

In-vivo hepatic procurement of tumor-free section followed by autotransplantation for large hepatocellular carcinoma with tumor thrombi extending into the inferior vena cava

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Abstract

In hepatocellular carcinoma (HCC) with thrombus formation in the major vasculature, to control unexpected life-threatening progression due to tumor extension into the inferior vena cava (IVC), ensure long-term survival, and improve quality of life (QOL), aggressive surgical approaches can be selectively adopted.

We utilized outstanding living donor liver transplant (LDLT) techniques to develop an alternative surgical procedure with new concepts in large HCCs with tumor thrombi that have extended into the supra-hepatic IVC from the right hepatic vein (RHV) and middle hepatic vein (MHV).

A 42-year-old man with a 10-cm HCC in the right lobe was transferred. We found tumor thrombi growing into the supra-hepatic IVC through the RHV, and a tumor thrombus that extended into the MHV through V8 was observed.

Surgically, we first procured the left lobe, which had no involvement of the tumor or tumor thrombi, to avoid the spread of tumor thrombi. After securing an adequate operation field, a total hepatectomy was performed with simultaneous total hepatic vascular exclusion. The LDLT technique with modified extended left lobe graft after MHV reconstruction was used for auto-transplantation.

Conclusively, this technique with new concepts for auto-transplantation offered our patient the potential to receive subsequent multidisciplinary treatments and an opportunity for improved QOL.

Abbreviations: AFP: alpha fetoprotein; CT: computed tomography; HCC: hepatocellular carcinoma; IVC: inferior vena cava; LDLT: living donor liver transplantation; MHV: middle hepatic vein; LHV: left hepatic vein; ¹⁸F FDG-PET/CT: ¹⁸F fluorodeoxyglucose positron emission tomography/computed tomography

Introduction

Hepatocellular carcinoma (HCC) is a highly malignant tumor with tumor thrombus formation in the major vasculature, such as the portal vein or hepatic vein, in advanced stages [1]. Tumor thrombi from any of the three main hepatic veins or the right inferior hepatic vein can easily extend into the inferior vena cava (IVC) or right atrium [2]. Traditionally, tumor extension into the IVC has been considered a contraindication of surgical treatment because of high operative risk and poor long-term survival. However, to control unexpected life-threatening progression due to tumor extension into the IVC, ensure long-term survival, and improve quality of life, an aggressive surgical approach can be selectively adopted in patients who are young or exhibit good general performance.

Notable developments of innovative surgical techniques in liver surgery, including living donor liver transplantation, have made

curative surgical approaches to tumors involving both the liver and IVC possible. Right or left trisectionectomies with IVC replacement, total hepatic vascular exclusion following venovenous bypass, *ex vivo* hepatic resections [3], and ante-situm hepatic resections [4] have been introduced as curative resection methods that may be implemented according to the tumor involvement in the three main hepatic veins and IVC.

With the development of liver transplantation, implantation of partial liver grafts became a useful treatment option for patients with end-stage liver disease or HCC [5]. Several surgical techniques have been shown to facilitate various anastomoses of partial liver grafts. After numerous attempts to utilize outstanding living donor liver

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Key words: hepatocellular carcinoma, IVC thrombi, autotransplantation, living donor liver transplantation

Received: April 04, 2017; **Accepted:** April 29, 2017; **Published:** May 04, 2017

transplantation (LDLT) techniques for extensive liver surgery, we eventually developed an alternative surgical procedure with new concepts for large HCC with thrombi that extend into the supra-hepatic IVC from the right hepatic vein and the middle hepatic vein (MHV) through V8.

Case report

A 42-year-old man who had a history of weight loss and fatigue was transferred for treatment of an incidentally detected large HCC. From this patient history, we assessed that he was a hepatitis B carrier who did not receive regular follow-up examination. Computed tomography (CT) scanning revealed a large mass that was >10 cm and occupied the entire right lobe. The tumor thrombi grew into the supra-hepatic IVC through the right hepatic vein (Figure 1A). A tumor thrombus also extended into MHV through V8 (Figure 1B). On ¹⁸F fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F FDG-PET/CT), we could ascertain that there was no distant metastasis. The patient's Child-Turcotte-Pugh score was 5 points. Aspartate transaminase and alanine transaminase levels were 344 and 86 IU/L. However, both total bilirubin and prothrombin time-international normalized ratio were within the normal ranges. The alpha-fetoprotein (AFP) level was 34410 ng/mL (normal: <7). Indocyanine green retention rate at 15 minutes was 17.7%.

Surgical procedure

Abdominal exploration was performed through an inverted T-shaped incision. First, the right portal vein and hepatic artery were ligated after cholecystectomy. The left portal vein as well as the left and middle hepatic arteries were individually isolated. The left lateral section of the liver was carefully mobilized, but we did not dissect the MHV and left hepatic vein (LHV). The V5 and V8 branches of the MHV were evaluated using intraoperative ultrasonography.

