# Case Report

# Cholangiocarcinoma in a 24-Year-Old Woman with Hepatolithiasis

Kawin Leelawat MD, PhD*,
Jerasak Wannaprasert MD*

** Department of Surgery, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand*

*Hepatolithiasis is well known to represent an etiology of cholangiocarcinoma. The average age of patients with a diagnosis of cholangiocarcinoma that occurs as a complication of hepatolithiasis is about 62 years old. Here, the authors present a case of cholangiocarcinoma that occurred in a 24-year-old woman who presented with the recurrent cholangitis from hepatolithiasis. Left hepatectomy with hepaticojejunostomy was performed because she had multiple stones in an atrophic left lobe of the liver. Histopathological examination revealed that it was cholangiocarcinoma located in the inflammatory left hepatic duct.*

***Keywords:*** *Bile ducts, Intrahepatic, Cholangiocarcinoma, Cholelithiasis, Cholestasis, Intrahepatic, Gallstones, Lithiasis*

***J Med Assoc Thai 2009; 92 (7): 983-6***
***Full text. e-Journal:*** *http://www.mat.or.th/journal*

Intrahepatic duct stones or hepatolithiasis are prevalent in East Asia[1]. Patients with intrahepatic duct stones present with a specific clinical course characterized by recurrent cholangitis which may cause sepsis or liver dysfunction resulting in biliary cirrhosis[2]. Moreover, the most unfavorable complication of this disease is a cholangiocarcinoma[3]. The average age of patients with a diagnosis of cholangiocarcinoma that occurs as a complication of hepatolithiasis is about 62 years[4]. The authors encountered a case of intrahepatic cholangiocarcinoma in a young Thai woman whose underlying was intrahepatic duct stones.

**Case Report**

A 24-year-old Thai female patient presented to the Department of Surgery, Rajavithi Hospital in August 2007 with a 7-day history of cholangitis. Results of laboratory tests were as follows; total bilirubin, 11 mg/L (normal range: 0-15 mg/L); direct bilirubin, 3 mg/L (normal range: 0-5 mg/L); aspartate aminotransferase (AST), 84 IU/L (normal range: 0-40 IU/L); alanine aminotransferase (ALT), 127 IU/L (normal range: 0-40 IU/L); alkaline phosphatase, 198 IU/L (normal range: 39-117 IU/L); and albumin, 42 g/L (normal range: 34-48 g/L). Tumor markers (AFP, CEA, and CA19-9) were all within normal limits.

A computerized tomography scan (CT) of the abdomen demonstrated multiple intrahepatic duct stones mainly in the left lobe of the liver. An atrophy of liver segments 2 and 3 was also identified (Fig. 1A). Endoscopic retrograde cholangiogram (ERC) revealed 0.5 cm common bile duct (CBD) without CBD stone. There were multiple stones at hepatic ductal confluence area and in the left intra-hepatic duct. There was a smooth narrow part just between the ducts of segment IV about 1 cm in length. Ducts of the segment II and III were dilated and filled with stones. Endoscopic sphincterotomy (EST) was done. Stone extraction was attempted. Some of the stones were removed from hepatic ductal confluence area. The 7 Fr, 10 cm pigtail stent was inserted over wire under fluoroscopy (Fig. 1B, 1C).

A preoperative diagnosis of intrahepatic duct stones with left lobe liver atrophy was made and the patient underwent left lobe hepatectomy with access limb-hepaticojejunostomy. On gross examination, the resected specimen was occupied with multiple brown pigment stones in an atrophic left lobe of liver. The stricture at main left hepatic duct and a nodular mass

*Correspondence to: Leelawat K, Department of Surgery, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok 10400, Thailand. Phone: 0-2354-8080, Fax: 0-2354-8080. E-mail: kawin.leelawat@gmail.com*

