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Aplastic Anemia Post Liver Transplant Due to Graft-versus-host Disease

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Aplastic Anemia Post Liver Transplant Due to Graft-versus-host Disease

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ABSTRACT

INTRODUCTION:
The patient was a 64-year-old male presented with a 2 day history of increasing fevers and altered mental status. He underwent orthotopic liver transplant for cryptogenic cirrhosis, probably secondary to non-alcoholic steatohepatitis, 46 days before. The head and neck imaging showed negative changes. CBC at admission showed pancytopenia with WBC 6.8 x 10^9/L, hemoglobin 6.8 g/dL and platelet 29 x 10^9/L.

METHOD:
Bone marrow biopsy demonstrated marked hypocellular marrow. Bone marrow culture showed no acid fast bacteria or fungal growing. EBV in-situ hybridization, CMV immunohistochemical (IHC) stain, Grocott’s methenamine silver stain and Ziel-Neelsen stain on bone marrow were all negative. CD3 and CD20 IHC stains showed significant increase of T cell but no B cell in bone marrow. HLA typing test of the bone marrow showed significant increase of T cell but no B cell in bone marrow. HLA typing test of the bone marrow showed significant increase of T cell but no B cell. No third HLA typing present ruled out transfusion-associated GVHD. The biopsy of skin rash on left arm showed vacuolar interface dermatitis with associated GVHD. The biopsy of skin rash on left arm showed vacuolar interface dermatitis with associated GVHD.

CONCLUSION

The differential diagnosis of aplastic anemia post liver transplant include: anaplastic anemia associated with non-A, non-B, non-C fulminant hepatic failure, medication, viral infection including parvovirus B19, CMV and EBV, post transplant lymphoproliferative disease, GVHD and some other etiology such as iron deficiency, renal insufficiency, hypersplenism, hemolysis. The incidence of GVHD post liver transplant is ≤1% and the mortality is 75-90%. The presentation includes fever, skin rash, diarrhea and pancytopenia. The diagnosis is demonstration of chimerism with the presence of both donor and recipient lymphocytes in PB and BM. The treatment includes immunosuppression and bone marrow transplant, but is usually ineffective.

CLINICAL COURSE

The patient is a 64-year-old male presented with a 2 day history of increasing fevers and altered mental status. His past medical history includes orthotopic liver transplant for cryptogenic cirrhosis, probably secondary to non-alcoholic steatohepatitis, 46 days before. The clinical course was uneventful after the liver transplantation. He was found to be C. difficile positive and was put on appropriate antibiotics. He still spikes every night, up to 102 F; accompanied with tremors and decreased mental status. The head and neck imaging is negative. His liver function test is close to the normal range. CBC shows pancytopenia with WBC 6.8 x 10^9/L, Hb 6.8 g/dL, MCV 82 fL, reticulocytes 0.3%, reticulocytes absolute 6 x 10^9/L, and platelet 29 x 10^9/L.

Figure 1: Peripheral blood smear shows severe pancytopenia

Figure 2: Bone marrow aspirate and biopsy. Bone marrow aspirates and biopsies shown in A and C. Bone marrow biopsy (C. 200X magnification and D. 400X magnification) shows severe hypocellular (variable, 1-10% cellularity) bone marrow with trilineage maturation. Intraepidermal necrotic keratinocytes are close to the normal range. CBC shows pancytopenia with WBC 0.6 x 10^9/L, Hb 0.6 g/dl, MCV 82 fL, reticulocytes 0.3%, reticulocytes absolute 6 x 10^9/L, and platelet 29 x 10^9/L.

Figure 3: Immunochemical staining for CD3 (A) and CD20 (B) demonstrate increased T cells infiltrating the bone marrow.

Figure 4: Immunochemical staining for CD3 (A) and CD20 (B) demonstrate increased T cells infiltrating the bone marrow.

Figure 5: Bone marrow aspirate and biopsy. Bone marrow aspirate shown in A. Bone marrow aspirate (A. 200X magnification and B. 400X magnification) shows hypocellular specimen in bone marrow composed mostly by stromal cells. Bone marrow biopsy: C. 200X magnification and D. 400X magnification shows severe hypocellular (variable, 1-10% cellularity) bone marrow with trilineage maturation.

Patient’s buccal mucosa

Patient’s current Bone Marrow

Table 1: By PCR-sequence specific primer (SSP), HLA typing of transplant liver (donor), patient’s buccal mucosa and patient’s bone marrow are identified.

<table>
<thead>
<tr>
<th>HLA A</th>
<th>HLA B</th>
<th>HLA C</th>
<th>HLA DRB1</th>
<th>HLA DQB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>A02, A26</td>
<td>B58, B44</td>
<td>C07, C16</td>
<td>DR07, DR15</td>
<td>DQ02, DQ06</td>
</tr>
</tbody>
</table>

FINAL DIAGNOSIS

Liver transplant-associated GVHD

DIFFERENTIAL DIAGNOSES

- Transfusion-associated GVHD
- Viral infection (Parvovirus B19, CMV, EBV)
- Medications (Tacrolimus, cyclosporine A, Sirolimus, MMF, Azathioprine)
- Aplastic anemia (non-A, non-B, non-C fulminant hepatitis due to unknown viral infection)
- Hemolysis following ABO-incompatible liver transplant
- Hypersplenism
- PTLD: 2% of liver transplant; poor prognosis
- Renal insufficiency: drug effect, diabetes, HTN

RISK FACTORS FOR GVHD AFTER LIVER TRANSPLANTATION

- Close HLA matching as a significant risk factor for GVHD
- Multiple HLA class I mismatches protect against GVHD
- More frequent in older patients (age >45 years) with younger donors (age difference of >40 years)

TREATMENT OF GVHD

- Increased immunosuppression with high-dose steroids and antibody preparations such as antithymocyte globulin, antithymocyte globulin and Prednisolone.
- Broad antibiotic and antifungal prophylaxis
- Restoration of the host’s immune system.

REFERENCES