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LETTER TO THE EDITOR

Transmission of idiopathic thrombocytopenic purpura during orthotopic liver transplantation

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Organ transplantation carries the risk of transmission of a disease from the donor to the recipient. Immune-mediated disorders can be transferred during solid organ transplantation via lymphoid tissue and passenger lymphocytes from the donor organ [1–3].

In this study, we report a patient who developed a severe, life-threatening thrombocytopenia after transplantation of a liver graft from a donor who died of a fatal intracranial hemorrhage resulting from acute idiopathic thrombocytopenic purpura (ITP).

A 44-year-old man, with diabetes mellitus type I and Crohn's disease, underwent re-transplantation of the liver for ischemic-type biliary lesions and recurrent cholangitis. Seven years earlier, the patient underwent a first liver transplantation for primary sclerosing cholangitis. His pre-operative platelet count was 424×10^9/l. There was no history of thrombocytopenia. The donor was a 53-year-old man, with arteriosclerosis. The day before his death, he presented with purpura and acute thrombocytopenia, with a peripheral platelet count of 2×10^9/l. Other laboratory results were within normal ranges. Because no other explanation was found for the extremely low platelet count, the sudden thrombocytopenia was diagnosed as ITP. One day after the diagnosis of ITP, the patient died as a result of spontaneous intracranial hemorrhage. His liver and both kidneys were offered for donation and accepted for subsequent transplantation. At the time of organ procurement, the donor's platelet count was 4×10^9/l. The liver transplantation was performed using the piggy back technique, without any complications. The estimated total blood loss during the procedure was 1500 ml. No blood products were transfused. The cold ischemia time was 400 min; the warm ischemia time was 37 min. ABO blood type of donor and recipient was identical (blood type B, Rhesus factor positive). There were no surgical complications, and the patients' condition remained stable throughout the procedure.

The initial recovery after the re-transplant was uneventful and early graft function was good. Postoperatively, the patient received tacrolimus and low-dose prednisone as immunosuppressive drugs and low-molecular-weight heparin as thrombo-prophylaxis, according to our protocol. Perioperatively, the patient received broad-spectrum antibiotics (vancomycin and imipenem) because of the patient history of recurrent and recent cholangitis.

During the first two postoperative days, the platelet count remained stable and within the normal ranges (Fig. 1a). On postoperative day 3, an acute drop in platelet count to values around 6×10^9/l was noted. Tacrolimus, vancomycin, and low-molecular-weight heparin were stopped immediately, because these drugs are known to be possible causes of drug-induced thrombocytopenia (9–12). Because of the history of ITP in the donor and the possibility of transmission of this disease, the dosing of prednisone was increased to 80 mg i.v. and intravenous immunoglobulins were administered at a standard dose for treatment of ITP (1 g/kg body weight daily for 2 days). For the subsequent 5 days, the platelet count remained extremely low (as low as 1×10^9/l). During this period, the patient received one unit of platelet concentrates daily until postoperative day 8. On postoperative day 8, a slight increase in platelet count was observed (Fig. 1a). On postoperative day 12, the patient's condition suddenly worsened because of acute portal vein thrombosis (PVT), eventually leading to his death. Due to a toxic liver syndrome, caused by the PVT and leading to hemodynamic instability, an emergency transplantectomy was performed and a temporary portocaval shunt was constructed. The patient was listed for urgent retransplantation. Unfortunately, no donor liver for urgent retransplantation had become available prior to his death. Postmortem laboratory studies demonstrated the presence of anti-platelet antibodies in serum of both the donor and recipient. Histological examination of the explanted liver graft revealed large areas of ischemia, as well as thrombosis of both arterial and portal branches in the liver (Fig. 1b–c). As other causes for the thrombocytopenia in the recipient were ruled out, we conclude that the patient contracted ITP through transmission of anti-platelet antibody-producing lymphocytes by the liver transplant procedure.

Although our liver transplant recipient did not die from hemorrhagic complications, it is conceivable that the PVT, leading to acute graft failure and subsequent death, was indirectly related to the severe postoperative

