Effect of cryoprecipitate transfusion without ABO group consideration: A nightmare experience

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Abstract:
The cryoprecipitate is an essential blood product as they are rich in factor VIII, fibrinogen, von Willebrand factor, factor XIII, and fibronecin, and their volume is too small. They play a significant role in the management of massive transfusion nowadays. Usually, they are used without ABO group consideration. We here report a case in which immunohematological problems arose due to out-of-group transfusion of cryoprecipitate. We suggest that the possibility of incompatibility subsequently is to be kept in mind during transfusion of large quantity cryoprecipitate, and ABO group compatible may be preferred.

Keywords:
ABO group, cryoprecipitate, immunohematological discrepancy, incompatibility

Introduction

Cryoprecipitate is precipitated proteins of fresh frozen plasma (FFP) which is rich in factor VIII and fibrinogen. They are obtained from a single unit of fresh plasma by rapid freezing within 6 h of collection.[1] Along with factor VIII and fibrinogen, they are rich in von Willebrand factor, factor XIII, and fibronecin. Cryoprecipitate was initially developed as a therapy for hemophilia “A” patients.[2] At present, these are commonly used in clinical setting with hemorrhage including cardiac surgery, trauma, liver transplantation, or obstetric hemorrhage. It is also used to replenish fibrinogen levels in patients with an acquired coagulopathy. Cryoprecipitate is a cornerstone of treatment for massive bleeding with chances of disseminated intravascular coagulation.

The American Association of Blood Banks (AABB)[3] and the Canadian Society for Transfusion Medicine (CSTM)[4] standards states that adult recipients can be transfused with any ABO group of cryoprecipitate. As per the joint UK blood transfusion and tissue transplantation services professional advisory committee guidelines, cryoprecipitate contains very little immunoglobulin, and hemolytic transfusion reaction has never been reported.[5] In India, cryoprecipitate is transfused across the ABO blood group.[6] In most of the centers across India, these are used irrespective of blood groups. We hereby report a case where 20 units of cryoprecipitate were transfused over 1 day without considering the ABO blood group, which led to hemolysis and immunohematological problems.

Case Report

A 27-year-old female presented to casualty with complaints of pain abdomen for 6 h, acute in onset, and diffuse in nature with passing of loose stools. She also had a history of fever, on and off type, for 1 month. Her pulse was 108/min at presentation, and her blood pressure was 96/62 mmHg with a saturation of 99% in room air. Her
abdominal examination showed diffuse tenderness. Ultrasonography done during admission showed free fluid predominantly in the pelvic area and gross moving echoes, which was suggestive of perforation peritonitis. Laboratory reports showed hemoglobin (Hb) – 8.2 g%, total leukocyte count – 11,200/μl, differential count – N90, L7, E1, M2, B0, with normal liver function test and renal function test. Her weight was 40 kg. The patient was taken up for surgery immediately, and ileocecal anastomosis was done. Blood was requested to our blood center. Pretransfusion workup revealed her blood group to be “B” positive with indirect Coombs test and direct Coombs test (DCT) being negative. Intraoperatively, the patient was transfused with two B-positive cross-match compatible packed red blood cells (PRBCs). Postoperatively, she was transfused with 2 units “B” positive PRBC and 4 units of “B” positive FFP. Further 10 units of cryoprecipitate were transfused in view of intraoperative bleeding and Hb of 6.6 gm/dl. The patient continued to have multiple episodes of fever and pain abdomen. She was again taken up for exploratory laparotomy after 3 days. Two units of PRBC, 4 units of FFP, and 10 units of cryoprecipitate were transfused again in the postoperative period. Due to severe anemia (Hb – 5.2), another PRBC was requested on postoperative day 4. This time, cross-match was incompatible [Figures 1-3] with all B-positive bags. Hence, immunohematology workup was initiated to resolve incompatible cross-match.

The following are the immunohematological findings [Table 1]:

i. Blood group: B positive with no grouping discrepancy
ii. Indirect Coombs Test (ICT): negative
iii. Direct Coombs Test (DCT): positive (3+)
iv. Autocontrol: positive (3+)
v. 3 cell panel and 11-cell antibody identification showed negative reactions with all the reagent cells
vi. Monospecific card testing showed: positive with immunoglobulin G and C3d
vii. Thermal amplitude: reactive at 37° Celsius and antihuman globulin phase.

