Cholangiocarcinoma or Caroli disease: a case presentation

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ABSTRACT
Early diagnosis and appropriate treatment of cholangiocarcinoma is problematic. Cross sectional imaging and tumor marker CA 19-9 are not absolutely reliable and tissue sampling is difficult. We present a patient with cholangitis and cystic dilation of intra-hepatic bile ducts that primarily diagnosed as Caroli's disease in imaging and needle biopsy but laparotomy and surgical biopsy revealed cholangiocarcinoma.

Keywords: Caroli's disease; Cholangiocarcinoma; Cholangitis.

Introduction
Cholangiocarcinoma is an invasive malignancy with poor prognosis that presents as cholestasis with or without apparent mass in imaging. This malignancy originates from interahepatic or exterahepatic biliary ducts and can present as obstructive gross dilatation of the intra or extrahepatic bile ducts. Extrahepatic cholangiocarcinoma is the most common form of this malignancy (1,2). Intrahepatic cholangiocarcinoma represents approximately 10% to 20% of all primary liver cancers and 20% to 25% of cholangiocarcinomas (3). The highest prevalence rates are found in parts of Asia, most notably certain regions of Thailand, Hong Kong, China, Japan, and Korea. Chronic infestation of the biliary tree with one of the liver flukes is thought to be the cause of these high rates (4). Early diagnosis of intrahepatic cholangiocarcinoma is unusual, and the annual mortality rate is almost identical to the annual incidence of the tumor (5, 6).

Caroli's disease is a rare disorder characterized by congenital non-obstructive gross dilatation of the segmental intrahepatic bile ducts (2, 5,6). The disease has been included in the classification of choledochal cysts (as type V) (2, 5, 6). This bile duct ectasia that may be diffuse or limited usually becomes symptomatic in early adulthood; more than 80% of patients present with symptoms before the age of 30 years.

As in our case that is presented below, differentiation between cholangiocarcinoma and limited Caroli’s disease that present as cholangitis and cystic dilation of biliary ducts is somewhat difficult.

Case Report
A 56 year-old male patient admitted to hospital due to intermittent epigastric and right upper quadrant (RUQ) pain associated with fever,
chilling, jaundice, and 10 kilogram weight loss for 5 months. On examination he was icteric, Blood pressure was 140/80 mm Hg, pulse rate was 96 per minute and temperature was 39° centigrade. Murphy sign was negative but epigastric and RUQ tenderness was remarkable. Laboratory findings are in table 1.

Trans-abdominal ultrasonogram, computerized tomography (CT) scan and magnetic resonance cholangio-pancreaticography (MRCP) revealed several various size turtose and tubular shape cystic structures without apparent mass lesion limited to left lobe of the liver (figure 1). Common bile duct (CBD), Port vein and intra-hepatic bile ducts of right lobe were normal. Thorax and other abdominal organs including the gallbladder, spleen, pancreas, kidneys and pelvic organs were normal. Regarding the clinical history (intermittent periods of fever, abdominal pain and jaundice) and paraclinic findings, diagnosis of cholangitis was made and Ceftriaxone and Metronidazole were prescribed. But after 3 days, patient’s conditions didn’t improve.

ERCP was performed for further evaluation of this febrile cholestatic disease; Ampulla of Vater appeared normal in duodenoscopy. CBD, right hepatic bile duct, left hepatic bile duct and intra-hepatic biliary ducts of the right lobe were normal in cholangiogram. But mentioned cystic lesion of biliary ducts in the left lobe that appeared in MRCP, weren’t visible in ERCP; there wasn’t any communication between mentioned cystic lesion and left hepatic bile duct. However minimal sphinctrotomy was done but there wasn’t any pus or stone in CBD.

