Objectives: Hepatocellular carcinoma with bile duct tumor thrombus is considered an aggressive malignancy, and the prognosis of liver transplant for it remains obscure.

Materials and Methods: A 42-year-old man with recurrent hepatocellular carcinoma and a history of surgical resection was admitted to our hospital with a 10-day history of yellowish urine and itchy skin. There were 3 lesions in the right lobe with the diameter of 2 cm each. A mass was found in the upper part of common bile duct, and the intrahepatic bile duct was dilated. His serum alpha-fetoprotein level was 2476 µg/L, total bilirubin level was 327 µmol/L, direct bilirubin level was 261 µmol/L, and alanine aminotransferase was 714 U/L. There was no main portal vein thrombus or extrahepatic metastases. Because of his poor liver function, he was listed for a liver transplant. During the wait (30 d), he underwent 9 episodes of plasmapheresis to decrease the serum level of bilirubin. He had an orthotopic liver transplant with the graft from a deceased donor. After the liver transplant, he received 5 cycles of chemotherapy with the regimen of oxaliplatin and 5-fluorouracil.

Results: This patient has survived without recurrence of hepatocellular carcinoma for more than 82 months and remains in good condition.

Conclusions: Liver transplant may have a favorable result for hepatocellular carcinoma patient with a bile duct tumor thrombus, within the Milan criteria.

Key words: Bile duct tumor thrombus, Portal vein tumor thrombus, Hepatocellular carcinoma, Liver transplant, Survival

Introduction

The incidence of bile duct tumor thrombus (BDTT) in hepatocellular carcinoma (HCC) ranges from 2.3% to 13% in surgical and autopsy cases.1,2 It has been characterized with aggressive behavior. Early diagnosis and radical surgical treatment in cases with compensated liver function may produce a favorable prognosis.3,4 However, owing to the underlying liver disease and cholestasis, most cases cannot be operated on. There have been few reports concerning liver transplant for HCC with BDTT. Most likely, these patients have outlined the Milan criteria of liver transplant for HCC. Here, we report a case with HCC and BDTT, within the Milan criteria, who has survived more than 82 months at the time of this writing after liver transplant without tumor recurrence. The outcome of this and the 10 other cases in the English literature are reviewed.4-6

Case report

This study was approved by the institutional review board for human research at Sun Yat-sen Memorial Hospital, and written informed consent was obtained from the patient himself. All protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. A 42-year-old man with the history of HCC and hepatitis B virus-related cirrhosis was admitted to our hospital because of a 10-day history of yellowish urine and itchy skin. Six years earlier, he had undergone a
left hepatectomy for an 8 cm × 10 cm tumor in the left lobe. Histologic analyses confirmed the tumor as poorly differentiated HCC. Fifteen months earlier, he underwent radiofrequency ablation for 2 recurrent HCC masses (2 cm in diameter each) in the right lobe. At this admission, his serum alpha fetoprotein level was 2476 μg/L, aspartic transaminase was 299 U/L, alanine aminotransferase was 714 U/L, total bilirubin was 324 μmol/L, and direct bilirubin was 261 μmol/L. Abdominal magnetic resonance imaging and ultrasound showed 3 lesions in the right lobe (2 cm in diameter each), a mass in the common bile duct, and dilation of intrahepatic bile duct.

Because of his poor liver function, he was listed for liver transplant. Three weeks later, his serum total bilirubin level increased to 478 μmol/L. At the time, he was given plasmapheresis to decrease the serum total bilirubin level. Totally, he had 9 episodes of plasmapheresis during the next 30 days. Ultimately, he underwent orthotopic liver transplant with the graft from a deceased donor. During the hepatectomy, we found that the common bile duct was full of thrombus. However, there was no direct connection between the thrombus and the lesions in the right side of the liver (type III according to Satoh’s classification). The bile duct was transected above the pancreas, and a hepaticojejunostomy with a Roux-en-Y loop was made for the bile duct reconstruction. Histologic analyses confirmed the intrahepatic lesions and bile duct thrombus as moderately differentiated HCC, and the wall of common bile duct was invaded by the tumor microscopically. His serum alpha fetoprotein returned to the normal range 21 days after surgery.

