

CLINICAL NOTE

Recurrence of hepatocellular carcinoma after liver transplantation presenting as anastomotic biliary stricture

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RESUMEN

Un varón de 52 años visitó nuestro hospital quejándose de anorexia y fatiga a los dos meses de haber recibido un trasplante hepático ortotópico a causa de un carcinoma hepatocelular. La analítica mostró un cuadro clínico de ictericia obstructiva. La colangiografía con tubo en T mostró una estenosis biliar sobre la anastomosis. Se intentó una dilatación transluminal percutánea con globo y colocación de endoprótesis, que fracasó. La colangiografía por resonancia magnética mostró una posible recurrencia tumoral sobre el lugar de la estenosis biliar anastomótica. Se extrajo una muestra de biopsia mediante aspiración bajo guía ecográfica y el estudio histopatológico mostró alteraciones inflamatorias y fibróticas. Al sospecharse la recurrencia del carcinoma hepatocelular, se realizó una exploración quirúrgica; un corte intraoperatorio congelado demostró dicha recurrencia. Así, diagnosticamos este caso como la recurrencia de un carcinoma hepatocelular después de un trasplante de hígado. Que sepamos, no se ha publicado anteriormente ninguna recurrencia tumoral precoz posterior a un trasplante hepático que fuera causa de estenosis biliar anastomótica.

Palabras clave: Estenosis biliar anastomótica. Trasplante hepático ortotópico. Recurrencia. Carcinoma hepatocelular.

ABSTRACT

A 52-year-old man visited our hospital complaining of anorexia and fatigue two months after receiving orthotopic liver transplantation for hepatocellular carcinoma. A laboratory investigation demonstrated a clinical picture of obstructive jaundice. T-tube cholangiography showed biliary stricture over the anastomotic site. Percutaneous transluminal balloon dilatation and stenting was attempted but failed. Magnetic resonance cholangiography showed possible tumor recurrence over the site of the anastomotic biliary stricture. A biopsy sample was obtained via ultrasound-guided aspiration and histopathological study revealed inflammatory and fibrotic changes. With high suspicion of recurrence of the hepatocellular carcinoma, surgical exploration was performed and an intraoperative frozen section proved the recurrence. We thus diagnosed this case as a recurrence of hepatocellular carcinoma after liver transplantation. To our knowledge, there have been no previous reports of early tumor recurrence after liver transplantation being the cause of an anastomotic biliary stricture.

Key words: Anastomotic biliary stricture. Orthotopic liver transplantation. Recurrence. Hepatocellular carcinoma.

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BACKGROUND

Since 1996, orthotopic liver transplantation (OLT) has been accepted as an effective treatment for hepatocellular carcinoma (HCC) in selected cases, with 4-year overall and recurrence-free survival rates of 85 and 92%, respectively (1). Despite adequate case selection improving survival rates, morbidity after liver transplantation remains a significant problem. Biliary complications, including anas-

tomotic stricture, have played an important role in liver transplant recipients with associated morbidity and graft loss (2). Furthermore, recurrence of HCC after OLT is a significant factor influencing survival. We report this interesting case to illustrate the need for early investigation and timely management of recurrent tumor after liver transplantation.

CASE REPORT

A 52-year-old man presented with obstructive jaundice and abdominal discomfort. He was diagnosed as HBV related HCC, T3N0M0, since 6 months ago and had received transarterial chemoembolization at that time. He

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went to offshore transplantation center and underwent OLT two months before. According to the referral sheet, a tumor sized 6-cm in diameter across to hepatic hilum area was noted at the time of transplantation. A lymph node dissection was not performed with any evidence of metastatic lymph nodes at the time of surgery. The postoperative pathological report revealed trabecular type HCC with grade II differentiation, piecemeal necrosis, focal bile ductules proliferation, and lymphovascular tumor thrombus. The postoperative tumor staging was T3N0M0, stage IIIA. He was referred to our hospital (Tri-Service General Hospital, National Defense Medical Center) for further evaluation and management. Laboratory investigations revealed the following biochemical picture: A total bilirubin of 5.2 mg/dL; direct bilirubin of 3.1 mg/dL; aspartate aminotransferase of 164 U/L; alanine aminotransferase of 283 U/L; alkaline phosphatase of 825 U/L; gamma-glutamyl transpeptidase of 614 U/L; hemoglobin of 11.0 g/dL; and a white blood cell count of 2,900/mm³. The alpha-fetoprotein concentration was 10.21 ng/mL.

His chest radiograph showed a mild pleural effusion over the right hemithorax. Abdominal ultrasonography (US) showed dilatation of the intrahepatic duct (IHD), but the common hepatic duct (CHD) and common bile duct (CBD) could not be traced. The T-tube cholangiography showed an abrupt narrowing over the CHD in the anastomotic area with dilatation of the proximal CHD and IHD (Fig. 1), suggesting a postoperative anastomotic stricture. Percutaneous transluminal balloon dilatation and stenting of the stricture was attempted via T-tube, but it failed,



Fig. 1. The T-tube cholangiography showed abrupt narrowing over the CHD in the anastomotic area with dilatation of the proximal CHD and IHD, suggesting a postoperative anastomotic stricture (arrow).

with no evidence of dilatation after the procedure. Magnetic resonance cholangiography (MRC) was arranged for further evaluation, and showed a segmental irregular narrowing over the CHD and CBD of about 3.8 cm in length. Dilatation of the proximal CHD and IHD was noted. In addition, severe segmental irregular narrowing of both the intrahepatic portal vein and the extrahepatic main trunk portal vein in the liver hilum region was noted. Postoperative fibrosis or metastatic lymph node encasement was highly suspected (Fig. 2). US-guiding aspiration was performed and two pieces of tissue were sent for pathological study. Histopathology of the aspiration specimen revealed fibrosis with a reactive inflammatory cell infiltration; no tumor cells were detected. Because the radiological intervention failed and tumor recurrence could not be ruled out clinically, even though the aspiration cytology was negative, the patient received an exploratory laparotomy with a bypass procedure.