Step 1: Left liver lobe procurement

An anterior approach for left hepatectomy was utilized (Figure 2A). Liver parenchymal dissection was meticulously performed with a Cavitron Ultrasonic Surgical Aspirator (CUSA, Valleylab). Following V5 ligation, we performed further parenchymal dissection, and the MHV was transected before V8 insertion to avoid upstream tumor thrombi. The final parenchymal dissection progressed from the left side of the MHV until the root of the LHV. The patient's left lobe and a portion of the MHV were procured and perfused with histidine-tryptophan-ketoglutarate solution.

Step 2: Total hepatectomy of remnant liver with large HCC and tumor thrombi

After procurement of the left lobe, approaching the supra- and infra-hepatic IVC was easy. Vascular clamps were applied above the level of the supra-hepatic IVC with the tumor thrombus and infra-hepatic IVC, simultaneously (Figure 2B). A total hepatectomy was completed following total hepatic inflow occlusion. An extracorporeal venovenous bypass from the left femoral vein and portal vein to the right internal jugular vein was used to prevent venous congestion and stabilize vital signs. Complete removal of tumor thrombi within the IVC and MHV (Figure 2C) was confirmed. The right hepatic vein orifice was then closed.

Step 3: Back-table surgery

The transected MHV of the procured left lobe was elongated with a 10-mm Dacron graft and joined with the LHV to form a common

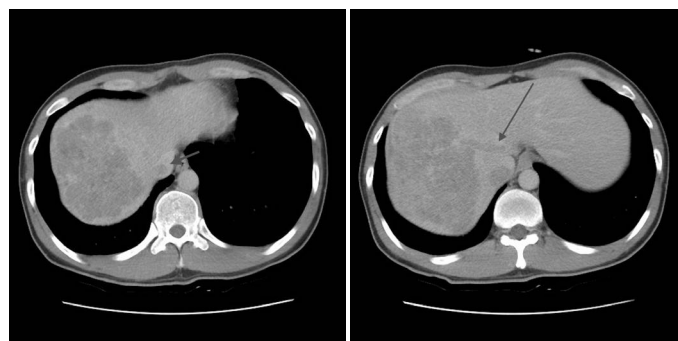


Figure 1. Pre-operative CT imaging demonstrating (A) Tumor thrombi in supra-hepatic IVC (short arrow), (B) Tumor thrombi that extended into middle hepatic vein (MHV) through V8 (long arrow)

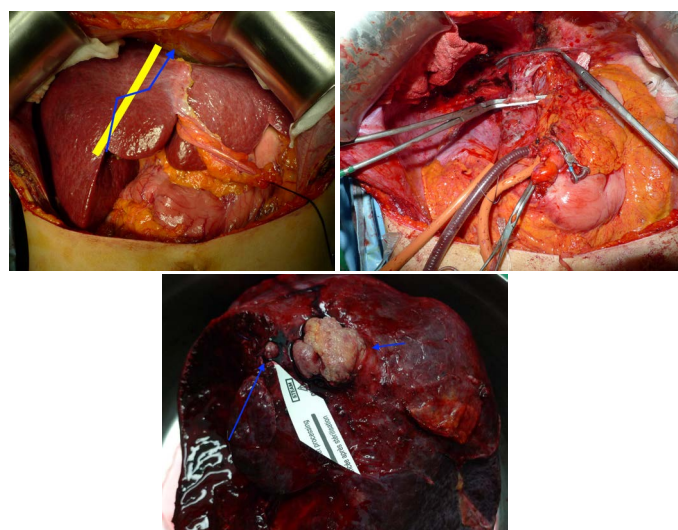


Figure 2. Operative findings (A) Transection line (arrow line) for V4b preserving left hepatectomy; MHV (thick line), (B) Total vascular exclusion with extracorporeal venovenous bypass after total hepatectomy, (C) Tumor thrombi that extended from RHV (short arrow) and MHV through V8 (long arrow)

trunk. We widened this common venous trunk with the left greater saphenous vein (Figure 3).

Step 4: Autotransplantation with a modified extended left lobe

Implantation of the reconstructed left lobe was performed using the left lobe living donor liver transplantation technique. The reconstructed common hepatic vein trunk was anastomosed with the patient's left common MHV and LHV outflow, and the left portal vein was reconstructed with the patient's main portal vein. After reperfusion, the hepatic artery was anastomosed with the left hepatic artery using a microscopic technique, and the hepatic duct was reconstructed with the patient's common hepatic duct using the duct-to-duct method with a T-tube. The total operation time was 455 minutes, and the cold ischemic time was 140 minutes. There was free RBC transfusion (Figure 4).

The in-hospital postoperative course for the patient was uneventful, except for medically controlled ascites. He was discharged, 23 days after autotransplantation. His AFP level declined to 272 IU/L, 3 months after autotransplantation. However, he died 12 months after autotransplantation because of intrahepatic recurrence and lung metastasis, despite trans-arterial chemoembolization and the administration of sorafenib (Nexavar[®]RR, Bayer).

