

Immune Hemolytic Anemia: A Report of Two Cases

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ABSTRACT

The transfusion-medicine specialists and physicians are often in a difficult situation when the patient has severe worsening anemia and all the blood is mismatched. This situation can arise in patients with red cell autoantibodies or alloantibodies due to previous transfusions. We report two cases of immune hemolysis – one due to warm auto antibodies and the second due to alloimmunization from multiple transfusions.

Keywords: Auto antibodies, hemolysis, alloimmunization, blood transfusion

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INTRODUCTION

Immune hemolysis is a shortening of red blood cell survival due, directly or indirectly to antibodies. These antibodies may be autoantibodies or alloantibodies. It is necessary to identify these atypical antibodies in the patient's serum in order to select appropriate blood for transfusion. Even in the most vexing situation encountered by a transfusion specialist where no compatible units are available for a patient with severe anemia, transfusion should not be denied. In such cases, transfusion requirement should be considered as a medical emergency even if serologic testing is incomplete.^[1]

CASE REPORT

Case 1

A 20-year-old female was referred to our hospital with complaints of icterus and breathlessness. She had similar complaints one year back and was treated for jaundice by a local physician. Prior to her referral, she had been transfused three units of AB positive blood over one week. On general physical examination, there was marked pallor, icterus, tachycardia and tachypnea. She had mild hepatosplenomegaly. Hematological investigations revealed severe anemia (Hb – 2.7 gm/dl). There was mild leucocytosis and blood film showed autoagglutination with the presence of nucleated red

cells (19/100 WBCs). Plasma and urine hemoglobin were raised. Liver function tests were deranged with indirect hyperbilirubinemia. Blood urea was also elevated (55 mg/dl). X-ray of the chest showed cardiomegaly. Patient had adequate urine output. The patient's sample was received in the blood bank for crossmatching. Cell and serum grouping showed a discrepancy with strong positive auto-control. Patient was typed as A Rh-positive with autoantibodies. Direct antiglobulin test with poly-specific Coomb's reagent (IgG + C3d) (Tulip diagnostics) was positive. Patient also had a positive antibody screen with all three reagent cells in the anti-human globulin test (Ortho cell panel, Ortho Diagnostics). Since the patient had life-threatening anemia with urgent requirement for transfusion, detailed phenotyping was not done and crossmatching was performed with several random A Rh-positive packed red cells but no compatible unit was detected. She received three 'least incompatible' A Rh-positive non-leuco reduced packed red cell units over three days as a life-saving measure after informed consent. No adverse events were reported during or after transfusion. Besides, she was also started on steroid therapy, antibiotics and diuretics. However, she developed sudden cardiorespiratory arrest on fifth day and could not be revived.

Case 2

A 57-year-old male presented with chest pain and breathlessness. The patient was a case of coronary

artery disease with off and on gastric bleed and a recipient of multiple transfusions in the past. Initial hemogram showed anemia (Hemoglobin 7.7 gm/dl). Peripheral blood smear showed dimorphic blood picture with moderate anisocytosis and poikilocytosis with mild hypochromia, microcytes, macro-ovalocytes and polychromasia. Reticulocyte count was 12%. Liver and renal function tests were normal. Blood group was O Rh-positive and two units of O Rh-positive packed cells were transfused. Since there was not much improvement in hemoglobin, another transfusion was requested but crossmatch was incompatible and antibody screen was positive. There was a difference in the strength of reaction at different phases and auto-control was negative. Direct Antiglobulin Test (DAT) was negative. Antibody identification studies suggested anti E, JKa and s as the implicating antibodies (Patient E-, JKa- and s-). Strong possibility of anti E was considered on 11 cell identification panel results. Meanwhile, patient improved clinically and was discharged at hemoglobin of 10.5 gm/dl with no further requirement for transfusion. Advice for future transfusions was given. Subsequently, he was readmitted with another bout of hematemesis and hemoglobin of 6.4 gm/dl. Patient received two transfusions by standard compatibility testing procedure since the blood bank was not informed about his previous immunohematological work up and hence a phenotypically matched blood was not given. However, there was a reaction with the first unit in the form of fever and mild jaundice (serum bilirubin 2.2 mg/dl), which recovered subsequently. Besides blood transfusion, the patient also received hematinics, antianginal drugs and diuretics.