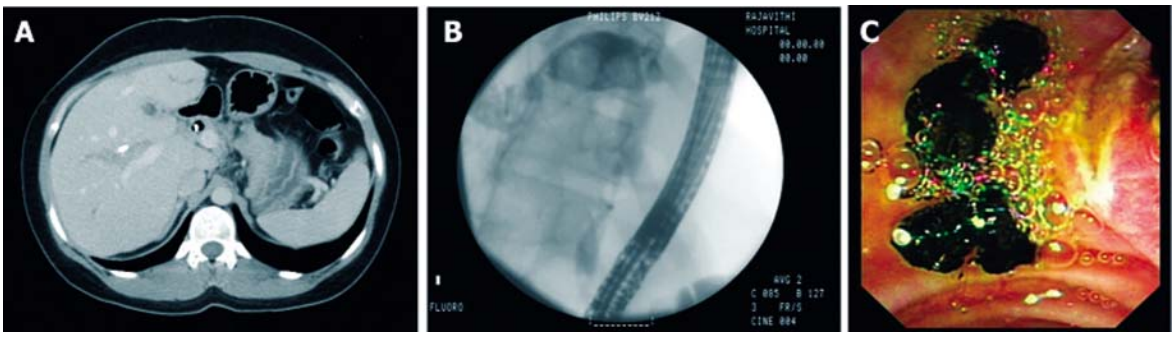


**Fig. 1** (A) The abdominal CT of the patient, demonstrating the presence of intrahepatic duct stones within the liver. The atrophy of left lobe of the liver is demonstrated. (B) Endoscopic retrograde cholangiogram revealed multiple stones at hepatic ductal confluence area and in the left intra-hepatic duct (C) Stone extraction was performed

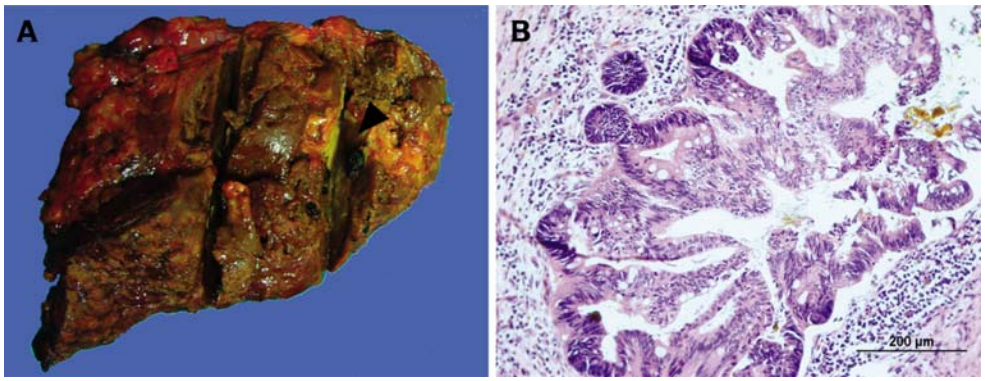


**Fig. 2** (A) A grosses appearance of a nodular mass and the pigment stones (arrow head) in the left lobe of the liver. (B) Photomicrograph of the resected specimen, showing that the tumor is well to moderately differentiated adenocarcinoma (H&E; original magnification; 40x)

was also noted (Fig. 2A). The histopathological examination revealed a focal point of well to moderately differentiated adenocarcinoma. There was no vascular and perineural invasion (Fig. 2B). The inflammatory and fibrotic changes around the bile duct wall were observed. Her postoperative course was uneventful.

## Discussion

Hepatolithiasis is a disease characterized by intrahepatic stones and recurrent attacks of abdominal pain, fever, chills, and jaundice[2]. Hepatolithiasis is a rare disease in the West but is an endemic area in East Asia. Symptoms of hepatolithiasis are abdominal pain, jaundice, and cholangitis. In addition to frequent cholangitis and chronic sepsis, it is widely known that longstanding intrahepatic stones lead to intrahepatic cholangiocarcinoma[3]. In the surveys conducted by Chijiiwa K, et al, the association of cholangiocarcinoma with hepatolithiasis was 5.8%[5]. Cholangiocarcinoma, a cancer arising from the bile duct epithelium, is the second most common primary liver cancer in the world except for Northeast of Thailand where this cancer is more common than hepatocellular carcinoma (HCC)[6]. A number of risk factors including liver fluke infection (*Opisthorchis viverini* and *Clonorchis sinensis*), choledochal cyst, hepatolithiasis, and primary sclerosing cholangitis have been identified to be important in the development of cholangiocarcinoma[7]. Most of these factors contribute to longstanding inflammation and chronic injury of the biliary epithelium. According to the previous study, the mean age of patient with hepatolithiasis who also have cholangiocarcinoma is 62 years old (range from 46-82 years old)[4]. Recently, Kim YT, et al suggested that cholangiocarcinoma should be suspected in patients with hepatolithiasis, especially when, the patient is over 40 years old, has a

