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Case Report

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Management of Hyperacute Rejection during Operation in Living Donor Liver Transplantation - A Case Report

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1. Abstract

Hyperacute rejection in solid organ transplantation is a catastrophic event and leads to graft failure immediately. It rarely happens in liver transplantation during operation. A 58-year-old male patient had salvage living donor liver transplantation for recurrent hepatocellular carcinoma. His wife was the donor. All the transplantation procedures were uneventful until bile duct anastomosis was done. The portal vein became tense without obvious thrombus. Portal flow ceased and small bowels were congestive. Hyperacute rejection was the impression and portal flow was diverted into systemic circulation by porto-femoral shunt. Postoperative serum showed positive for anti-donor antibodies. The patient had re-transplantation on next day with a hepatitis B antigen (+) deceased graft. The excised liver graft in the 1st liver transplantation showed multiple focal hemorrhagic necrosis, extensive thrombus in portal vein and positive for C4d. It was a hyperacute rejection and was rare in liver transplantation. Herein, we reported how the patient was rescued during the operation.

2. Introduction

Hyperacute rejection in solid organ transplantation is a catastrophic event and leads to graft failure immediately. It is a well-known immune reaction in kidney transplantation and happens when recipients have preformed anti-donor antibodies [1, 2]. Hence, a panel-reactive antibody will be measured and cross-matching between donors and recipients will be performed prior to transplantation to prevent hyperacute rejection. If hypersensitized candidates are identified, desensitized procedures will be proceeded to remove preformed anti-donor antibodies and reduce the possibility of hyperacute rejection.

The liver is the largest organ in the abdomen and has the large sinusoid surface which may have the ability to absorb anti-donor antibodies. Hence, the liver is recognized as an immune privilege organ and is easy to accept allogeneic organs. Matches of human leukocyte antigen typing are usually not required and hyperacute rejection rarely happens in liver transplantation. Herein, we reported an intra-operative non-ABO incompatible hyperacute rejection in ABO-incompatible living donor liver transplantation and how the patient was rescued.

3. Case Report

A 58-year-old male hepatitis B patient had right hepatectomy for hepatocellular carcinoma (HCC) on 5/24/2018. Tumors recurred one and a half years after liver resection. Three times of transcatheter arterial chemoembolization (TACE) were performed to treat the recurrent tumors. Because new tumors developed repeatedly, the patient and family were willing to perform living donor liver transplantation since tumors were still with Milan criteria [3]. His wife was the donor. Pre-operative donor assessment revealed that the liver

parenchyma was normal without fatty change. Anatomy of hepatic artery, portal vein, and biliary tact was all normal, too. Estimated liver volume was 1259.6cm3 by computed tomography volumetry and right lobe was allocated by 63% [4, 5]. Estimated graft-to-recipient weight ratio was 0.86%. As her blood type was A and recipient's blood type was B, this would be an A to B-incompatible living donor liver transplantation.