DISCUSSION

Autoimmune hemolytic anemia is a fairly uncommon disorder with estimates of the incidence at 1–3 cases per 100 000 per year.^[2,3] In contrast, alloimmune hemolytic anemia requires exposure to allogeneic red cells through pregnancy, transfusion or transplantation. The incidence of acute hemolytic transfusion reactions has been estimated to be 0.003–0.008%, while 0.05–0.07% of transfused patients develop a clinically recognized delayed hemolytic transfusion reaction.^[4-6] Delayed serologic transfusion reactions are more common and are a frequent finding in patients who receive multiple transfusions.^[7]

Warm autoantibodies are responsible for 48–70% of autoimmune hemolytic anemia cases.^[8,9] Positive direct antiglobulin test may be the first serological evidence. Anemia is of variable severity and some patients present with fulminant hemolysis, jaundice, pallor, hemoglobinuria

and hepatosplenomegaly.^[10] In the first case, the patient was erroneously grouped and transfused AB positive blood before referral to our center. She presented with severe life-threatening anemia, jaundice, mild hepatosplenomegaly and evidence of hemolysis. The direct and indirect antiglobulin tests were positive. Initial antibody screen and auto-control was also strongly positive. Approximately 57% of patients with warm autoimmune hemolytic anemia have free serum autoantibody and a positive indirect antiglobulin test.^[11] Due to pan agglutinin in the serum of patients with autoimmune hemolytic anemia, crossmatching blood is a difficult and time-consuming process since the pan agglutinin reacts with all donors' red blood cells. Moreover, the most pressing problem is detection and identification of RBC alloantibodies that may be masked by the autoantibodies.^[12] In our patient, the anemia was life threatening with time constraints to perform adsorption studies with subsequent identification of underlying alloantibodies.

Even after thorough serological evaluation, the optimal blood for transfusion is still likely to be mismatched. Clinical reluctance to administer transfusions to such patients due to serological mismatch or an incomplete workup can have devastating consequences. Factors such as rate of onset of hemolysis and anemia, presence or absence of accompanying hypovolemia and the underlying health status and cardiorespiratory reserve must be taken into account to determine the transfusion trigger.^[12] Our patient had received 'least incompatible' transfusions due to severe anemia with imminent clinical deterioration. When a decision to transfuse mismatched blood is taken, transfusion of small aliquots to provide relief of symptoms and avoid fluid overload has been recommended.^[12] It has also been recommended to transfuse using leucocyte-reduced blood products and pre-medication with antihistaminics and antipyretics to prevent febrile and allergic reactions, respectively, in patients with multiple antibodies.^[13] Provision of prophylactic antigen-matched donor blood where feasible has also been advocated.^[14]

The second patient was a recipient of multiple transfusions with difficulty in finding a compatible unit. Antibody screen was positive with difference in the strength of reaction in immediate spin, 37°C, and in the antihuman globulin phase. The patient had multiple alloantibodies, which did not cause any clinical evidence of delayed hemolytic transfusion reaction except mild subclinical jaundice. However, in spite of repeated transfusions, there was not much improvement in the hemoglobin. The reason could be that the antibody titer was low initially but subsequent to transfusion, an anamnestic response led to rise in antibody titer and hence subsequent crossmatching did not give a compatible unit.

When the patient's sample was received in the first instance, crossmatch was compatible. Antibody screening was done with a subsequent request for blood when crossmatching yielded incompatibility. The incidence of alloimmunization in random multi-transfused patients has been reported to be 0–34%.^[15-19] It is more in transfusion-dependent patients, such as those with sickle cell disease, aplastic anemia, myelodysplastic syndrome and other congenital or acquired anemia.^[20] In a prospective study on the incidence of red cell alloimmunization following transfusion, 8.4% of patients developed antibodies within 24 weeks of transfusion.^[21]

However, all alloantibodies are not clinically significant.^[22] Takeuchi and coworkers^[23] have reported a delayed hemolytic transfusion reaction due to anti E, anti C and anti JKa that are clinically significant antibodies. Such patients present a challenge for elective transfusions particularly if multiple clinically significant alloantibodies are present. If such a situation arises, transfusion should be withheld until suitable antigen-negative donor units are located. Patients with multiple alloantibodies should receive phenotypically matched red blood cells to avoid transfusion reaction and they should be given a card indicating the antibody specificities so that he can receive antigen negative blood.

In either case, a good communication must be established between the clinician and the transfusion specialist to assess the clinical urgency and the complexity of serological studies. The final decision to transfuse should depend on the evaluation of the patient's clinical status and the benefits must be weighed to the potential risks of transfusion.

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