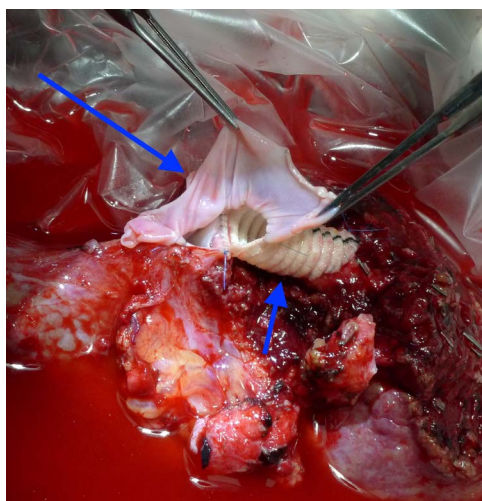


Figure 3. Back-table surgery: MHV that was elongated with Dacron graft (short arrow) and common venous trunk that was reconstructed with greater saphenous vein (long arrow)

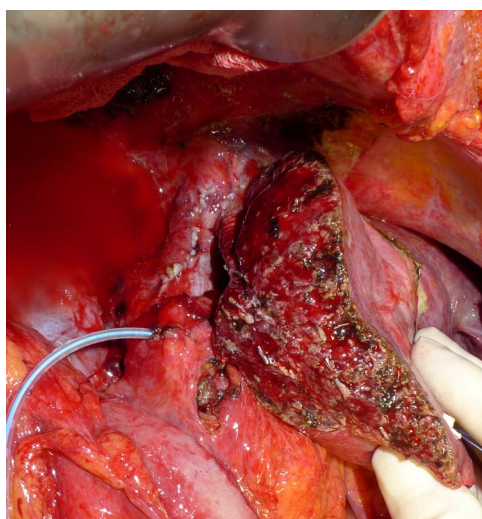


Figure 4. Auto-transplantation with modified extended left lobe graft

Discussion

In patients with IVC thrombi that developed from HCC, surgical removal of the involved IVC combined with hepatectomy is the treatment of choice. This decreases the risk of systemic metastasis, sudden death due to pulmonary embolism, and tumor thrombus-related symptoms, such as edema and ascites [6,7]. Hence, although technically challenging, hepatic resection can be considered an acceptable treatment for HCC with tumor thrombus in patients with resectable primary tumors and sufficient hepatic reservoirs [8,9]. In order to accomplish these objectives, technically developed surgical procedures have been suggested, including left or right trisectionectomy with IVC reconstruction and either *ex vivo* liver resection or hypothermic ante-situm resection followed by autotransplantation.

However, the prognoses of patients who received such aggressive operations are generally poor and depend on the extension of the tumor thrombi. Patients with thrombi within hepatic veins alone have better prognoses than those with tumor thrombi extending into the IVC because of early distant organ metastasis [8]. In other words, it is very important to minimize the spread of tumor thrombi extending into the IVC. Therefore, we needed to utilize a “no-touch technique” and an

“anterior approach” to avoid excessive rotation and traction of the liver. Hypothermic ante-situm resection followed by autotransplantation is a useful alternative surgical option. However, this procedure was rejected by our team for two reasons. First, there was the possibility of intraperitoneal seeding during extravasation of blood containing tumor thrombi during perfusion of the preservation solution. Secondly, MHV reconstruction with an artificial graft should be performed in a limited intra-abdominal operative field.

In our patient with Child A liver cirrhosis, a sufficient functional liver volume was of paramount importance in the prevention of postoperative hepatic failure. MHV reconstruction was necessary to maintain appropriate hepatic venous outflow. *Ex vivo* liver resection is a useful surgical option. The reconstruction of vascular structures takes place in a bloodless field and can be conducted without time restrictions. However, we did not choose this option because the risk of morbidity, including bile leakage, is high, the cold ischemic time is needlessly long, and full liver mobilization and unnecessary IVC reconstruction are required even when there is no excessive involvement of the IVC from the three major hepatic veins.

For *ex vivo* liver resection or ante-situm resection, total hepatic vascular exclusion is necessary. Without full liver mobilization, it is very difficult to clamp the supra-hepatic IVC. Occasionally, a median sternotomy and pericardiectomy are required. Full liver mobilization can potentially cause tumor dissemination, and sternotomy can induce mediastinitis, which is a grave infection.

We herein described an enhanced hepatic autotransplantation technique using new concepts. First, we perfused with preservation solution after excision of the future remnant liver without the tumor and reconstructed the MHV in back table surgery. Following total hepatic vascular exclusion under better operative field, it was easier and safer to remove the diseased liver with the tumor and tumor thrombi. Finally, we performed hepatic autotransplantation using the LDLT technique.

The disparity between the number of liver transplant candidates and the supply of deceased donor organs is the major cause for the development of LDLT. LDLT has been markedly improved by the innovation of surgical techniques [5]. We performed this operation based on wide LDLT experience and achieved satisfactory results.

Conclusively, a few reports note that intrahepatic recurrences or lung metastases occur in most patients after surgery [10]. However, this aggressive surgery offered our patient a chance to receive subsequent multidisciplinary treatments, such as transcatheter arterial chemoembolization and molecularly targeted therapy as well as an opportunity for improved quality of life and prolonged survival.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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