As an ABO-incompatible adult liver donor liver transplantation was going to be carried out, ABO isoagglutinin was measured prior to liver transplantation. Recipient's serum anti-A isoagglutinin IgM was 1: 32 and IgG was 1:128. According to our desensitizing protocol [6], rituximab, 375mg/m^2, was given on 7/28/2020 to deplete B-cells and bortezomib, 3.5mg was given on 8/11/2020 to deduce anti-A isoagglutinin IgM to 1:32 and IgG to 1:64. Salvage living donor liver transplantation was performed on 8/18/2020. Donor operation was smoothly to take right lobe of the liver which weighted 665gm. In recipient operation, liver graft was implanted in right liver fossa. Graft right hepatic vein was anastomosed to right hepatic vein of the recipient, and portal vein was reconstructed as end to end. Portal flow was 1200cc/min after reperfusion, which was measured by flowmeter (Transonic flowmeter, Transonic System Inc.). Hepatic artery was reconstructed microscopically and flow was 120cc/min. Bile duct was reconstructed as end to end manner. After bile duct was reconstructed, insufficient hepatic artery flow was found by flowmeter. During hepatic artery re-anastomosed, small bowel became progressive congestion and operation field became smaller and smaller. Portal vein was felt very tense and flow ceased. Hyperacute rejection was the impression. The condition became very critic because the bowels become severe edema and venous congestion. At this moment, diversion of portal flow was decided to be done. A bypass from portal vein to right femoral vein was performed by using DLP® aortic root cannulae and a 6mm ringed cortex conduit to drain portal flow. Bowel congestion was subsided and the abdominal wound was covered by a plastic sheet. The patient was sent back intensive care unit and waited for the opportunity of re-transplantation. Anti-B isoagglutinin titers were measured and revealed IgM at 1 : 4 and IgG at 1 : 16. Anti-HLA donor specific antibodies (DSA) were measured and showed negative. However, anti-donor non-HLA antibodies were positive (figure 1) Fortunately, the patient had an opportunity of re-transplantation with a HBs Ag (+) deceased liver graft [7] on 8/20/2020. The 2nd transplantation was uneventful and the patient was discharged 3 weeks after transplantation. The excised liver graft of the 1st transplantation was multiple focal hemorrhagic necrosis, extensive thrombus in portal vein and positive for C4d (figure 2). This case study was approved by institutional review board of Chang-Gung Memorial Hospital (IRB No. 202100193B0).

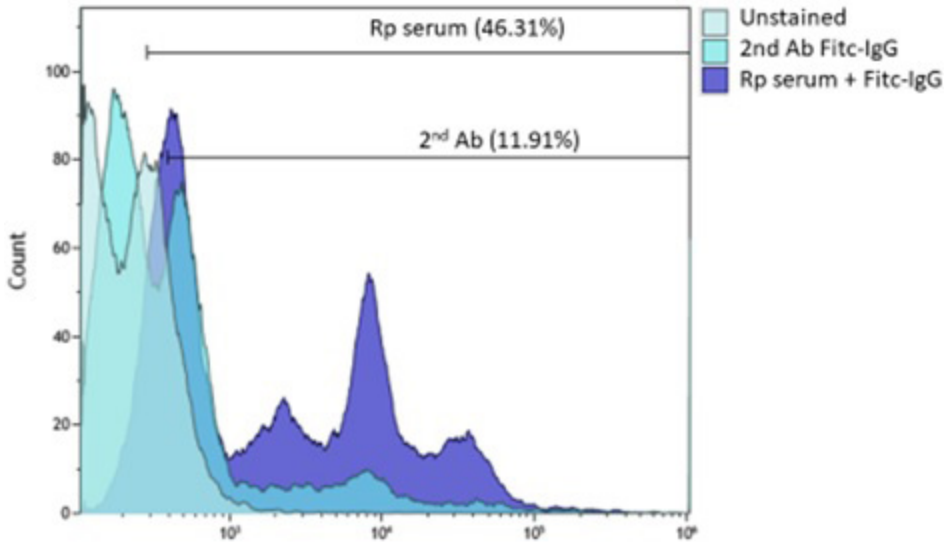

Figure 1: Flow cytometry of anti-donor antibodies. To detect anti-donor antibodies, decomplement recipient's serum was added to donor's peripheral blood monocytes and incubated at room temperature for an hour. Fitc-conjugated goat anti-human antibody was added and showed positive anti-donor antibody.

