Int Surg 2013;**98**:424–427
DOI: 10.9738/INTSURG-D-13-00082.1

Case Report

Repeat Liver Resection for Hepatocellular Carcinoma Complicating Primary Biliary Cirrhosis

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The incidence of hepatocellular carcinoma (HCC) complicating primary biliary cirrhosis (PBC) is between 0.7% and 16%. Repeat liver resection for recurrent HCC complicating PBC is not usually performed and not published because this approach is not generally applicable due to liver dysfunction. We applied repeat liver resection for these diseases. Three patients were diagnosed with PBC. The first HCC was noted at a mean of 6 years (4–17 years) after diagnosis of PBC. The second HCC occurred at a mean of 2.5 years (0.4–3 years) after the first surgery. All patients were treated with curative resection on first and second surgery. The mean overall survival time after the first liver resection was 46 months. Repeat liver resection for recurrent HCC complicating PBC is an option and may improve the outcome.

Key words: Primary biliary cirrhosis – Hepatocellular carcinoma – Liver resection

Introduction

The incidence of hepatocellular carcinoma (HCC) complicating primary biliary cirrhosis (PBC) is between 0.7% and 16 %,[1–4] and often the stage has progressed to advanced cancer when HCC is discovered.[5] Liver resection and liver transplantation have been used for this condition, but the appropriate treatment is controversial.[6] Repeat liver resection for recurrent HCC complicating PBC is not usually performed because this approach is not generally applicable due to progressive liver dysfunction. It is reported that repeat liver resection is an independent prognostic factor for HCC.[7] However, we have found no previous report of a patient with repeat liver resection for HCC complicating

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PBC. We applied liver resection twice for three patients with these diseases.

Case Reports

Case 1 was a 71-year-old man in whom chronic nonsuppurative destructive cholangitis (CNSDC) was found histologically in 1989. Test findings did not exclude PBC and met the diagnostic criteria for PBC. He received treatment with ursodeoxycholic acid (UDCA), and imaging diagnosis was scheduled every four months. HCC development was detected in liver segment 4 in 2006. The Child-Pugh score was A, and anatomical segment 4 liver resection (medial segmentectomy) was performed. The pathologic diagnosis was well-differentiated HCC with a 1.4-cm diameter without hepatic cirrhosis. The Scheuer stage was III. After 5 months, a 1.4-cm recurrent HCC was found in liver segment 8 and repeat liver resection was performed. The pathologic diagnosis was moderately differentiated HCC with findings of noncancerous liver tissue similar to those in the first surgery. As of 38 months after the first surgery, the patient was dead with recurrence of HCC (Table 1).

Case 2 was a 66-year-old woman who was diagnosed with PBC in 2000 based on findings similar to those in Case 1. In 2006, HCC was found in liver segment 3. The Child-Pugh score was A, and wedge liver resection of segment 3 was performed. The pathologic diagnosis was a 1.8-cm well-differentiated HCC of Scheuer stage III (Figure 1). Repeat liver resection was performed for recurrent HCC in 2009. Liver function aggravated to Child-Pugh score B. The pathologic diagnosis was moderately differentiated HCC with a 2.5 cm of diameter, and the Scheuer stage was IV. The patient died of pneumonia 60 months after the first surgery.

Case 3 was a 61-year-old man who was found to be antimitochondrial antibody (AMA)-positive with histology not excluding PBC and without histologic CNSDC in 2005. He had been under medication with UDCA. The first anatomical subsegmentectomy was performed for HCC in liver segment 8 in 2009. The pathologic diagnosis was moderately differentiated HCC with a 3.4-cm diameter and Scheuer stage I. Repeat liver resection was performed for 2 recurrent HCCs in segments S4 and S8 moderately differentiated HCC with a 3.4-cm diameter. Repeat liver resection was performed for 2 recurrent liver cancers in segments 4 and 5 in 2012. HCCs with diameters of 1.5 and 2.2 cm were present in segment 4 and 5, respectively. Both were moderately differentiated HCC with no change in Scheuer stage. As of 39 months after the first surgery, the patient is alive without recurrence of HCC.

Discussion

Of 614 HCC patients who underwent initial liver resection between 2001 and 2010 in our institute, three (0.5%) had accompanying PBC. The first HCC was pointed out at a mean of 6 years (4–17 years) after diagnosis of PBC. The second HCC occurred at a mean of 2.5 years (0.4–3 years) after the first surgery. All patients were treated with curative resection on first and second surgery. The mean overall survival time after the first liver resection was 46 months.

The number of PBC patients has increased due to wider performance of the AMA test. Many PBC cases (80%) are asymptomatic and several cases (20%) are discovered as progression of nonspecific liver dysfunction-induced symptoms. Asymptomatic conditions are maintained by oral UDCA treatment in most cases of asymptomatic PBC, but systemic malaise and jaundice develop in about 10% of cases and progress to liver failure after several months to several years.[1,2]

HCC is increasingly being discovered during course observation of PBC due to improved internal medical treatment of PBC and advances in imaging diagnosis.[8] Many previously reported cases of HCC based on PBC were accompanied by advanced liver dysfunction, and were treated with liver resection and liver transplantation, similarly to treatment for HCC.[5,6]

In present report, frequency occurring HCC with PBC was 0.5%. All 3 patients were diagnosed with PBC and received treatment with UDCA and scheduled periodically imaging diagnosis. Therefore, their initial and recurrent cancers were detected in small sizes. Early diagnosis may increase the chance of repeat liver resection. We selected liver resection for the first HCC based on their hepatic functional reserve. The indications and procedures for liver resection were in accordance with Makuuchi's criteria[9] and the Japanese Guideline on Liver Cancer Examination and Treatment.[10] A meta-analysis reported that liver resection is superior to radiofrequency ablation for small single HCC.[11] Moreover, the predominance of liver resection in the latest large cohort study was shown.[12]

