

## Letters to the Editor

### Graft versus host disease as a complication after liver transplantation: A rare but serious association

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*Key words: Graft versus host disease. Liver transplant.*

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*Dear Editor,*

The acute graft-versus-host disease (GVHD) after liver transplantation (LT) is a rare complication with a prevalence < 1%. There are multiple treatment options ranging from increasing doses of immunosuppressive drugs, the dose reduction or stopping, or the addition of new immunosuppressive drugs. However, the results are very poor, with high mortality rate (75-85%) (1-4).

#### Case report

A 68-year-old man underwent LT due to alcoholic cirrhosis with a 42 year-old ABO identical cadaveric donor. The postoperative period was uneventful with progressive normalization of liver function.

Six days later, he is readmitted presenting diarrhea (6-10 watery stools/day), renal failure, scaly and itchy rash on the trunk, arms and palms (Fig. 1), and fever (37.7 °C).

Laboratory tests were normal except for an increased serum creatinine (4.38 mg/dl). Blood and stool cultures were negative, as well as CMV antigenemia and C-reactive protein. Gastroscopy and colonoscopy showed mucosal ulcerations with irregular,

nodular and friable surface in duodenum, ileum and colon. Biopsies were reported as ulcerations with loss of surface epithelium,



Fig. 1. Typical erythematous-scaly itchy skin lesions located on the hand's palm.

crypt destruction and apoptosis appearance without the presence of viral inclusions, what was suggestive of GVHD. Biopsy of skin lesions showing vacuolar degeneration in the basal plane of cells with apoptotic dyskeratotic cells and infiltrating lymphocytes also corresponded to GVHD (Fig. 2).

With the diagnosis of GVHD grade III, we started steroid boluses getting an initial improvement, but when we started the descending pattern the patient's status deteriorated. As a second option we withdrew immunosuppression, though no response was obtained and ultimately we added basiliximab (two doses of 20 mg). The patient suffered progressive worsening, requiring admission to the ICU due to respiratory failure. He fatally evolved presenting severe thrombocytopenia (12,000 platelets), severe lower gastrointestinal bleeding and finally cytolysis (AST 400 U/L, ALT 200 U/L) and died on the 90<sup>th</sup> post-transplant day due to multiorgan failure.

Necropsy showed CMV infection affecting the liver, adrenal, gastrointestinal tract, lungs and kidneys, as well as esophageal herpes infection.

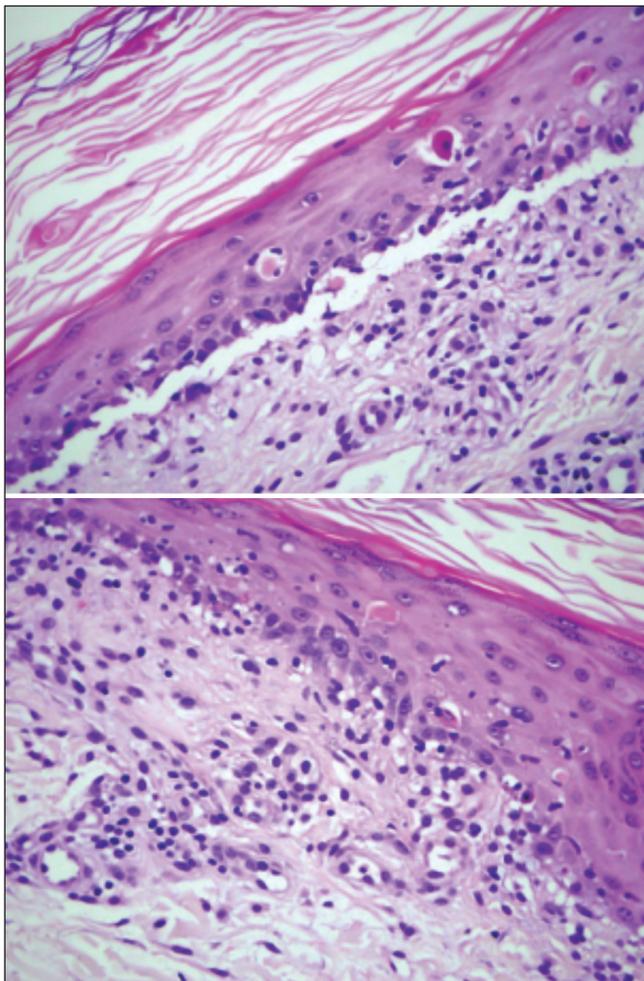


Fig. 2. Skin biopsy with the presence of mild hyperkeratosis with focal parakeratosis, vacuolar degeneration of basal layer separation grooves, apoptotic keratinocytes in the basal layer, exocytosis of lymphocytes.

## Discussion

GVHD after LT is a rare but serious complication, with high mortality rate (75-85%) (1-3). It is more common after bone marrow, intestinal or multivisceral transplantation. One feature of this entity after LT is that liver function tests remain normal, affecting gastrointestinal tract and skin, and the blood system in severe cases, what implies extremely poor prognosis. Its onset usually starts between 2-4 weeks after LT and typically after a normal initial post-transplant period as it occurred in our patient (3).

For early diagnosis it is important to have a high index of suspicion based on clinical signs: Diarrhea, fever, erythematous scaly and itchy skin lesions (characteristic at palmar hand's side). The diagnosis can be achieved with endoscopy and biopsy of the gastrointestinal tract and biopsy of skin lesions (3,4). Typical histological signs are ulcerations with loss of surface epithelium, crypt destruction and presence of apoptotic cells without viral inclusions in the gastrointestinal tract; and vacuolar degeneration in the basal lamina, dyskeratotic apoptotic cells and infiltration of lymphocytes in the skin (5). We can confirm the diagnosis with chimerism (presence of donor cells) in the blood of the recipient of more than 30% (6).

There is no consensus on HVGD treatment. Some authors proposed a reduction or even withdrawal of immunosuppression in order to restore the recipient's immune system to fight the immune attack of the donor (7). Some others immunosuppression increase with different patterns: increased basal immunosuppression, adding methyl-prednisolone boluses (2,4), or the use of antilymphocyte therapy such as anti-thymocyte globulin, anti-lymphocyte globulin, OKT3, daclizumab or basiliximab, guest cell infusion, rapamycin (3,8-13).

It is also very important the intensive care along with the association of broad-spectrum antibiotics, antifungal therapy and antiviral treatment to prevent the superimposed infection which is the main cause of death (1-4). However, the prognosis is very poor with a high mortality rate (> 75%) mainly due to viral infectious complications (CMV in our patient).

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