CASE REPORT

Delayed Serological Transfusion Reaction After Platelet Transfusion Due to Anti-e

Deepti Sachan¹ · Aswin Kumar¹ · Dinesh Jothimani² · Mohamed Rela²

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Abstract Delayed serological transfusion reaction (DSTR) is defined as absence of clinical signs of hemolysis and demonstration of new, clinically-significant antibodies against red blood cells after a transfusion, by either positive direct antiglobulin test or positive antibody screen with newly identified RBC alloantibody. Various delayed hemolytic transfusion reaction cases are reported after red cell transfusions. However, the incidence of DSTR after platelet transfusion due to non-Rh(D) antibodies is not much documented. We report here a case of DSTR due to anti-e Rh antibody in a multiply red cell alloimmunized female patient after single donor platelets transfusion.

Keywords Delayed serological transfusion reaction · Rh alloimmunization · Anti-e · Red cell antibody

Introduction

Delayed hemolytic transfusion reaction (DHTR) occur in patients who have previously been immunized but in whom the antibody is not detectable during pretransfusion testing. Transfusion provides a secondary immunogenic stimulus that causes the antibody titer to rise. Destruction of sensitized donor red cells is usually gradual, with the clinical symptoms of hemolysis, including anemia, fever, and

jaundice, evident 5–10 days after transfusion [1]. A more appropriate term delayed serologic transfusion reactions (DSTRs) is used for cases with serologic findings consistent with DHTR but with no evidence of hemolysis.

Various DHTR cases are reported after red cell transfusions, mostly due to Kidd and Rh antibodies [2–4]. However, the incidence of DSTR after platelet transfusion is not much reported. We present here a case of delayed serological transfusion reaction due to anti-e Rh antibody in a patient after a single donor platelets (SDP) transfusion.

Case Report

A 64 years old female from Bahrain, a case of Hepatitis C related End stage liver disease was referred to our centre. She had history of multiple pregnancies, and history of many episodes of blood transfusions was present with last transfusion 1 year before. All transfusions were uneventful.

On admission for therapeutic paracentesis, her haemoglobin (Hb) was 8.3 g/dl, PCV—28 %, total count 2230/cmm, platelet—40,400/cmm, T. Bilirubin—1.06 mg/dl, direct bilirubin—0.12 mg/dl, INR—1.36. A request was received for single donor platelets. Her type and screen results showed blood group was A Rh(D) Positive. Indirect antiglobulin test was performed using commercially available 3-cell ID Diacell (DiaMed, Cressier sur Morat, Switzerland) which showed positive agglutination in P1 (3+), P2 (0), P3 (3+). Antibody identification was performed using 11 cell Panel (ID-Diapanel, Biorad) with showed 3+ reaction with P1,2,4,6 with Negative auto-control which were suggestive of anti-C and anti-K (Fig. 1a). Cold antibodies were not detected. Extended antigen phenotyping of patient was done using Rh + K phenotype cards (Biorad), and was found to be R2R2

✉ Deepti Sachan
deepti.vij@gmail.com

¹ Department of Transfusion Medicine, Global Health City, #439, Cheran Nagar, Perumbakkam, Chennai, Tamil Nadu 600100, India

² Institute of liver disease and transplantation, Global Health City, Chennai 600100, India

Fig. 1 a Antibody identification on admission (anti-C + K), b on 13 days post SDP transfusion showing additional anti-e antibody

(C-c+E+e-K-) phenotype. A Rh(D) positive SDP was issued and was transfused uneventfully and patient was discharged on same day.

Thirteen days later, another blood request was received for one unit of packed red cells. On blood grouping, ABO discrepancy was found with a 4+ reaction in Pooled A, B and O cells (Fig. 2). Antibody screening using 3 cell Panel (ID-Diapanel, Biorad), showed positive and antibody identification using 11 cell Panel (ID-Diapanel, Biorad), showed 4+ positive reaction against all panels except panel 3 suggestive of anti-e which was reactive at AHG phase (Fig. 1b). ON cold antibody detection, presence of IgM anti-e antibody was confirmed with negative autocontrol. Antibody titre was checked using conventional tube method using select cells and was 8128 and 64 for anti-e, C and K respectively. The anti-e was both IgG and IgM in nature and was reacting at 4 C causing ABO discrepancy.

