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A Strategy to Allow Red Blood Cell Transfusion in Major ABO-Mismatch Hemopoietic Stem Transplantation in a Patient with Multiple Anti-Erythrocyte Antibodies and Transfusion Block: A Case Report

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Abstract

ABO-mismatch between donor and recipient impacts on clinical outcomes, such as Red Blood Cell (RBC) requirements. Major mismatch is defined when the recipient carries antibodies against the donor erythrocyte antigens. Adverse effects associated with this type of ABO-mismatch are acute hemolysis and delayed erythroid engraftment. Herein, we describe the case of a patient (blood type O) with aplastic anemia and multiple acquired anti-erythrocyte antibodies who underwent HCST from a type A donor (major ABO-mismatch) in which we established a transplantation and chemotherapeutic strategy to promote a faster erythroid engraftment in order to reduce the need of RBC transfusion.

Keywords: Bone marrow transplant; ABO-mismatch; Pure red cell aplasia; Transfusion block

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Introduction

ABO-mismatch between donor and recipient is not considered a major barrier for Hematopoietic Progenitor Cell Transplantation (HPCT) [1]. However, it impacts on clinical outcomes, such as Red Blood Cell (RBC) requirements [2-4]. ABO-mismatch is present in approximately 40% to 50% of HPCT and is classified as major, minor or bidirectional [2,5]. Major mismatch is defined when the recipient carries antibodies against the donor erythrocyte antigens. Adverse effects associated with this type of ABO-mismatch are acute hemolysis and delayed erythroid engraftment [6]. Also, multi-transfused patients often develop anti-erythrocyte antibodies that, depending on their specificities, can difficult, or even impede, the finding of RBC units for transfusion. Herein, we describe the case of a patient (blood type O) with aplastic anemia and multiple acquired anti-erythrocyte antibodies who underwent HCST from a type A donor (major ABO-mismatch) in which we established a transplantation and chemotherapeutic strategy, such as the use hematopoietic progenitor cell from mobilized peripheral blood, to promote a faster erythroid engraftment in order to reduce the need of RBC transfusion.

Case Presentation

A 51-year-old woman was diagnosed with severe aplastic anemia (nine years before HPCT) [7]. During this period, she received regular RBC transfusion and immunosuppression (cyclosporine and rabbit anti-thymocyte globulin) with partial response in the beginning. During the follow-up, the patient was also diagnosed with Paroxysmal Nocturnal Hemoglobinuria (PNH) and was treated initially with Eculizumab and, afterwards, with Ravulizumab. In the last months, the disease relapsed (neutrophil <500/μL and platelets <20.000/μL). She proceeded to HPTC with an HLA-identical sibling donor. The conditioning regimen was FluCy+ATG+TBI [8].

The patient had alloantibodies including anti-K, anti-Cw anti-Dia, auto anti-E and auto anti-C. For adequate transfusional support until engraftment, type O RBC were selected. Additionally, type A and AB platelets were chosen to adsorb anti-A antibody. Another strategy to decrease the titers of anti-A and acquired anti-erythrocyte antibodies included plasma exchange (one plasma volume removed, replaced with 4% albumin solution) before the conditioning regimen (Day-7). Six days

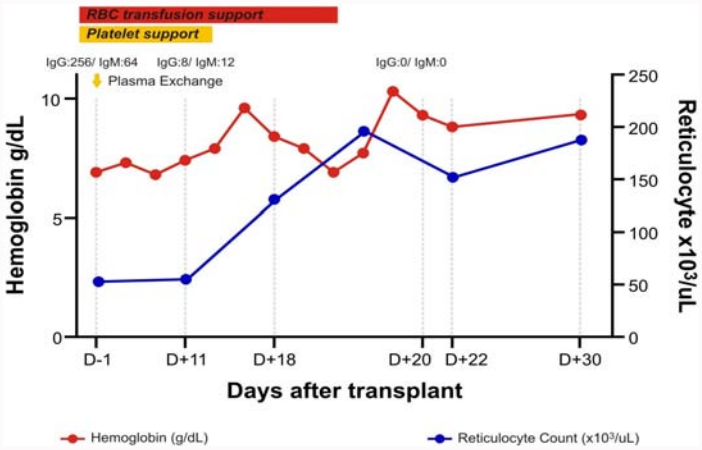

Figure 1: Hemoglobin (Hb) concentration along the transplantation period. The yellow arrow indicates the plasma exchange session on Day-7. IgG and IgM titers refer to antibodies against blood type A antigen.

later, a new antibody titration showed a reduction of anti-A IgG/IgM titer from 256/64 to 16/8 around Day 0 and to zero around Day 20 (Figure 1).

Discussion

Major ABO-mismatch is common in allogeneic hematopoietic progenitor cell transplantation, of which a possible complication, besides immediate hemolysis, is the Pure Red Cell Aplasia (PRCA), due to anti-donor erythrocyte antibodies [9]. PRCA is more often associated with anti-A isoagglutinin, probably because of the frequency of blood type A, which is higher than type B, and the fact that A-antigen expression and the anti-A antibody titers and affinity are higher compared with B antigen and anti-B antibody [9]. Furthermore, major ABO-mismatch transplantation requires more RBC transfusion than Isogroup transplantation, which was a concern in this specific case since the presence of various a variety of anti-erythrocyte antibodies (anti-A and others), which resulted in difficulty in finding compatible RBC.

In severe aplastic anemia, bone marrow is the preferred graft source for transplantation compared to mobilized peripheral blood stem cell because of the lower incidence of Graft-*vs*-Host Disease (GVHD) [10,11]. Nevertheless, the choice of PBSC as a source for transplantation was considered a better option, as it usually provides a faster engraftment, especially important in a case with transfusion block [11].

Another strategy to surpass transfusion block was the plasma exchange, which could provide a reduction of the titers of the anti-erythrocyte antibodies, associated with transfusion of blood type A plasma to adsorb anti-A antibodies, so further reducing its titers (Figure 1) [12-14].

Neutrophil engraftment occurred on day +22. On day +32, it was identified donor-derived RBC type A. The last platelets and RBC transfusion were performed on day +12 and day +18, respectively. This strategy resulted in a significant reduction of anti-erythrocyte antibodies, which allowed RBC transfusions (total of 9) during the aplastic period, with no evidence of hemolytic reaction. Despite the use of PBSC, the patient did not have GVHD.

Transfusion block associated with major ABO-mismatch can be overcome with strategies to reduce anti-erythrocyte antibodies, such as plasma exchange and antibody adsorption and defining the peripheral blood as the source of hematopoietic progenitor cells [12-15].

Major ABO-mismatch is associated with delayed RBC recovery [1,16], probably due to the antibody anti-A or B antigens, which results in increased need of RBC transfusion. Additionally, to PBSC, we performed plasma exchange to reduce the titers of anti-A and the titers of acquired anti-erythrocyte antibodies, allowing a safer and more efficacious RBC transfusion. Antibody adsorption by donor type is effective in preventing acute hemolysis due to major ABO-incompatibility. All these strategies allowed decreased red cell transfusion, and its complication, iron overload, transfusion reaction [12].

In conclusion, this case highlights the feasibility of the adoption of combined strategies to circumvent transfusion block due to anti-erythrocyte antibodies, such as the peripheral blood as the source of hematopoietic stem cells, plasma exchange and plasma type A transfusion, which resulted in robust engraftment (neutrophil on day 22), even if somewhat slower than expected, solved the transfusion block and avoided PRCA.

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