long history of hepatolithiasis with weight loss, a higher level of serum alkaline phosphatase, a lower level of the serum albumin, a serum carcinoembryonic antigen (CEA) level exceeding 4.2 ng/mL, and hepatolithiasis that is located either in the right or both lobes of the liver[8]. The present study reported the occurrence of cholangiocarcinoma in a 24-year-old female patient who underwent left hepatectomy because of recurrent cholangitis from hepatolithiasis. She had high serum alkaline phosphatase but normal levels of the serum albumin. Her serum CEA level was also within the normal limit. This might be explained by the very early course of this cancer. In this case, the pathology report showed well-differentiated cholangiocarcinoma associated with chronic inflammation of the bile duct epithelium. Thus, tumor transformation from chronic inflammation of the biliary epithelium might explain its origin. Factors responsible for cholangiocarcinoma may be partly mechanical stimuli from intrahepatic stones and partly chemical irritation to the bile duct epithelium by the infected bile. However, genetic study should be further investigated to identify the exact mechanism responsible for cholangiocarcinogenesis in this young patient. The brown pigment intrahepatic duct stones were identified in this patient. While previous study demonstrated that cholangiocarcinoma was associated in 2.8% of patients with brown pigment stones and 30% of patients with cholesterol stones[5], the risk of cholangiocarcinoma is supposed to be even higher in patients with primary calcium bilirubinate stone than those with primary cholesterol stone[9,10]. However, the exact causal relationship between the kind of stones and cholangiocarcinoma remains unclear. The prognosis of cholangiocarcinoma is very poor. In the vast majority of cases, it follows a course toward lethal progression. Therapeutic options for cholangiocarcinoma have been limited due to the poor responses to chemotherapy and radiation therapy. Surgery is perhaps the only effective treatment for cholangio carcinoma[11]. Three-year survival rates of 35% to 50% are achieved in only a few patients when negative histological margins are attained at the time of surgery[11-13]. Moreover, there has been no effective method to prevent development of a cholangiocarcinoma in patients with hepatolithiasis. Early detection and surgical treatment of these patients is currently the best strategy[14].

## Conclusion

In summary, although the occurrence of cholangiocarcinoma in the young-age hepatolithiasis patient is rare, physicians should recognize this rare entity because the early detection raises the possibility that a patient can be selected as a surgical candidate and may consequently improve their prognosis.

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## *โรคมะเร็งทางเดินน้ำดีในผู้ป่วยหญิงอายุ 24 ปี ที่มีภาวะนิ่วในตับ*

***กวิญ ลีละวัฒน์, จีรศักดิ์ วรรณประเสริฐ***

*ภาวะนิ่วในตับ จัดเป็นสาเหตุของการเกิดมะเร็งทางเดินน้ำดี ส่วนใหญ่ของผู้ป่วยมะเร็งทางเดินน้ำดีซึ่งมีสาเหตุจากภาวะนิ่วในตับ จะมีอายุเฉลี่ยที่ 62 ปี รายงานนี้ รายงานผู้ป่วยหญิงอายุ 24 ปี ได้รับการวินิจฉัยเป็นนิ่วในตับร่วมกับมีตับซีกซ้ายฝ่อ ผู้ป่วยได้รับการรักษาโดยการผ่าตัดตับซีกซ้ายออก ผลการตรวจทางพยาธิวิทยาพบว่ามีจุดของมะเร็งทางเดินน้ำดีอยู่ในท่อน้ำดีของตับซีกซ้าย*