Case Report

Delayed hemolytic transfusion reaction with multiple alloantibody (Anti S, N, K) and a monospecific autoanti-JK^b in intermediate β-thalassemia patient in Tabriz

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Abstract:

It appears that delayed hemolytic transfusion reactions may occur several days after the administration of donor red cells is true even though they have been shown to be compatible in cross match tests by the antiglobulin technique. A specific case was observed in our center, which confirms the fact. The patient was a 37-year-old male suffering from intermediate β-thalassemia. He had a history of two previous transfusions, with unknown transfusion reaction. In the last transfusion, laboratory data showed: Hb 7.8 g/dL and Hematocrit (Hct) 24.2%. The patient received two units of cross matched, compatible concentrated red blood cells (RBCs). After eight days a severe reaction was observed with clinical evidence of tachycardia, fatigue, fever, back pain, chest discomfort, jaundice, nausea and anorexia. Accordingly delayed hemolytic transfusion reaction was suspected, and anti-RBC antibodies were tested. Laboratory tests revealed the presence of three alloantibodies: Anti-N, anti-S, anti-K, and a monospecific autoanti-JK^b.

Key words

Alloantibody, autoanti-JK^b, delayed hemolytic transfusion reaction, β-Thalassemia

Introduction

Delayed hemolytic transfusion reaction (DHTR) syndrome is presumed to occur after alloimmunization to red blood cells (RBC) antigen(s), and occurs within few days to two weeks after administration of donor red cells although they were shown to be compatible in cross match tests by the antiglobulin technique.[1-3] DHTR can be considered as one of the clinical features of hyperhemolysis (hemoglobinuria, jaundice, and pallor) combined with symptoms, which suggests severe vaso-occlusive crisis (pain, fever, and sometimes acute chest syndrome).[1,4]

The pathophysiology of the reaction has not been clarified yet, although, the number of cases with no detectable antibody were not infrequent. In 50% of cases the direct antiglobulin test (DAT) was positive and screening tests show auto- or alloantibodies.[1,4] The selection of blood type suitable for transfusion to such patients is complex. A male patient with DHTR, anti-JK^b autoantibody and anti-S, N, K alloantibodies are presented.

This is an interesting case as the anti-JK^b autoantibody were not the cause for anemia and three alloantibodies were detected, of which anti-S was involved in a delayed hemolytic reaction. We describe the treatments used and we suggest the management strategy for such patients.

Case Report

A 37-year-old male with intermediate β-thalassemia syndrome was admitted to Ghazi Tabatabai Hospital. The patient's blood type was O, Rh positive and his medical history included two previous transfusions. Throughout the past transfusions, not done in our center, he had unknown and unfamiliar transfusion reactions without any follow-up. At the time of admission to our center, laboratory data showed Hb 7.8 g/dl, RBC count 3.33×10^6/μL, White Blood Cell (WBC) count 4.33×10^3/μL, Hct 24.2% and serum Ferritin 840 ng/mL. The patient received two units of cross matched compatible and concentrated RBCs.

Eight days later a severe reaction was observed with clinical evidence which included tachycardia, fatigue, fever, back pain, chest discomfort, jaundice, nausea and anorexia. The patient was referred to an intensive care unit, and medication to modulate the immune system, including corticosteroid

(Prednisolone 2 mg/kg) and high dose immunoglobulin (IV Immunoglobulin, 0.4 g/kg/day, for 7 days) were initiated.

Laboratory data showed: Hb 4.8 g/dL, Hct 15.9%, Urea 40 mg/dL, creatinine 0.8 mg/mL; total billirubin 2.8 mg/dl, direct billirubin 0.5 mg/dl, and reticulocyte count 0.7%. He had a mild Hepatomegaly, and severe Splenomegaly (186 × 104 mm). DHTR was suspected. Coombs Test for antibodies against RBC Antibody Identification was performed. Laboratory tests showed the presence of three alloantibody: Anti-N, anti-S, anti-K, and a monospecific anti-JK^b autoantibody, which is a warm auto antibody with single specific in the serum of patient, due to an autoimmune process.

DAT was performed. Red cells from the EDTA tube were washed three times and a 3% cell suspension was made. A drop of cell suspension and the anti-Human Globulin (LORNE Laboratories Ltd, UK) was mixed in a tube and then centrifuged. The eluate was tested with panel cells by indirect antiglobulin test to know whether there were antibodies in patients' serum which react with RBCs *in vitro*. Anti-Human Globulin reagents (LORNE Laboratories LTD., UK) and commercial panel cells (Iranian Blood and Transfusion Organization, Iran) were used.

Seven days later, red cell units lacking anti-JK^b, N, K, and anti-S antigens were transfused. He had mild reaction to these red cells, like mild pain in the back, fever, and hemoglobinuria. Further, RBC transfusions were stopped and the patient's Hb stabilized at approximately 8 g/dL.

Discussion

Alloimmunization against red cell antigens is not a rare occurrence in multi-transfused patients. Moreover, in alloimmunized patients the probability of additional antibodies increases threefold.[2] The antibody produced by the primary immune response may be undetected, however, subsequent exposure to the same antigen usually leads to a secondary response in which the antibody level rises rapidly within 48-72 h after the transfusion and reaches a peak at 7-10 days.[3]

The antibodies like Immunoglobulin G (IgG) usually react with the transfused RBCs in the patient's circulation causing their destruction; an event known as a DHTR. Unfortunately there is no single test to diagnose DHTR and the DAT is often negative.[3,5] DHTR can occur even after transfusions that were cross-matched at least in the ABO, Rhesus (RH), and Kell antigen (KEL) systems, which gave a negative serological cross-match test; negative immunological tests do not exclude a DHTR.[1] *Talano et al*. identified seven pediatric patients who had Sickle Cell Disease and experienced a DHTR event 6-10 days after RBC transfusion. All the patients presented with fever and hemoglobinuria. Vaso-occlusive pain in back, abdomen, or legs was present in all but one patient, which is a common sign and complications of an ongoing hemolytic process, which were found in our patient too. These symptoms could be easily mistaken for a simple vaso-occlusive crisis. Therefore, the clinician must have an awareness of DHTR in patients who recently had blood transfusions.[3,5]

Blood transfusion is a standard therapy for severe anemia in patients with intermediate β-thalassemia syndrome. However, in this patient, only a minimal increase in hemoglobin occurred after transfusion of red cell which lacked anti-JK^b autoantibody and anti-S, N, K alloantibodies, probably from persistent red cell anti-S antibody-induced hemolysis.[6] Whole blood exchange transfusion can effectively, rapidly, and safely correct anemia in antibody-associated hemolysis and hyper volemia.[6,7]

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