Passenger lymphocyte syndrome after minor ABO–incompatible stem cell transplantation: A case report

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INTRODUCTION

Passenger lymphocyte syndrome (PLS) is a complication of organ transplantation or stem cell transplantation in which donor B lymphocytes or plasma cells produce alloantibodies against recipient red blood cell (RBC) antigens, leading to the development of haemolytic anaemia. Although PLS is a self-limiting disease, it affects the success and survival rate of transplantation due to the occurrence of haemolytic disease, disseminated intravascular coagulation, and organ failure. Present studies have demonstrated that PLS occurs in individuals after liver, renal, or cardiac transplantation, but only a few studies reported that PLS occurs in individuals who undergo minor ABO-incompatible stem cell transplantation. In our study, serological ABO, Rh typing, and direct coombs test were used to identify a better strategy to administer blood transfusion in a patient with PLS.

CASE REPORT

A 14-year-old boy was diagnosed with type II mucopolysaccharidases and received stem cell transplantation. The patient’s blood type was A, of the CcDEe phenotype, and the donor’s blood type was O, of the CcDEe phenotype. The patient had intermittent fever, with the highest body temperature (38.2 °C) noted on day 5 after stem cell transplantation. On day 7, the occult blood test showed black-coloured stools (2+) and a rash was noted on the patient’s chest and back. Type O washed RBCs were given on day 6, and AB+ apheresis with radiation treatment was given on day 9. All whole blood specimens containing ethylene diamine tetraacetic acid (EDTA) were analyzed on day 6, 9, and 10.

Serological ABO forward typing (anti–A, anti–B, Immucor Inc., USA), ABO reverse typing (ABO typing cells, Shanghai Blood Tech, China) and a chloroform elution test was performed to analyze the patient’s red blood cells to identify the presence of anti–A or anti–B antibodies produced by donor lymphocytes, and the eluted solution was incubated with A cells, B cells, and screen cells. Capillary tube centrifugation was performed to separate the patient’s own aged RBCs at the end of the capillary tube and donor’s RBCs from the stem cells in the middle of the capillary tube.

After stem cell transplantation, anti–A alloantibodies were noted in the patient’s plasma, and the agglutinin titres became elevated within days (Table 1). On day 6, the haemoglobin level declined to 55 g/L, and the serological anti–A and anti–A1 typing showed mix-field appearance (before transfusion), as the specimen was mixed with the stem cells from the donor’s blood. The same results were observed on days 9 and 10 as the...
specimen was mixed with the donor’s RBCs. The blood sample on day 6 after capillary tube centrifugation demonstrated CcDee after Rh typing (Rh typing card, Jiangsu Libio Biotech CO. Ltd, China) of the patient’s own aged RBCs (from the end of the capillary tube) and CcDee after Rh typing of the donor’s RBCs from the donor’s stem cells (from the middle of the capillary tube). The results of the patient’s Rh typing on day 6, 9, and 10 are shown in Table 2.

### Table 2 Rh serological result in the patient

<table>
<thead>
<tr>
<th>Collected date</th>
<th>anti–A</th>
<th>anti–B</th>
<th>anti–H</th>
<th>anti–A1</th>
<th>A cell</th>
<th>B cell</th>
<th>O cell</th>
<th>Auto–control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 6</td>
<td>4+mf</td>
<td>Less free cells</td>
<td>0</td>
<td>W+</td>
<td>4+mf</td>
<td>Less free cells</td>
<td>0</td>
<td>3+</td>
</tr>
<tr>
<td>Day 9</td>
<td>4+mf</td>
<td>0</td>
<td>W+</td>
<td>4+mf</td>
<td>W+</td>
<td>4+</td>
<td>0</td>
<td>W+</td>
</tr>
<tr>
<td>Day 10</td>
<td>4+mf</td>
<td>0</td>
<td>W+</td>
<td>4+mf</td>
<td>1+s</td>
<td>4+</td>
<td>0</td>
<td>1+</td>
</tr>
</tbody>
</table>

mf: mix field, 0: negative, W+: weak positive.

dcp: double cell population.

