

Letters to the Editor

Severe thrombocytopenia in liver transplantation

Key words: Severe thrombocytopenia. Liver transplantation. Post-transfusion purpura.

Dear Editor,

Thrombocytopenia is a common disorder in the early postoperative period of liver transplantation (LT). It usually recovers when the liver function is restored (1). In the first two weeks after LT the incidence of thrombocytopenia is 22%. The nadir of the drop in the platelet count commonly occurs on posttransplant day 4 (2). However, severe thrombocytopenia with platelet count below 10.000/mm³ is anecdotal.

Some studies have showed that thrombocytopenia is correlated with poorer patient and graft survival (2).

Case report

We present the case of a liver transplant patient who developed a severe thrombocytopenia in the early post-transplant period.

The patient is a 64 year old woman diagnosed with HCV liver cirrhosis in 1988 with Child Class C and MELD score 19 at the time of the LT. The pre-LT ultrasound showed signs of cirrhosis, with partial thrombosis of the portal vein, splenomegaly and ascites. The platelet count was 90.000/mm³. The past medical history of the patient included type 2 diabetes mellitus, and hysterectomy with bilateral oophorectomy. This surgery took place 22 years earlier and required blood transfusion, which could have been the possible source of the HCV infection.

The donor was a 69 year old woman who died of a hemorrhagic stroke. Her past medical history included only arterial hypertension and two cesareans.

During the LT the patient required transfusion of 6 units of packed red blood cells, 2 units of fresh frozen plasma, 2 platelet pools and 3 g of fibrinogen. After the LT, immunosupresion with tacrolimus and corticosteroids was initiated, maintaining a good renal and liver function.

During the first five postoperative days (POD) the platelet count remained stable. On POD 6 the platelet count reduced to 2,000/mm³, with the lowest platelet count (nadir) of 1,000/mm³ on POD 8. Clinical examination revealed generalized skin hematomas and melena with anemia, which required red blood cells transfusion. She did not present infectious symptoms. She developed transfusion reaction after platelet transfusion that needed premedication prior to subsequent transfusions. The platelet count did not increase after multiple transfusions of platelet pools. On POD 8, we suspected immune etiology. Therefore we started treatment with high doses of immunoglobulins (0.4 g/kg/day) and corticosteroids, and ceased all medication associated with thrombocytopenia (tacrolimus, furosemide, and omeprazole). Abdominal ultrasound only showed known splenomegaly. Bone marrow aspiration showed a hypercellular bone marrow with trilinear hyperplasia with correct cell maturation. Indirect antiplatelet antibodies IgM and IgG were positive and antiHLA I-II were negative. The microsatellite study (STR) using DNA techniques (10 loci and 20 alleles analyzed) in peripheral blood from two post-transplant samples (on POD 7 and POD 60) from the recipient and one sample from the donor suggested the absence of chimerism. The HCV viral load was 11,000,000 UI/mL and the CMV viral load was undetectable in a CMV PCR test. On POD 14 the platelet count grew up to 12.000/mm³. At this moment the treatment with immunoglobulins was discontinued, the corticosteroid doses were reduced and the tacrolimus therapy was reinitiated. After this time, the platelet count grew up progressively.

Discussion

Mild to moderate thrombocytopenia in the early postLT is a common disorder. Many factors can contribute, such as reduced

Table I. Severe thrombocytopenia in the early postLT

Author (Ref. No)	Age(y)/Sex/ Liver disease	Cause of thrombocytopenia	Donor characteristics	Time to severe thrombo-cytopenia onset (POD)	Nadir platelet count	Antibodies	Treatment / Comments
West (5)	43/F/PBC	Alloimmune thrombocytopenia caused by antibodies produced by donor's B lymphocytes	Multiparous woman homozygous for HPA-1b	11	12.000/mm ³	AntiHPA-1a positive	Thrombocytopenia resolved after a severe episode of rejection, suggesting that the donor's B lymphocytes that were producing the antiplatelet antibodies were also rejected
Friend (6)	47/F/PBC	ITP transmitted by the donor	ITP refractory to multiple treatments. Donor death from ICH	2	2.000/ mm ³	IgG anticomplex GP IIb-IIIa positive	Thrombocytopenia resolved after a severe episode of rejection.
Díaz (7)	67/M/HCV	ITP transmitted by the donor	ITP refractory to multiple treatments. Donor death from ICH	1	6.000/ mm ³	IgG e IgM indirect antiplatelet negative	The most aggressive case. The platelet count only improved after liver retransplantation. The recipient expired from septic complications.
De la Torre (8)	52/M/HCV	ITP transmitted by the donor	ITP refractory to multiple treatments. Donor death from ICH	1	2.000/ mm ³	Direct antiplatelet positive	The best evolution case. The platelet count improved with high doses of immunoglobulins.
Takatsuki (9)	5/F/ biliary atresia	ITP transmitted by the donor	Healthy living donor (her mother)	1	18.000/mm ³	IgG antiplatelet positive	The platelet count improved with high doses of immunoglobulins She had already suffered of ITP pre-LT (suspected CMV induced)
Our case	64/F/HCV	Post-transfusion purpura	Multiparous woman. Arterial hypertension. Donor death from ICH	6	1.000/ mm ³	IgG e IgM antiplatelet positive	The platelet count improved with high doses of immunoglobulins In the absence of B cell chimerism we excluded the possibility of alloimmune thrombocytopenia transmitted by the donor

F: female. M: male. POD: postoperative day. PBC: primary biliary cirrhosis. HCV: hepatitis C virus. ITP: Idiopathic thrombocytopenic purpura. ICH: intracerebral hemorrhage.

hepatic thrombopoietin production, allograft sequestration, hypersplenism (1,3,4), hemorrhage, heparin-induced thrombocytopenia, immunologic reactions, hemolysis, drugs, infections, platelet consumption secondary to DIC and sepsis (3,4). However most of these factors are not usually the cause of severe thrombocytopenia.

Few cases of severe thrombocytopenia in the early postoperative period of LT have been described in the literature. These are cases of immune thrombocytopenias (Table I) (5-9).

In our case, we excluded the previously mentioned common causes of thrombocytopenia. In the absence of B cell chimerism and the absence of idiopathic thrombocytopenic purpura (ITP)

in the donor, since the patient was a multiparous woman who presumably has been sensitized during pregnancy, or after platelet transfusions, the temporal sequence of the development of thrombocytopenia and the presence of antiplatelet antibodies leads us to diagnose post-transfusion purpura.

Post-transfusion purpura is a rare bleeding disorder characterized by severe thrombocytopenia that usually occurs between the 5th and the 10th transfusion day. The majority of affected patients are multiparous women and politransfused patients. The pathogenesis remains unclear, although it is strongly associated with alloimmunization against platelet-specific antigens. The treatment of pos-transfusion purpura includes intravenous immunoglobulins, corticosteroids, and plasmapheresis (10).

In summary, severe thrombocytopenia is uncommon in liver transplantation recipients. When it occurs we should investigate the possibility that this is a case of immune thrombocytopenia related to post-transfusion purpura.

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