is usually hypoattenuating. On MRI, they appear as hypoattenuating lesions on T1 and demonstrate T2 hyperintensity typically seen with any fluid-filled mass. Enhancement of the septations was seen in our case along with calcifications as reported in the past [13, 14]. However, the T1 and T2 signal intensity can be variable depending on the amount of protein in the fluid and on whether blood products are present. Calcifications within the cyst walls can also be seen. MRCP can provide an idea of the extent of the tumor and provide guidance for the surgeon as the tumor might not be completely opacified on ERCP.

The main differential diagnoses are biliary cystadenocarcinoma, simple hepatic cyst, hydatid cyst, Caroli disease, undifferentiated sarcoma, intraductal papillary mucinous tumor and hepatocellular carcinoma. Positive serology can distinguish a hydatid cyst with or without peripheral eosinophilia. Imaging cannot completely rule out biliary cystadenocarcinoma. Preoperative diagnosis may be very difficult in some cases based on clinical characteristics and imaging studies. A treatment algorithm involving CEA, CA19-9 and cyst wall biopsy has been proposed [8], however its utility needs to be validated in larger studies. No definite diagnostic criteria for CA19-9 and CEA levels are established largely due to lack of statistically convincing data with comparisons of levels to simple cysts. Complete resection of the whole cyst with negative resection margins is advised due to the risk of malignant transformation to cystadenoma or sarcoma [9, 15].

We report a rare tumor, biliary cystadenoma, that presented with an extension to the left hepatic and common hepatic duct. Nonspecific abdominal pain may be the only presenting symptom and diagnosis can be suspected based on CT or MRI. Complete surgical resection is advised for cure in view of the risk of transformation to cystadenocarcinoma or sarcoma.

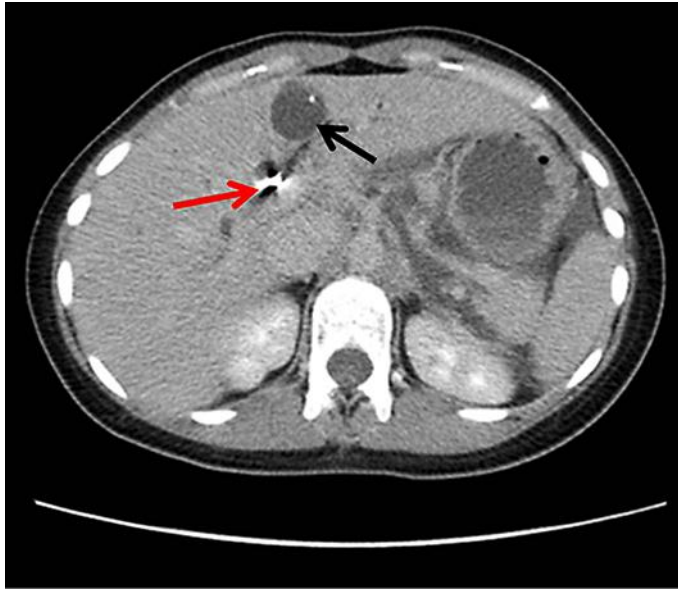


Fig. 1. CT scan showing biliary cystadenoma. The cystic lesion (black arrow) in segment 4 of the liver with a central focus of high density is seen representing the biliary cystadenoma. A bile duct stent placed during ERCP can also be seen (red arrow).

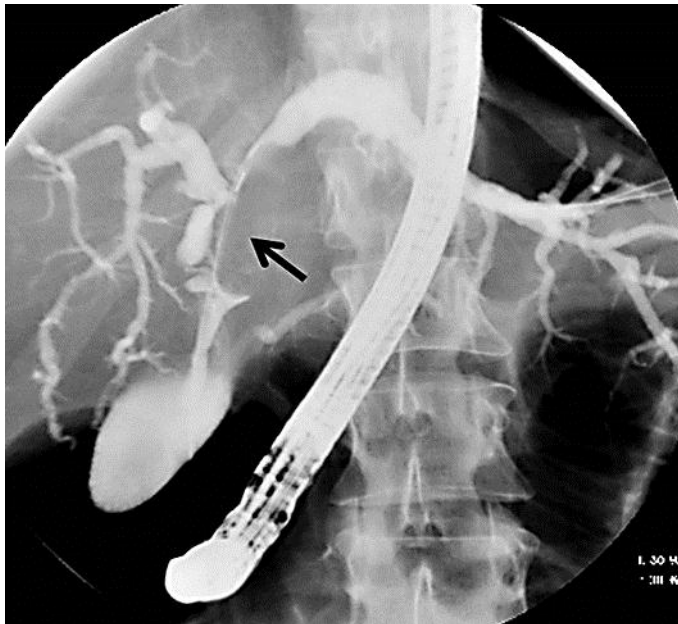


Fig. 2. Appearance of biliary cystadenoma during ERCP. A filling defect extending from the common hepatic duct to the left hepatic duct is seen (arrow).