The recurrence rate of HCC within 5 years after treatment is $\geq$80% because HCC often develops in a multicentric carcinogenesis pattern.[13] Chen *et al* recommended repeat liver resection for recurrent

Table 1 Clinical characteristics of the patients

Case	1	2	3
Age/Sex	71/male	66/female	65/male
First hepatic resection			
Number	1	1	1
Location	S4	S3	S8
Diameter (cm)	1.4	1.8	3.4
Child-Pugh score	A	A	A
ICG R15 (%)	10	18	8
Hepatectomy procedure	MS	WR	SS
PBC Scheuer stage	III	III	I
Second hepatic resection			
Number	1	1	2
Location	S8	S3	S4, S5
Diameter (cm)	1.4	2.5	1.5, 2.2
Child-Pugh score	A	B	A
ICG R15 (%)	10	24	15
PBC Scheuer stage	III	IV	I
Hepatectomy procedure	WR	WR	WR
Prognosis after first operation	death/38 months	death/60 months	alive/39 months

ICGR15, indocyanine green retention rate at 15 minutes; MS, medial segmentectomy (anatomical segment 4 resection); WR, wedge resection; SS, anatomical subsegmentectomy; PBC, primary biliary cirrhosis.

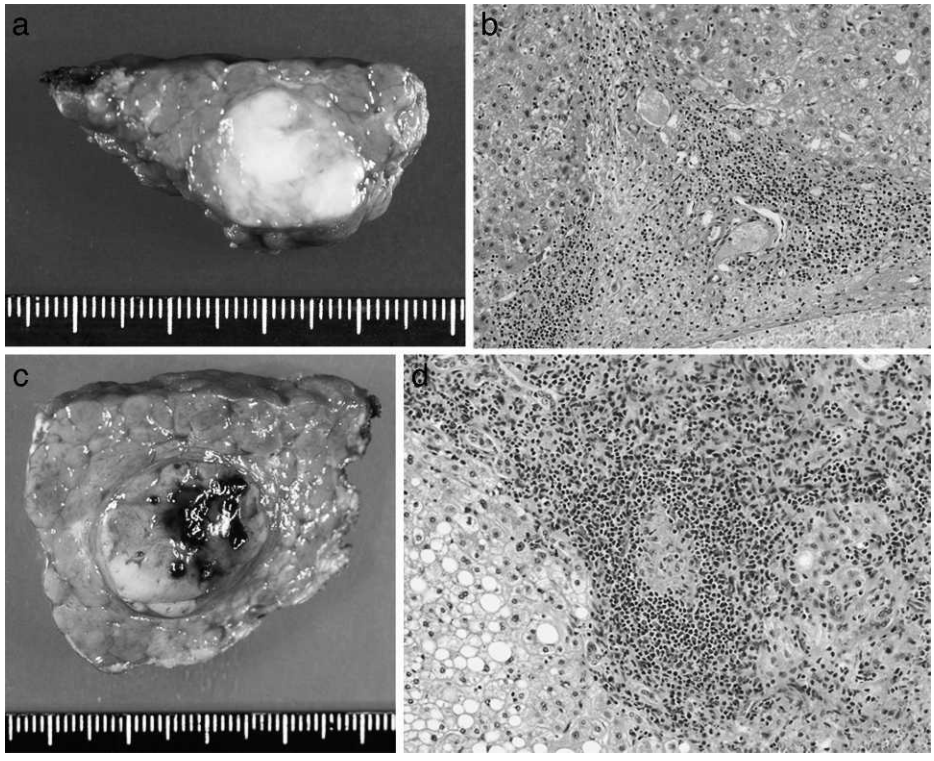

Fig. 1 (A) A solid mass of 1.8 cm with yellow-white nodular lesion was found in the resected specimen of Case 2. (B) The histopathologic diagnosis of (A) was well-differentiated hepatocellular carcinoma without vascular invasion. Reduction of interlobular bile duct in portal tract was seen. (H&E, ×20) (C) A solid mass of 2.5 cm with simple nodular lesions was found in the secondary resected specimen of Case 2. (D) The histologic diagnosis of (C) was moderately differentiated hepatocellular carcinoma. Appearance of epithelioid cell in portal tract was seen (H&E, ×40).

HCC, because of prognostic improvement.[7] However, the recommendation of repeat liver resection for patient with HCC complicating PBC is not yet clear. At our institution, we perform repeat liver resection following the Japanese Guideline on Liver Cancer Examination and Treatment when the liver function allows this procedure.[10] In the 3 patients, repeat liver resection was safely performed without a major complication and they survived for 3 years or more. In several cases of PBC, liver dysfunction progresses over several months to several years and liver tissue fibrosis and Scheuer stage may progress after the first liver resection. Although oral UDCA treatment was performed in 3 patients, Scheuer stage progressed from III at the first liver resection to IV at repeat liver resection in one patient. And the values of indocyanine green retention rate at 15 min (ICGR15) turned worse in 2 patients. The decision to treat with liver resection was made based on the value of ICGR15, showing the value of this test for evaluation of liver function in PBC.

Conclusions

!Repeat liver resection for the recurrent HCC accompanying PBC is an option and may improve the outcome of the patients.

Acknowledgments

The authors have no conflicts of interest to declare. This work was supported by Grant-in-Aid for Scientific Research (A) 24249068 and Research (C) 25350856 from the Ministry of Education, Culture, Sports, Science and Technology (MEXT).

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