At operation, tumors were located over the grafted liver hilum area with external compression of the CHD and CBD. The segmental compression of the CHD and CBD was about 2.5 cm in length. An intraoperative frozen section was sent for pathological study and the report revealed recurrence of the HCC. The metastasis was confined to the abdomen without evidence of other distal lesions. We removed the tumors and converted the choledochocolocholestomy to a hepatojejunostomy. The specimen consisted of 2 tiny pieces of liver tissue measuring up to 2.5 cm in length. Grossly, they were brown



Fig. 2. Magnetic resonance cholangiography (MRC) showed segmental irregular narrowing over the CHD and CBD. Severe segmental irregular narrowing of both the intrahepatic portal vein and extrahepatic main trunk portal vein in the liver hilum region was also noted. Postoperative fibrosis or metastatic lymph node encasement was highly suspected (arrow).

in color and soft in consistency. Microscopically, the sections show a picture of metastatic hepatocellular carcinoma characterized by small nested and clusters of hyperchromatic tumor cells with focal plasmacytoid patterns infiltrating in the lymphoid tissue with extensive necrosis and capsular destruction. Postoperatively, the symptoms of obstructive jaundice and abdominal discomfort subsided. The total bilirubin level was 2.4 mg/dl on postoperative day 5. The patient was discharged in good health on postoperative day 7.

DISCUSSION

Bile duct stricture is a significant complication after biliary reconstruction and leads to postoperative morbidity and mortality. There are several factors predisposing for anastomotic biliary stricture, including difficult anastomosis, poor circulation to the anastomotic site, inflammation, fibrosis, the use of a T-tube or stent in end-to-end choledochocholedochostomy, and severe preoperative liver dysfunction (3). The clinical presentation in patients with bile duct strictures includes jaundice, deterioration of liver function tests, and symptoms similar to those of cholangitis. Because an anastomotic biliary stricture causes patient discomfort and potential graft loss, this condition should be treated as serious and managed aggressively. Initial management includes the use of radiological intervention with stenting or dilatation; it has a higher success rate in treating early postoperative biliary stricture than late stricture. Bypass surgery, i.e., hepatojejunostomy, is suggested when percutaneous procedures fail or the approach is difficult (2).

Patients with HCC are candidates for OLT if the tumor stage meets the Milan criteria –a single lesion less than 5 cm in diameter or no more than 3 tumor nodules all less than 3 cm in diameter (1). Patients who are outside the Milan criteria have a higher risk of postoperative recurrence. While recurrence of HCC may present in the transplanted liver, the majority of recurrences are extrahepatic. The most common involved sites are lungs and bones. Only 16% of patients present with the grafted liver as the sole site (4). The possible mechanism of recurrence is tumor seeding via bloodstream, because vascular invasion increases the likelihood of recurrence and shortens the recurrence-free time (5). When recurrence of tumor is diagnosed after OLT, surgical resection of the recurrent HCC is the treatment of choice if the tumor is localized and resectable. With the exception of multiple metastases, surgery is independently associated with a longer survival period (6).

The early recurrence of HCC after liver transplantation presenting as external compression of the CHD and CBD and leading to symptoms similar to anastomotic stricture is an unusual situation. Most early recurrences of HCC following liver transplantations are metastatic lesions, presenting as metastases to lung, bone, liver, and multiple or-

gans. The factors influencing the early recurrence of tumor include a tumor size of more than 3 cm, staging outside of the Milan criteria, and a tumor with a capsule (7). With regard to the localized recurrence of HCC over the anastomotic site at an early time after transplantation, there has been no comprehensive survey reported in the literature. The possible factors that influence the early recurrence of tumor localized over the site of the biliary anastomosis are worthy of discussion. Unexpected tumor rupture may lead to seeding of cancer cells into the abdominal cavity. One of the reasons that tumors rupture intraoperatively is excessive manipulation by the surgeon, especially when the tumor is located peripherally. Another important factor is the preoperative tumor staging. Postoperative recurrence of HCC occurs earlier when the preoperative tumor staging is underestimated. Micrometastases to regional lymph nodes in the hilum or hepaticoduodenal ligament may be another predisposing factor to anastomotic-site recurrence. Preoperative tumor staging should be performed carefully to detect both intra- and extrahepatic lesions, as extrahepatic lesions are sources of early recurrence and contraindicate liver transplantation.

In summary, we report a rare and interesting case of recurrence of HCC after OLT presenting as anastomotic biliary stricture. There are several factors leading to the anastomotic biliary stricture after OLT. Tumor recurrence should be considered even in the relatively early postoperative stages, as the causes of stricture influence the therapeutic strategy. Since liver transplantation has been accepted as treatment for patients with HCC, the number of livers available remains insufficient for the people on the waiting list. Clinicians should evaluate the preoperative tumor staging carefully and avoid underestimating the stage, as the survival rate significantly decreases when there is tumor recurrence. We believe that this report will contribute to the management of anastomotic biliary stricture of unknown origin.

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