The bile duct was transected above the pancreas, and a hepaticojejunostomy with a Roux-en-Y loop was made for the bile duct reconstruction. Histologic analyses confirmed the intrahepatic lesions and bile duct thrombus as moderately differentiated HCC, and the wall of common bile duct was invaded by the tumor microscopically. His serum alpha fetoprotein returned to the normal range 21 days after surgery. The immunosuppressant protocol included tacrolimus and steroids, and the steroids were removed 45 days after surgery. The trough serum level of tacrolimus was around 3 μg/mL ever since 6 months after surgery. He had 5 cycles of chemotherapy with the regimen of oxaliplatin and 5-fluorouracil.

He returned to the hospital regularly so we could monitor his liver function and tumor recurrence. As of this writing, he has been in good condition for more than 82 months without the recurrence of HCC.

Discussion

Hepatocellular carcinoma usually spreads intrahepatically via the portal vein branches, and the incidence of portal vein invasion is 34% to 40% in surgical resected series.8,9 Dissemination through the lymphatic system and bile ducts is rare.

Liver transplant is the ideal treatment for HCC, as it may cure the tumor and the underlying cirrhosis. However, tumor recurrence is the main problem after liver transplant. To exclude the HCC with aggressive behavior and decrease the risk of tumor recurrence, selection criteria of HCC for liver transplant has been studied intensively. Generally speaking, Milan criteria or UNOS criteria has been accepted internationally.10 In China, Hangzhou criteria and Shanghai Fudan criteria have been made.11,12 The number and size of the tumor, serum alpha fetoprotein level, and histologic grade are considered important factors that decide prognosis. Among these criteria, tumor thrombus in the main portal trunk, lymph node, and extrahepatic metastases were the contraindications. However, the status of BDTT has not been included in all of above criteria.

In 2004, Peng and associates6 reported 1 case of liver transplant for HCC with BDTT, and it was within Milan criteria. This patient survived for 27 months and then died of tumor recurrence. In 2006, Lee and associates5 reported 4 cases of HCC with BDTT treated by living-donor liver transplant, and all the cases were within Milan criteria. During the median follow-up of 20.6 months (range, 17.6-28.1 mo), only 1 patient died of a tumor recurrence 20 months postoperatively. In 2009, Luo and associates4 reported 5 patients with HCC and BDTT who underwent liver transplant. Three of these had multiple primary liver foci and extensive tumor thrombi in the bile duct, with the operation was unable to be completed in the remaining 2 patients owing to severe liver decompensation. These 5 patients have survived 11, 20, 26, 30, and 37 months; 3 patients are still alive at the time of this writing. In this report, in spite of the fact that the patient had a tumor thrombus in the extrahepatic bile duct, he was still within the Milan criteria. Among these 11 patients with HCC and BDTT, 6 patients were clearly within the Milan criteria, and 2 of 5 cases reported by Luo and associates4 also were possibly within Milan criteria (Table 1).

Hepatocellular carcinoma with BDTT has an aggressive biological behavior, and most cases present with vascular tumor thrombi at the same time.3 This may explain why few HCC patients with
BDTT undergo liver transplant as they outline the selection criteria based the vascular factors. However, bile duct tumor thrombus was not definitely accompanied by portal vein tumor thrombus. Among 38 cases of HCC with BDTT that underwent surgical treatment, ESAKI and associates found that the degree of bile duct tumor invasion was not related to the incidence of portal vein involvement and intrahepatic metastases, and HCC patients with macroscopic bile duct invasion (tumor thrombus located in no more than the second order branch of the bile duct) had a more favorable long-term postoperative result than did patients with microscopic BDTT (the tumor thrombus located higher than the second branch of the biliary tree). This suggests that tumor thrombus extending to the extrahepatic bile duct may not be an independently negative factor for the prognosis after radical surgical treatment.

In the present case, the immunosuppressive protocol, postoperative chemotherapy, or even preoperative plasmapheresis also may have played a role in his long-term tumor-free survival after liver transplant. It is well known that lower level of immunosuppression is important in preventing HCC recurrence after liver transplant. In this case, whether preoperative plasmapheresis and postoperative chemotherapy were coincidentally positive factors in the prognosis should be investigated.

In conclusion, we reported an HCC patient with BDTT having survived more than 82 months at the time of this writing after liver transplant without tumor recurrence. The bile duct is a specific pathway for HCC dissemination, but BDTT alone may not be a negative factor for the prognosis after liver transplant for HCC.

References


