

Early Hepatocellular Carcinoma Presenting with Biliary Ductal Invasion —A Case Report

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Abstract

Early and small hepatocellular carcinoma (HCC) rarely presents with biliary ductal invasion. We present a case of early HCC presenting with biliary invasion, in the absence of a mass on computed tomographic scanning. The patient, a hepatitis B carrier, was initially diagnosed to have “liver fluke infection” after a “leaf-like structure” was found within the right hepatic duct on endoscopic retrograde cholangiopancreatography (ERCP). The specimen was retrieved with a Dormia basket. Histology revealed HCC. This report highlights an unusual case of early and small HCC presenting with biliary ductal invasion. A high index of suspicion has to be entertained in the background of hepatitis B regardless of the atypicality of presentation.

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Introduction

Hepatocellular carcinoma (HCC) is a common malignant tumour worldwide. The local incidence of HCC is 40 per 100,000 in males and 20 per 100,000 in females.¹ Its geographical distribution parallels that of hepatitis B infection. The highest prevalence is encountered in the Far East and sub-Saharan Africa. Most HCCs present late as large hepatic tumours with necrotic centres and satellite lesions. It is uncommon for early HCC to present with obstructive jaundice, cholangitis or biliary dilatation. Most are detected as small hepatic nodules during the screening of hepatitis carriers, by ultrasound imaging or computer tomographic (CT) scan. An unusual case of early HCC which presented with biliary obstruction is described.

Case Report

A 59-year-old Chinese female, who was a hepatitis B carrier for the past 10 years, presented to the medical service with atypical chest pain radiating to the epigastrium for a duration of 3 months. She was investigated with a treadmill test, oesophago-gastroduodenoscopy and barium meal, all of which were normal. Serum alkaline phosphatase was mildly raised at 141 IU/L (normal range 32 to 103 IU/

L), while serum bilirubin, alanine and aspartate transaminases were normal. Serum amylase was normal. Alpha-fetoprotein was mildly raised at 11.4 ng/ml (normal range 1 to 10 ng/ml). Ultrasound of the liver was normal. CT scan, however, revealed biliary ductal dilatation on the right with no evidence of a space-occupying lesion or stone disease. The patient's pain persisted despite treatment with famotidine and buscopan. An endoscopic retrograde cholangiopancreatography (ERCP) was done because of the persistent pain, dilation of the biliary system and elevated alkaline phosphatase. ERCP revealed a “leaf-like” filling defect at the liver hilum. Sphincterotomy was performed and an elongated clot-like structure was withdrawn via a Dormia basket. This was thought to be a parasite. The clinical impression was that of a liver fluke or schistosoma infection and the patient was started on praziquantel.

However, histology of the extracted tissue revealed hepatocellular carcinoma. The patient was referred for surgery. A magnetic resonance cholangiogram was performed to delineate the intrahepatic biliary anatomy. This revealed a mass just adjacent to the right hepatic duct with right intrahepatic biliary ductal dilatation. A laparotomy

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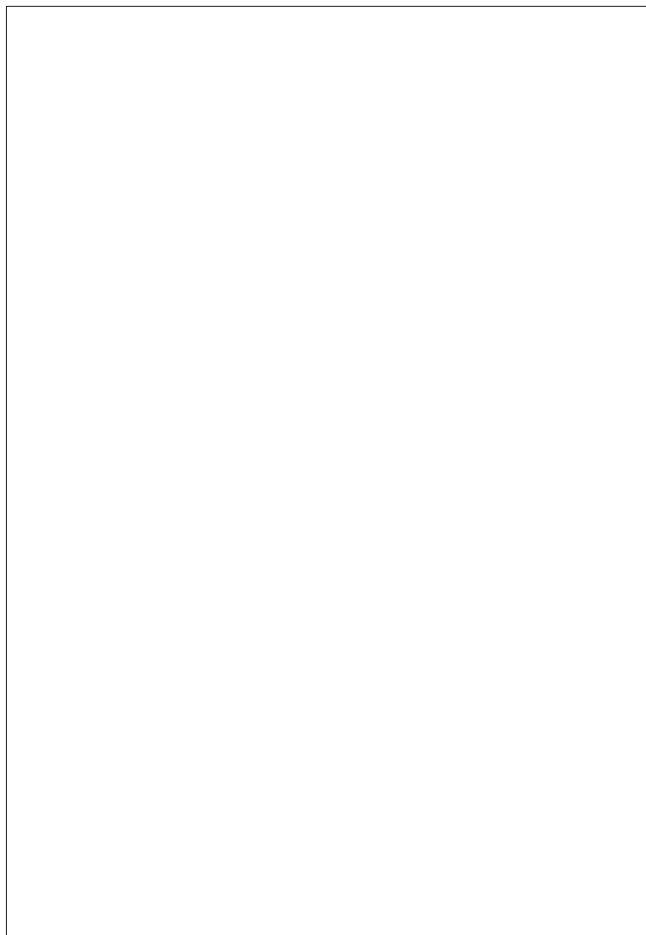