Root cause analysis of the incompatibility was initiated. History was analyzed. Cross-matching was done further with more 6 units of “B” positive, but all came incompatible. Allantibodies were ruled out as there was no history of the previous transfusion, and all screening and identification panels were negative. Cross-match was repeated with “O” positive bags and was found to be compatible. All transfusions in the patient were analyzed. She was transfused with 20 units of cryoprecipitate without considering the ABO group. Out of these 20 units, 10 were “O” positive, 4 were A positive, and 6 were B positive. Each unit had a volume of around 15–20 ml. It was suspected that the anti-B of the above blood product was the culprit for immunohematological (IH) discrepancy and drop of Hb in the patient. Elution was performed on DCT positive cells. The eluate was tested with pooled A, B, and O cells and found reactive with B cells. It was proved that anti-B, which was present in cryoprecipitate, was the reason for IH discrepancies.
and contributed for a drop in Hb. The patient continued with transfusion of O-positive PRBC. After 5 days, DCT became negative, and cross-matches were compatible with B-positive PRBC units. This can be explained by the fact that the dissolved B antigen present in plasma in the patient had neutralized the anti-B antibodies. Further cryoprecipitate transfusions were group compatible. No further discrepancy was observed.

**Discussion**

Out-of-group transfusion is allowed for cryoprecipitate transfusions. Various reasons include (i) the presence of the insignificant amount of naturally occurring antibodies in the plasma suspended in cryoprecipitate (ii) dilution of antibody while pooling (iii) dilution of less amount of plasma transfused in the patient with a blood volume of 4–5 l adults. Various standards such as AABB[3] and CSTM[4] recommend transfusion of cryoprecipitates irrespective of ABO group consideration. Some studies have shown the safety of transfusion of cryoprecipitate without the need for blood group matching in adult recipients.[2] However, as per Australian Red Cross guidelines, “compatibility tests before transfusion are not necessary. Preferably, ABO compatible with the recipient’s red cells but ABO-incompatible cryoprecipitate can be used with caution, particularly with large volumes.”

In the present case, a large amount of cryoprecipitate was transfused (10 units twice, 24 h apart, approximate volume around 150–200 ml each time). When a large volume of cryoprecipitate is transfused, the amount of antibodies present in the plasma that is passively transfused also increases. Such excess amount of anti-B antibodies (passively transfused from Groups O and A cryoprecipitate) reacted with the B antigen present in the recipient’s red cells. This explains the DCT positivity in our patient posttransfusion. These antigen-antibody complexes thus activate complement and cause lysis of red cells. Drop in Hb after blood transfusions and incompatible cross-matches with B-positive PRBC can be explained by ABO-incompatible cryoprecipitate transfusion. There was no incompatibility with O-positive blood bag units because passively transfused anti-B antibodies did not react with O cells. This also explains why our three cells and 11 cells were negative. Hence, careful precaution is to be taken when more (>10 units) out-of-group cryoprecipitate are being transfused to the patient. Patients receiving a large volume of ABO-incompatible cryoprecipitate should be monitored for passive hemolysis by performing DCT. In these cases, strict vigilance may be done for any signs of hemolysis due to the naturally occurring antibodies in high-volume transfusions.

**Conclusion**

Cryoprecipitate which is usually transfused across the group may lead to hemolysis and immunohematological discrepancies when transfused in large volumes. The possibility of incompatibility subsequently is to be kept in mind when larger volumes of cryoprecipitate are transfused.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Saran RK. Transfusion Medicine: Technical Manual. New Delhi:
2. Hadjesfandiari N, Levin E, Serrano K, Yi QL, Devine DV. Risk analysis of transfusion of cryoprecipitate without consideration of ABO group. Transfusion 2021;61:29-34.

3. Shehata N, Delores Y. Hemotherapy Decisions and their outcomes. In: Cohn CS, Delaney M, Johnson ST, Katz LM, editors. AABB Technical Manual. 20th ed. Bethesda: American Association of Blood Banks;2020.

4. CSTM. Standards for Hospital Transfusion Services. Ver. 4. Markham, Canada: Canadian Society for Transfusion Medicine; 2017.

5. Norfolk D. Handbook of Transfusion Medicine, United Kingdom Blood Services. 5th ed. Norwich, UK: TSO Information and Publishing Solutions; 2015.

6. Blood Component Information: An Extension of Blood Component Labels. Australian Red Cross, Lifeblood; 2019. Available from: https://transfusion.com.au/BCL [Last accessed on 2021 Jul 08].