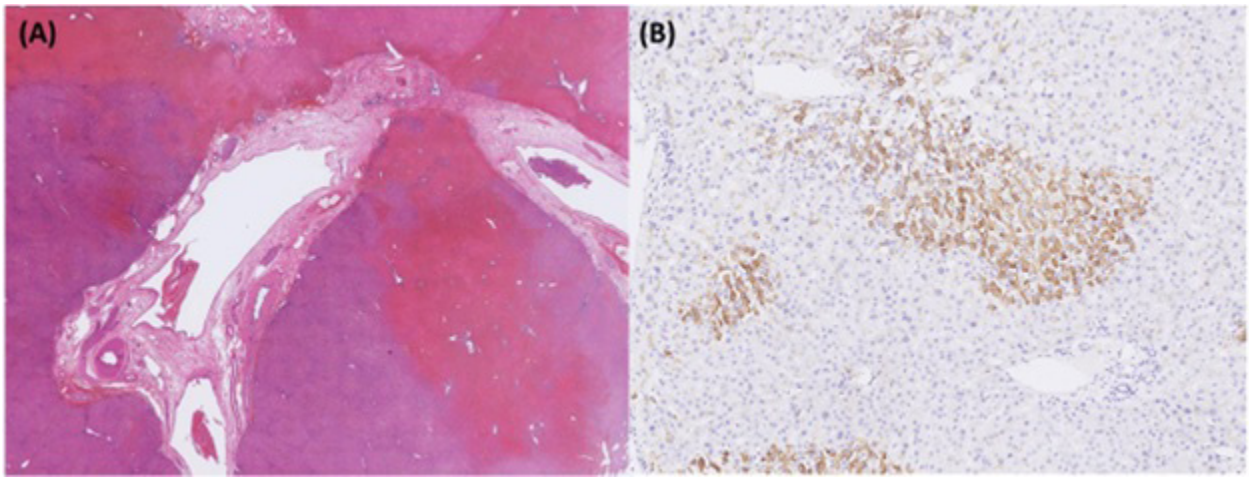

Figure 2: Pathological figures of the excised liver graft. The excised liver graft of the 1st transplantation showed multiple focal hemorrhagic necrosis, extensive thrombus in portal vein (A) and positive for C4d (B).

4. Discussion

Hyperacute rejection during operation in liver transplantation is extremely rare. Clinical diagnosis of hyperacute rejection during operation is not well defined yet. Recognition of hyperacute rejection during operation for liver transplantation is difficult. In our previous study, we mentioned that cease of portal flow without portal vein thrombus implied antibody-mediated hyperacute rejection [8]. In this case, tense portal vein without obvious thrombus combined rapid small bowel congestion was noted. Hyperacute rejection was highly impressed. After operation, anti-donor antibody was detected in the serum. The excised liver graft also showed typical acute antibody-mediated rejection with multiple focal hemorrhagic necrosis and positive for C4d staining. Herein, we would like to emphasize the clinical presentations of hyperacute rejection included tense portal vein, no obvious thrombus in portal vein and congestive small bowel.

How to manage hyperacute rejection during operation has not been mentioned before. In this case, we performed porto-femoral shunt and successfully diverge portal flow into systemic circulation, and let the patient had the opportunity to be re-transplanted. When hyperacute rejection happened during operation, portal flow ceased and the small bowel became congestive immediately. Diverging portal flow into systemic circulation would be the most important procedure at this stage to decongest bowels and maintain circulations. Portocaval or mesocaval shunt might be the other optional procedure to divert portal flow. However, portocaval and mesocaval shunt would become difficult to perform when small bowels were congested and operation field was compromised. Under such circumstance, porto-femoral shunt would be the better choice.

Hyperacute rejection is mediated by pre-formed antibodies. As this is an ABO-incompatible liver donor liver transplantation, hyperacute rejection related to ABO-incompatibility was the first impression. Anti-blood type issoagglutinin was measured immediately after the operation. However, the IgM and IgG isoagglutinin titers were only 1: 4 and 1:16, respectively. DSA were also measured but showed negative results. But, anti-donor antibody was positive by flow cytometry when donor white blood cells were used as targets. DSA has been emphasized to be related to antibody-mediated rejection. In this case, hyperacute rejection was related to anti-donor antibodies, but not anti-HLA antibodies. The preformed anti-donor antibodies are speculated that donor and recipient are spouse.

In conclusion, intra-operative hyperacute rejection rarely happens in liver transplantation. It is difficult to make a precise diagnosis at once. The clinical presentations of tense portal vein, no obvious thrombus in portal vein and congestive small bowel might imply hyperacute rejection. To diverge portal flow into systemic circulation, and let the patient had the opportunity to be re-transplanted will be the optimal management for hyperacute rejection.

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