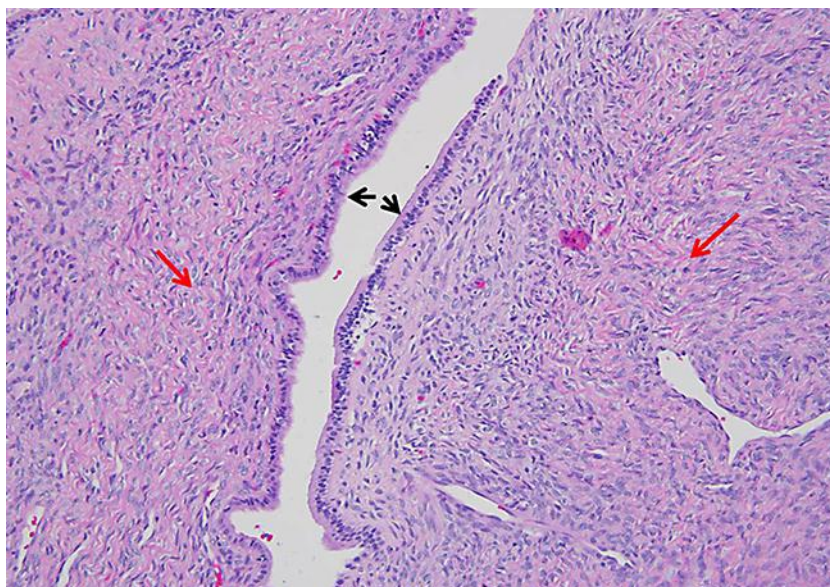


Fig. 3. Histology of biliary cystadenoma: high power view (20×) showing mucinous lining of the cyst (black arrows) along with the ovarian like stroma (red arrows). Epithelial lining is bland with basal nuclei and abundant mucin-filled cytoplasm with no evidence of stromal invasion or malignancy.

References

- 1 Henson SW Jr, Gray HK, Dockerty MB: Benign tumors of the liver. VI. Multilocular cystadenomas. *Surg Gynecol Obstet* 1957;104:551–554.
- 2 Ahanatha Pillai S, Velayutham V, Perumal S, Ulagendra Perumal S, Lakshmanan A, Ramaswami S, Ramasamy R, Sathyanesan J, Palaniappan R, Rajagopal S: Biliary cystadenomas: a case for complete resection. *HPB Surg* 2012;2012:501705.
- 3 Delis SG, Touloumis Z, Bakoyiannis A, et al: Intrahepatic biliary cystadenoma: a need for radical resection. *Eur J Gastroenterol Hepatol* 2008;20:10–14.
- 4 Kim K, Choi J, Park Y, et al: Biliary cystadenoma of the liver. *J Hepatobiliary Pancreat Surg* 1998;5: 348–352.
- 5 Soochan D, Keough V, Wanless I, Molinari M: Intra and extra-hepatic cystadenoma of the biliary duct. Review of literature and radiological and pathological characteristics of a very rare case. *BMJ Case Rep* DOI: 10.1136/bcr.01.2012.5497.
- 6 Devaney K, Goodman ZD, Ishak KG: Hepatobiliary cystadenoma and cystadenocarcinoma. A light microscopic and immunohistochemical study of 70 patients. *Am J Surg Pathol* 1994;18:1078–1091.
- 7 Lewin M, Mourra N, Honigman I, et al: Assessment of MRI and MRCP in diagnosis of biliary cystadenoma and cystadenocarcinoma. *Eur Radiol* 2006;16:407–413.
- 8 Koffron A, Rao S, Ferrario M, Abecassis M: Intrahepatic biliary cystadenoma: role of cyst fluid analysis and surgical management in the laparoscopic era. *Surgery* 2004;136:926–936.
- 9 Wang C, Miao R, Liu H, Du X, Liu L, Lu X, Zhao H: Intrahepatic biliary cystadenoma and cystadenocarcinoma: an experience of 30 cases. *Dig Liver Dis* 2012;44:426–431.
- 10 Dixon E, Sutherland FR, Mitchell P, et al: Cystadenomas of the liver: a spectrum of disease. *Can J Surg* 2001;44:371–376.
- 11 Diaz de Liano A, Olivera E, Artieda C, et al: Intrahepatic mucinous biliary cystadenoma. *Clin Transl Oncol* 2007;9:678–680.
- 12 Gadzijev E, Ferlan-Marolt V, Grkman J: Hepatobiliary cystadenomas and cystadenocarcinoma. Report of five cases. *HPB Surg* 1996;9:83–92.

- 13 Mortelé KJ, Ros PR: Cystic focal liver lesions in the adult: differential CT and MR imaging features. *Radiographics* 2001;21:895–910.
- 14 Seidel R, Weinrich M, Pistorius G, et al: Biliary cystadenoma of the left intrahepatic duct (2007:2b). *Eur Radiol* 2007;17:1380–1383.
- 15 Sang X, Sun Y, Mao Y, Yang Z, Lu X, Yang H, Xu H, Zhong S, Huang J: Hepatobiliary cystadenomas and cystadenocarcinomas: a report of 33 cases. *Liver Int* 2011;31:1337–1344.