Case Report

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Masquerading of mismatched blood transfusion by underlying autoimmune hemolytic anemia

Priyanka Samal, Sarita Pradhan[1], Sudipta Sekhar Das[2]

Abstract:

Mismatched blood transfusion due to immunohematological discrepancy is relatively uncommon and in most instances occurs due to Type IV blood group discrepancy which is the discrepancies between forward and reverse groupings. Here, we present a case of a 15-year-old girl with preexisting autoimmune hemolytic anemia (AIHA) who inadvertently received 3 units of wrongly matched packed red blood cell (PRBC), followed by severe intravascular hemolysis. On detailed immunohematological investigation, the patient was found to be autoimmunized and diagnosed with "mixed AIHA" and the patient's blood group was confirmed as "A" positive. Three units of group-specific "best match" PRBC was transfused under close observation without any adverse effect. This highlights the importance of carrying out both forward and reverse blood groupings to avoid mismatched blood transfusion.

Keywords:

Mismatched blood transfusion, mixed autoimmune hemolytic anemia, life threatening complication

Introduction

Mismatched blood transfusion due to immunohematological discrepancy is an uncommon phenomenon. In most instances, ABO-incompatible transfusion occurs due to Type IV blood group discrepancy which is the discrepancies between forward and reverse groupings. It occurs mostly due to miscellaneous causes such as warm or cold autoantibodies, unexpected ABO isoagglutinins, unexpected alloantibodies, and polyagglutination. It is more commonly attributable to the autoantibodies in a case of autoimmune hemolytic anemia (AIHA).[1] Such mismatched transfusion may at times be fatal with incidences reported between 5.5% and 30%.[2] We report a case of mismatched blood transfusion in a young girl with underlying AIHA who survived intravascular hemolysis following three units of ABO-incompatible blood transfusion after appropriate resuscitation. Herein, we discuss the need of communication with blood bank personnel about underlying AIHA while performing blood grouping for transfusion and also stress upon the fact that a blood grouping is incomplete without performing the reverse (serum) grouping/typing of the blood.

Case Report

A 15-year-old girl (consented) presented in the emergency department with fever with chills, respiratory distress, and passage of coca-colored urine. The patient had a history of three units of "AB-" positive packed red blood cell (PRBC) transfusion at a local hospital. On evaluation, she had severe pallor and icterus and was hypotensive, dehydrated, restless, and dyspneic. Laboratory values revealed hemoglobin (Hb, 3.8 g%), reticulocytosis (12.7%), total serum bilirubin (s. bili, 12.2 mg/dL), serum LDH (sLDH, 2850 U/L). Peripheral blood

Department of Clinical Hematology, IMS and SUM Hospital, [1]Department of Pathology, Division of Hematology, IMS and SUM Hospital, Bhubaneswar, Odisha, [2]Department of Transfusion Medicine, Aapollo Gleneagles Hospital, Kolkata, West Bengal, India

Address for correspondence:
Dr. Sarita Pradhan, IMS and SUM Hospital, Bhubaneswar, Odisha, India.
E-mail: dr.sarita26@gmail.com

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smear shows marked agglutination of red cells. With existing *in vivo* hemolysis and severe anemia, requisition and blood samples were sent to blood bank for blood transfusion. Owing to incompatible crossmatches, detailed immunohematological investigation was performed in the blood bank [Table 1]. The patient was found to be autoimmunized and diagnosed with "mixed AIHA." In AIHA, the forward group discrepancy is caused by autoantibody-coated red cells which nonspecifically react with all monoclonal antisera used. In addition, the free autoantibody in the patient's serum is the cause of reverse group discrepancy where autoantibodies react nonspecifically with the reagent "A," "B," and "O" cells used for reverse grouping.[3,4] Based on this principle, the patient's red cells were subjected to cold acid elution, and serum was subjected to alloadsorption. The eluted red cells and adsorbed serum were then used for forward and reverse groupings, respectively, to solve the discrepancy. This confirmed the patient's blood group as "A" positive, and 3 units of group-specific "best match" PRBC was transfused under close observation without any adverse effect.