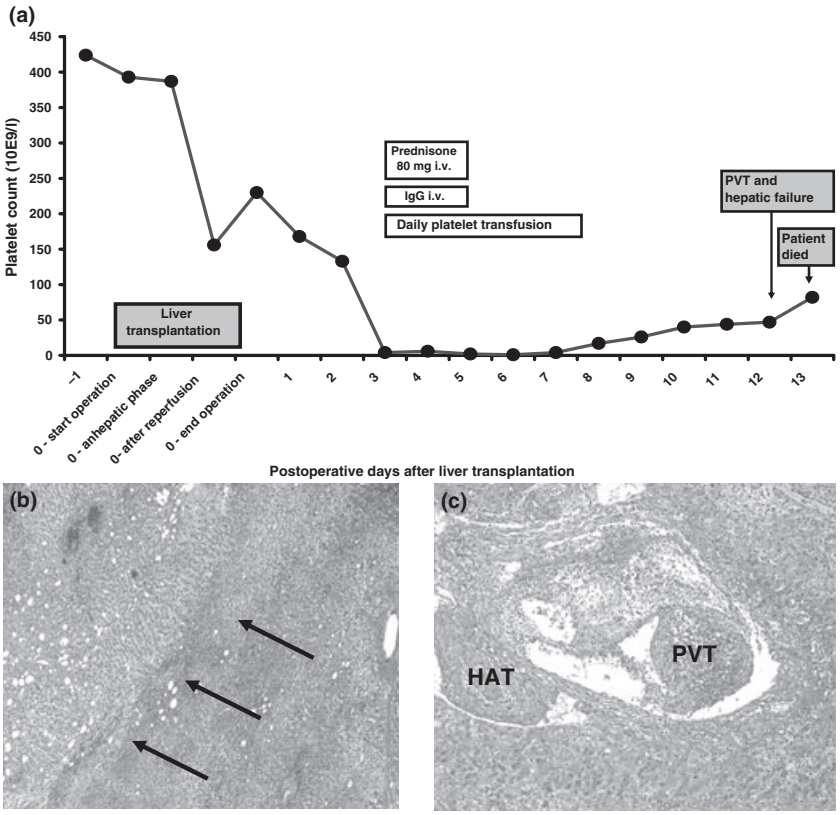

Figure 1 (a) Peri- and postoperative changes in platelet count in a patient who received a liver graft from a donor who died from massive intracranial hemorrhage because of idiopathic thrombocytopenic purpura (ITP). A sharp decrease in platelet count was observed on postoperative day 3. The platelet count remained extremely low despite treatment with high-dose prednisone, immunoglobulins, and daily platelet transfusion (one unit from five random donors per day). After a spontaneous recovery of the platelet count was noted, the patient died on postoperative day 13 because of acute portal vein thrombosis, resulting in graft failure with severe hemodynamic instability. (b) Histologic studies (hematoxylin/eosin staining) of the liver graft. Overview showing large areas of hepatocellular necrosis (arrows). (c) Histologic studies (hematoxylin/eosin staining) of the liver graft. Example of a portal area of the liver, showing occlusion of both arterial and portal branches. PVT, portal vein thrombosis; HAT, hepatic artery thrombosis.

thrombocytopenia in this patient. Potentially, cessation of thrombo-prophylaxis and administration of platelet concentrates and intravenous immunoglobulins have contributed to the development of the PVT.

To the best of our knowledge, this is only the fourth liver transplant recipient reported in whom the early postoperative course was complicated by severe, life-threatening thrombocytopenia because of the transmission of ITP. The first patient who developed a donor-derived ITP after liver transplantation was reported by Friend *et al.* [4]. Similar to our patient, this patient was treated with intravenous immunoglobulins and daily platelet transfusions, without any effect on platelet count. The same anti-platelet antibodies were detected in the serum of the donor and recipient. The second patient, reported by West *et al.* [5], developed ITP as a result of antibodies against platelets produced by passenger lymphocytes from a HPA-1a-mismatched donor. This thrombocytopenia was uneventful and resolved after a period of severe rejection of the liver graft. In addition to the liver transplant recipient, West *et al.* [5] also reported ITP in the two recipients of a kidney from the same donor. In these patients, the same antibodies against platelets were detected. We contacted the two centers in which the kidneys of our liver donor were transplanted and none of these two patients had developed ITP up to 6 months after kidney transplantation. The lack of response in the recipients of the kidneys from the same donor could be explained by the smaller amount of lymphoid tissue in kidneys compared with that in the liver [1–3]. The third patient, recently reported by Diaz *et al.* [6], developed transplantation-mediated alloimmune thrombocytopenia following liver transplantation using an allograft from a donor with ITP, which was resistant to medical and

surgical therapy, resulting in allograft failure caused by a massive subcapsular haematoma requiring re-transplantation.

In an era of donor organ shortage, it remains difficult to conclude that livers from donors with ITP should not be used for transplantation. We believe that our patient may have survived with a good functioning graft if his recovery had not been interrupted acutely by PVT. However, the evidence put forward in this case report corroborates previously published cases. Livers from donors who have died from ITP seem to be dangerous for the recipients, and therefore should not be used, even in an era of donor shortage. Although the condition is likely to be self-limiting (depending on the persistence of donor B- and T-cells), current evidence suggests that patients receiving such a donor liver would have difficulties in surviving the intervening period.

Ilona T. A. Pereboom,[1,2] Marieke T. de Boer,[1]
Elizabeth B. Haagsma,[3] Frans van der Heide,[3]
Leendert Porcelijn,[4] Ton Lisman[1,2]
and Robert J. Porte[1]
1 Department of Hepatobiliary Surgery and Liver Transplantation
2 Surgical Research Laboratory and
3 Department of Gastroenterology and Hepatology,
University Medical Center Groningen,
Groningen, the Netherlands
4 Depatment of Immunohematology
Diagnostic Services, Sanquin Diagnostic Services,
Amsterdam, the Netherlands
E-mail: i.t.a.pereboom@chir.umcg.nl

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