Fig. 1. ERCP showing a space-occupying lesion at the confluence of the left and right hepatic ducts extending into the common hepatic duct, as indicated by the arrow. G: gallbladder; L: left hepatic duct; R: right hepatic duct; C: common bile duct.

was planned but the following preoperative problems had to taken into consideration:

- (i) Although the patient's preoperative status was that of Child's-Pugh's A, the volume of the left lobe of the liver was considered just adequate. Hepatic reserve was thus suspect.
- (ii) The exact hilar extension of the tumour could not be accurately determined on the magnetic resonance cholangiogram. Thus a decision could only be made intraoperatively whether to do a segmentectomy or a right hepatectomy, depending on the extent of invasion of the tumour.
- (iii) Tumour extension into the confluence at the common hepatic duct would have necessitated resection of the left hepatic duct with reconstruction to ensure adequate margins.

Laparotomy was performed after adequate preoperative preparation and optimisation. Intraoperatively, there was micronodular liver cirrhosis. Ultrasound revealed a tumour mass 1.5 cm in diameter invading the right main hepatic duct. The liver was split with a cavitron ultrasonic

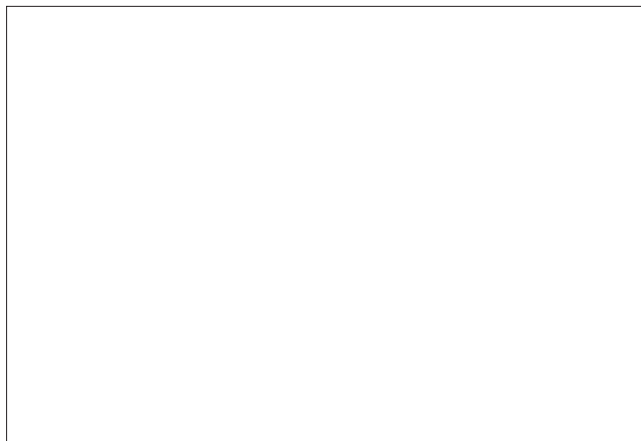


Fig. 2. MRI cholangiogram showing a mass adjacent to the right hepatic duct with right intrahepatic biliary ductal dilatation. L: liver; G: gallbladder; Arrow: mass; R: right hepatic duct.

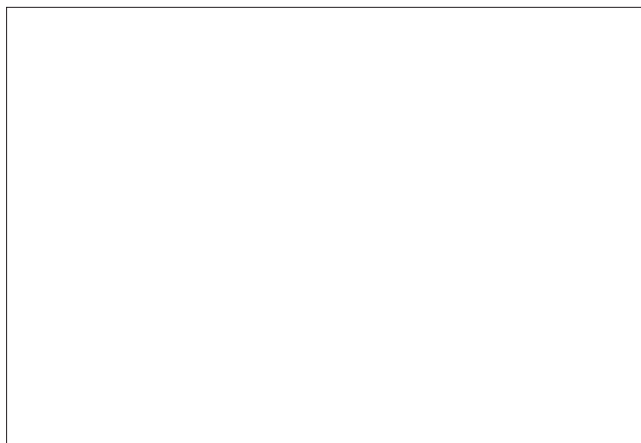


Fig. 3. Right hepatectomy specimen split open to reveal the right hepatic duct along its longitudinal axis. Tumour invasion into the right hepatic duct is demonstrated.

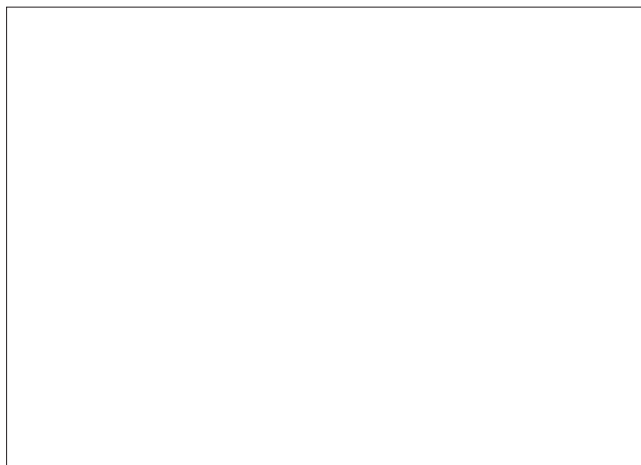


Fig. 4. The right hepatic duct at higher magnification (H&E 400x), showing loose clumps of hepatocellular carcinoma lying within its lumen, as indicated by the arrows.

suction and aspirator (CUSA) without vascular control along Cantlie's line and the bile ducts were examined. Choledochoscopy revealed the edge of the tumour in the right hepatic duct. The porta hepatis lymph nodes were not

enlarged. The gallbladder and the peritoneum were normal. Frozen section done on the tumour mass confirmed HCC. Right hepatectomy was then performed, ligating the right hepatic artery, right portal vein and the right hepatic duct at the confluence. Postoperatively, the patient was initially managed in the high dependency unit. She made an uneventful recovery, with normalisation of the liver function over 1 week and was discharged home on the 11th postoperative day. There was no recurrence of tumour at 3 months' follow-up. Histology showed a 1.7-cm hepatocellular carcinoma with invasion into the hepatic duct. Tumour emboli was present in the portal vein. The rest of the liver was cirrhotic with liver cell dysplasia.