The patient was managed optimally by blood transfusion and steroids. Adequate diuresis was maintained for clearing the metabolites of mismatched transfusion. The patient improved clinically and symptomatically and maintained a Hb of 10.3 g% within 4 days of treatment. On the 5th day, she again became pale and Hb dropped to 5.2 g%. She received further 3 units of "best match" PRBC and rituximab in view of the high titer (1:1024) of cold agglutinin. There was no further fall in Hb, and laboratory values depicted a reduction in the *in vivo* hemolysis. At discharge, the patient was stable with Hb, s. bili, and sLDH of 12.5 g%, 2.1 mg/dL, and 750 U/L, respectively. She was advised to visit the hematology outdoor after a week.

Discussion

Determination of ABO blood group in AIHA is a frequent problem encountered by the blood bank personnel due to discrepancy between forward and reverse groupings. Zhu *et al*. performed ABO typing in 38 AIHA patients and found 11 cases (31.6%) showing ABO discrepancy, and all these patients were highly reactive for indirect agglutination test.[5] Garratty in 1993 described false-positive Rh typing results in AIHA when using reagents containing potentiators (e.g., albumin).[6] In the present case, the blood group was mistyped as "AB" positive probably due to nonspecific agglutination of the patient's red cells with the antisera used and failure to perform a reverse group and pretransfusion testing as per recommended protocol. This led to transfusion of "AB-" positive PRBCs in the "A-" positive patient.

Life-threatening complications of mismatched blood transfusion are rare but can occur.[2] Important factors that determine the severity of hemolytic reaction due to mismatched transfusion include blood volume, rate of infusion, patient age, comorbid conditions, isoagglutinin titer, and rapidity of initiation of appropriate treatment. Janatpour *et al*. observed severe signs and symptoms of transfusion reaction in patients receiving >50 mL of ABO-incompatible blood. They also discussed that deaths only occurred in patients who received >50 mL of incompatible blood although the finding was not statistically significant.[7] The patient survived the high-volume incompatible transfusions because of her young age, low isoagglutinin titer (anti-B titer: 1:32), the absence of comorbid conditions, and the rapidity of commencement of management.

Immunoglobulin M (IgM) antibodies have low-affinity interactions and less specificity compared to IgG antibodies. High concentration of free IgG autoantibodies in this patient, which have high affinity and multiple specificities to self-antigens, might have reduced the ABO antigen–antibody interaction leading to a less severe form of ABO-incompatible hemolytic transfusion reactions.[8]

The patient under study had a high titer of serum warm and cold autoantibodies reacting at wide thermal amplitude [Table 1]. These free autoantibodies interfered with the pretransfusion testing as well as activated the complement pathways strongly. Severe extravascular and intravascular hemolysis was caused by the significant red cell bound IgG and complements (C3d). No underlying alloantibody was detected using alloadsorption technique.[9]

Despite significant serological incompatibility, we transfused several units of PRBC based on the clinical condition. Das and Chaudhary discussed that no critical patient should be denied blood transfusion due

Table 1: Immunohematological details of the patient

Red cell study			Serum study					Crossmatch details		Transfusion details	
Blood group	DAT	Antibody type	Anti-B titer	IAT	Autoantibody titer	Autocontrol	Alloantibody	Units crossmatch	Best match units	Units transfused	Side effect
A+	4+	IgG + C3d	1:32	4+	Anti-IgG: 256 Anti-IgM: 1024	3+	ND	15	4	3	None

DAT=Direct antiglobulin test, IAT=Indirect agglutination test, IgG=Immunoglobulin, ND=Not detected

to serological incompatibility, and the patient may be transfused "best match" units after performing few important simple tests.[10]

Conclusion

A blood grouping is incomplete without performing the reverse (serum) grouping/typing. It is mandatory to perform reverse grouping using the known "A," "B," and "O" cells. The sensitized red cells and free autoantibodies in serum in a case of AIHA may cause blood group discrepancy (Type IV). In the index case, sensitized red cells were subjected to cold acid elution and serum subjected to alloadsorption. The eluted red cells and adsorbed serum were then used for forward and reverse groupings, respectively, to solve the discrepancy.

Declaration of patient consent

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

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Conflicts of interest

There are no conflicts of interest.

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