| Table 1 Patient’s laboratory findings |
|---------------------------------------|
| **Parameter**                        | **Patient** | **Normal value** |
| White Blood Cell (×/mm³)              | 15 × 10³    | 3.5–9.1 × 10³    |
| Hemoglobin (g/dL)                     | 11.8        | 13.3–16.2        |
| Platelet (×/mm³)                      | 485 × 10³   | 165–415 × 10³    |
| Prothrombin Time (sec)                | 12          | 12.7–15.4        |
| Partial Trombine Time (sec)           | 34          | 26.3–39.4        |
| Aspartate Transaminase (U/L)          | 85          | 7–41             |
| Alanine Transaminase (U/L)            | 64          | 7–41             |
| Alkaline Phosphatase (U/L)            | 822         | 33–96            |
| Total Bilirubin (mg/dL)               | 16          | 0.3–1.3          |
| Direct Bilirubin (mg/dL)              | 11          | <0.3             |
| Blood Culture                         | Negative    | Negative         |
| Amylase (U/L)                         | 76          | 20–96            |
| Lipase (U/L)                          | 32          | 3–43             |
| Creatinine (mg/dL)                    | 0.9         | 0.5–0.9          |
| Blood Urea Nitrogen (mg/dL)           | 16          | 7–20             |
| Fasting Blood Sugar (mg/dL)           | 98          | 75–100           |
| CA 19-9 (U/L)                         | 165         | <37              |

Fever, jaundice and abdominal pain intensified at the next 3 days after ERCP. At this time imipenem was prescribed. After one week, abdominal pain was decreased markedly, serum level of bilirubin was decreased to 7 mg/dl and fever discontinued. At this time a percutaneous CT guided core biopsy was done and revealed hepatic fibrosis with bile duct ectasia consistent with Caroli's disease. Patient was scheduled for resection of the left hepatic lobe.

A large mass revealed in left lobe of the liver at laparotomy that surgeon had taken a wedge biopsy from it only. Histopathologic assessment of this surgical biopsy confirmed cholangiocarcinoma. Due to vascular invasion, tumor was unresectable and the patient scheduled for palliative chemotherapy.
Discussion

Preoperative diagnosis in our case was Caroli disease but because of recent significant weight loss, high level of serum CA19-9 and particularly no communication between left hepatic bile duct and intra-hepatic cystic structures in ERCP (obstructive bile duct dilation), Caroli disease wasn’t an appropriate diagnosis for our patient. Clinical manifestation and imaging findings of cholangiocarcinoma and Caroli’s disease may be similar somewhat. Communication between intra-hepatic cystic lesions and right or left hepatic duct in endoscopic retrograde cholangiopancreaticography (ERCP) in patient with cholestasis and intrahepatic cystic lesions is a key point for the differentiation of Caroli disease that is a non-obstructive biliary disease from cholangiocarcinoma that is an obstructive lesion; Visualization of cystic like dilated intra-hepatic bile ducts in ERCP indicates the presence of free communication between ectatic bile ducts and right or left hepatic duct; this is consistent with localized Caroli disease rather than cholangiocarcinoma. Due to special laminar growth of cholangiocarcinoma into adjacent tissues, this tumor may be not visualized in cross sectional imaging such as CT scan. So this malignancy can present as a multi-cystic lesion (due to bile duct obstruction) without apparent mass in imaging. This situation can lead to misdiagnosis with Caroli disease. Surgical resection is the only curative treatment in cholangiocarcinoma but because of delay in diagnosing, most cases are unresectable. Patients with Caroli’s disease typically present with recurrent episodes of fever and abdominal pain caused by cholangitis. Gallstones form in the ectatic ducts in one third of patients. The result of these complications may be cholangiocarcinoma, which develop in less than 10% of patients. Attacks of cholangitis in Caroli’s disease require treatment with antibiotics. Endoscopic retrograde cannulation of the biliary system may be used to facilitate removal of sludge or stones from the accessible part of the biliary system, and the cysts may be drained by an endoscopic or percutaneous route. Liver resection for unilobar Caroli’s disease and liver transplantation for diffuse Caroli’s disease are associated with excellent long-term patient survival and a low rate of complications.

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