All samples demonstrated negative results on antibody screening tests (Screen cells, Sanquin, Switzerland) and on the LISS–coomb test (Anti–IgG, C3d gel column test, BioRad, USA). However, reverse/forward typing showed an elevation in A-cell agglutinin levels on day 6. The results of the patient’s direct antiglobulin (coombs) test (DAT) and eluted test are shown in Table 3. Type O washed red blood cells were transfused after stem cell transplantation, and the haemoglobin level elevated to 73 g/L on the day 7 without transfusion reaction.

### DISCUSSION

PLS is a kind of post–transplantation hemolytic disease. Organ transplantations such as liver, renal and cardiac transplantation occur frequently in contrast to stem cell transplantation. PLS shows high association with B lymphocyte count from donors due to the antibody formation rate corresponding to B lymphocyte causing a higher immune response level.

Classifying PLS from hemolytic disease is a challenge. The first specimen in our study was from day 6, from which this retrospective and perspective investigation to confirm the PLS was conducted. Free RBCs from the mix field of serological forward anti–A, anti–A1, anti–c and anti–E tests elevated with date due to donor’s stem cell hemostasis RBCs and extra RBC products transfusion.

The features of PLS are: ① PLS occurs in various blood groups and occurs easily in ABO incompatible transplantations, especially in minor–incompatible. The case in our study is a blood type A recipient who received blood type O donor’s stem cells. Published studies have demonstrated the incidence of PLS to be 44% in recipients with blood type A and 18% in recipients with blood type B, which may be explained by the average of A antigens count being more than that of B antigens. ② In general, PLS presents from day 7 to day 14 post transplantation which relates to B lymphocyte physiology. The published study reported PLS in ABO over the course of 3 months in contrast to PLS in Rh for 1 year. ③ Clinical symptoms in PLS: hemoanemia, uremia and bilirubin. ④ The DAT for PLS reports a reaction to anti–IgG or anti–C3d or mixed anti–C3d and anti–IgG. The eluted solution from the case showed anti–A, B with anti–IgG agglutinin in DAT at day 6; and anti–A and anti–B, B with stronger both anti–C3d and anti–IgG agglutinin in DAT at day 9.

There is no precision therapy for PLS, and steroids are generally used to suppress the immune response to blood transfusion for oxygen metabolism support. Type O washed RBCs is preferable to instead of ABO–matched transplantation due to unexpected anti–A or anti–B. The case in our study was major incompatible with A washed RBCs and major compatible with O washed RBCs.

PLS is a temporary disease, showing a huge association with the recipient’s immune response and drug treatment. The symptoms release with the destruction of the donor’s lymphocyte. DAT is a sensitive and di-
rective tool to screen PLS and identify the level of seriousness for the clinical symptoms. Our study suggests DAT should be added in routine test for transplantation procedures to monitor the antibody sensitized RBCs before and after transplantation. Meanwhile, blood transfusion staffs are recommended to make important responses to the diagnosis of PLS by keeping up to date with progress relating to post transplantation PLS research and practices.

References


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Diagnosis of Hemolytic Disease of the Newborn

**ABO、Rh(D) Antigen Testing Card Newborn**

**Intended Use:**

The product is suitable for clinical tests on ABO and Rh (D) blood typing and direct antiglobulin test (DAT) for newborns and suspected hemolytic disease patients. It is only applicable for clinical test, but not for blood screening.

**Case:**

- **Pregnant woman with Blood Type O**
  - Few RBCs
  - Blood group antibodies
  - IgG anti-A

- **Placenta**
  - O × A

- **Fetus with Blood Type A**
  - Few RBCs
  - Binding to the surface of the RBC

**Hemolysis**