As the patient did not receive any red cell transfusion during this period from our or any other hospital. A case of

Fig. 2 ABO discrepancy due anti-e (IgM) antibody

delayed serological transfusion reaction due to anti-e Rh antibody after SDP transfusion was suspected.

The transfused apheresis product was collected from collected by a Trima Accel cell separator (TerumoBCT, Lakewood, CO, USA), and the platelet donor was checked for Rh phenotype and was found to be R₁R₁ phenotype with e+ antigen. The routine quality control results showed presence of red cells in SDP products in acceptable range.

Discussion

International Society of Blood Transfusion (ISBT) working party on hemovigilance defines DSTR as absence of clinical signs of haemolysis and demonstration of new, clinically-significant antibodies against red blood cells, after a transfusion by either positive direct antiglobulin test (DAT) or positive antibody screen with newly identified RBC alloantibody. The reaction can be of definite imputability if new alloantibody is identified between 24 h and 28 days after cessation of transfusion and transfusion performed by your facility is the only possible cause for seroconversion [5, 6].

The overall risk estimates of DHTR in various studies vary from 0.007 to 0.6907 per 1000 red cell units transfused [7–9]. The data on overall incidence of DHTR vary in different studies because DHTR is difficult to diagnose and most often, it is asymptomatic or may even be similar to the clinical signs and symptoms of the patient so that it remains under-diagnosed and underreported. A number of factors which influence the incidence of DHTRs, includes the average length of stay for inpatients, the average number of RBC transfusions per inpatient, and the adoption of new antibody detection systems.

Ness et al. [10] reported the incidence of DSTRs associated with posttransfusion red cell sensitization 1 per 1605 units transfused (0.06 %) or 1 per 151 patients with post-transfusion samples available for testing. The true incidence of DSTR in multiply transfused patients would require a prospective study of all patients.

In this case, anti-e was detected 13 days after SDP transfusion in a previously alloimmunised female patient. The primary sensitization to Rhe antigen occurred probably during her pregnancies or transfusions given 1 year back which were not detectable during pretransfusion antibody screening. The only presumptive cause of this anamnestic response is history of transfusion of single donor platelets. This strongly suggests that trivial amounts of RBCs in platelet concentrates are able to trigger sensitization or secondary immune response to highly immunogenic Rh antigens and induce the formation of Rh antibodies. Our case had anti-e antibodies which were both IgG and IgM antibodies and were reactive at both AHG as well as saline

phase and causing ABO discrepancy. It was clear that DAT was negative as minimal e+ sensitised red cells in SDP were cleared by patient circulation rapidly.

It is reported that, in alloimmunized patients, the probability of additional antibody formation increases approximately threefold [11, 12]. This alerts us that the transfusion dependent patients with existing alloantibody are at risk of developing multiple alloantibodies in further course of time. Our case was also red cell alloimmunized with presence of anti-C and anti-K and 3rd red cell alloantibody anti-e was developed after platelet transfusion as DSTR.

Moncharmont et al. [13] showed that in French haemovigilance system 48 cases (1.3 % of adverse events) of RBC alloimmunisation after platelet transfusion were reported between 2007 and 2011 as delayed adverse reaction. Anti-E and anti-D were most frequently involved. Cid et al. [14] reported 78 cases of Red cell alloimmunization after platelet transfusion including 49 (4.8 %) anti-D and 29 (2.9 %) with other specificities in a study over 10 year period.

Several factors are involved in RBC alloimmunization after platelet transfusion: type of platelets, the volume of residual RBC in the PC, immune status of patients. Kitazawa et al. [15] showed that RBC derived microparticles can provoke non-D Rh antibody formation in spite of very low RBC contamination of Apheresis platelets as they are volumetrically comparable and can induce sufficient antibody stimulus. The authors estimated that platelets collected by apheresis had a residual RBC volume and RBC derived microparticle volume in range of 0.4–0.8 and 0.1–1 µl, respectively.

We suggest that Rh phenotyping and antibody screening to be performed in pre-transfusion screening for all blood components for timely detection of rare phenotype as well as minimizing the risk of haemolytic transfusion reaction by preventing sensitization. DSTR cases are benign compared to DHTR however; these patients are susceptible to severe reactions in the future, which would justify the documentation of these reactions and the notification of physicians and patients of their potential clinical significance.

Compliance with Ethical Standards

Conflict of interest None.

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained from patient included in the study.

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