Discussion

HCC is a common malignant tumour worldwide. Most HCCs present late as large hepatic tumours with necrotic centres and satellite lesions. The incidence of ductal invasion is reported to be 4% of cases.² However, early and small HCCs presenting with ductal invasion are rare, with only a small number of case reports in the literature.³⁻⁷ Jaundice is present in only 19% to 44% of patients at the time of diagnosis, common causes being underlying liver cirrhosis or the extensive hepatic parenchymal destruction by tumour.^{2,8} Differential diagnoses relevant in this case include gallstones, biliary strictures and neoplasm of the head of pancreas or cholangiocarcinoma. In fact, Huang et al⁹ expressed that the differential diagnosis between cholangiocarcinoma and HCC still poses a problem for clinicians. Seven out of 9 patients in their series were initially misdiagnosed to have cholangiocarcinoma because of the early involvement of the common bile duct, and could not be excluded even after ultrasound and CT examinations. HCC was only suspected because of the elevated alpha-fetoprotein (AFP) levels.

Definitive diagnosis was only reached after liver biopsy or resection. Our patient poses this very same diagnostic problem. The factors that aroused suspicion for diagnosing HCC were her hepatitis B carrier status and mildly raised AFP. In fact, her presentation was very much like that of cholangiocarcinoma or a parasite infection. Furthermore, even with the entire standard imaging procedures, no mass lesion was found. It was the MRI that demonstrated the mass lesion. On retrospective analysis of the CT scan, the cuts were taken at 12-mm intervals. This was too big an interval to be able to visualise the tumour mass, which is only 17 mm in diameter. Current practice involves taking cuts at 10-mm intervals. Finer cuts at 5-mm intervals will have to be taken in cases with suspected small lesions or biliary ductal pathology. Moreover, studies have shown that MRI and magnetic resonance cholangio-pancreatography (MRCP) exhibit similar if not higher diagnostic accuracy than CT scan and ERCP for HCC with

or without biliary ductal involvement.¹⁰⁻¹³

HCC with bile duct involvement and no obvious mass lesion is clinically difficult to differentiate from cholangiocarcinoma. Helpful features include patient's risk factors like hepatitis B or C infection for HCC and the association of cholangiocarcinoma with *Clonorchis sinensis* infection. Tumour markers like AFP and CA 19-9 may be elevated in HCC and cholangiocarcinoma, respectively. Cholangiocarcinoma tends to affect the central bile ducts, with obstructive jaundice and deranged liver function test. Cholangiocarcinomas occurring at the periphery of the liver are uncommon. HCC can be both central and peripheral. The liver function test is often unaffected or mildly deranged. Laparotomy in this case aims to be both diagnostic and therapeutic. It is important that the offending duct and subserving area of liver is removed, i.e. hepatectomy. Nevertheless, once a diagnosis is made of HCC with intrabiliary extension, most authors have demonstrated a poor prognostic outlook, similar to that for patients with metastatic liver tumours who manifest jaundice.¹⁴⁻¹⁶ Most of the cases have come from Taiwan and the Taiwanese have coined the term 'icteric type hepatoma' two decades ago to describe this type of clinical presentation.⁹ However, there are patients in the Taiwanese series that had small-sized tumours suitable for curative resections. These patients had improved prognosis and survival, with a survival time of 16 to 63 months as compared to patients with inoperable tumours, who only survived for another 17 months. Most of these patients have a guarded prognosis as biliary ductal involvement usually indicates advanced disease despite small tumour size.¹⁷⁻²⁰ However, Taiwanese and Korean clinicians have reported improved prognosis in a group of patients whose tumours are small enough to be adequately resected as compared to patients with inoperable tumours.^{9,21} There were no emboli in the other bile ducts. This was confirmed by intraoperative choledochoscopy. There was also no vascular invasion grossly but tumour emboli were found in the portal vein. Postoperative adjuvant chemotherapy can be useful in controlling biliary and haematological spread but further studies need to be done in order to provide objective evidence of its advantage. Cho et al²¹ have also described a case of extrahepatic bile duct HCC without a primary hepatic parenchymal lesion who has survived for more than a year with local resection of the tumour. Palliative drainage procedures, whether radiological or surgical have not been shown to improve survival, with a survival time of only half a year post-procedure.^{15,16}

Conclusion

A high index of suspicion for the diagnosis of HCC is needed in high risk patients with hepatitis B and chronic liver disease, regardless of how atypical the presentation

may be. Although the prognosis of HCC with intrabiliary invasion is generally poor, patients with small tumours amenable to curative resection have improved survival.

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