Sickle Hyper-hemolytic Transfusion Reaction Syndrome

Neha Hurkat

Assistant Professor, Department of Transfusion Medicine, Prathima Institute of Medical Sciences, Karimnagar,Telangana,India.

Address for correspondence: Dr.Neha Hurkat, Assistant professor, Department of Transfusion Medicine, Prathima Institute of Medical Sciences, Karimnagar,Telangana,India.

Email: nehahurkat@gmail.com

ABSTRACT

A 17-year-old female with sickle cell disease (SCD) presented with vasoocclusive crisis and jaundice, she received conventional treatment and one unit of compatible PRBC after a negative antibody screen was documented. After 48hrs of receiving a blood transfusion, her clinical picture was consistent with hemolysis. Immunohematology workup demonstrated evidence of a new antibody i.e anti-E. Delayed hemolytic transfusion reaction (DHTR) is a well-known complication of RBC transfusion. As her hemoglobin was declining , she was transfused with E antigen negative PRBCs. Despite this, hemolysis was ongoing and accelerated. Thus she was treated with steroids for presumed hyperhemolysis. Clinicians should have a high index of suspicion for hyperhemolysis in sickle cell patients with evidence of hemolysis after a recent transfusion. Differentiating hyperhemolysis from other hemolytic syndromes in SCD patient is critical; transfusions in a hyperhemolytic episode can accelerate hemolysis causing life-threatening anemia.

Keywords: Delayed hemolytic transfusion reaction , hyperhemolysis , Antibody screening, red blood cell, Hemoglobin.

INTRODUCTION

Sickle cell disease (SCD) is characterized by chronic hemolysis and intermittent vaso-occlusion, leading to tissue hypoxia and organ dysfunction.

Although red cell transfusions are not usually required in steady-state patients, they remain a mainstay therapy for many complications such as severe anemia, acute chest syndrome, stroke and splenic sequestration.

Allo-immunization, hemolytic transfusion reaction and iron overload are the distinct adverse effects of red cell transfusions in patients with SCD. Delayed hemolytic transfusion reaction (DHTR) is a classic complication in patients with SCD who undergo frequent blood transfusions, and this condition may lead to hyperhemolysis syndrome (HS).

In this article we report a case of delayed hemolytic transfusion reaction in a SCD patient with resultant hyperhemolysis syndrome. This case highlights it as an uncommon but potentially life-threatening complication. Therefore, it is important to understand the aim of transfusion therapy and to be aware of the potential side-effects.

CASE REPORT

A 17 yr old female with sickle cell disease was admitted with presenting complaints of chest pain, back pain, joint pains and jaundice.

On Day 1 of admission, her laboratory parameters tabulated in table 1.

Table 1. Day 1 laboratory parameters

Hemoglobin	7.3 g/dl
WBC	19,200 cells/cumm
Platelet count	2.5 lakhs/cumm
Retic count	4.5%
Total Bilirubin	10.2mg/dl
Unconjugated Bilirubin	7 mg/dL
HbS level	76.3%
DAT	Negative
IAT	Negative

On pretransfusion testing, her direct antiglobulin test (DAT) and indirect antiglobulin test (IAT) for antibody screening were negative. She was treated with intravenous fluids, analgesia, antibiotics and received one unit of coombs crossmatch compatible packed RBCs with no complications during the transfusion.

On Day 3, her Hb dropped to 5.7 g/dl, bilirubin raised to 19.8mg/dl (unconjugated 17.8 mg/dL), LDH 2098 U/L, no hemoglobinuria or dark colored urine. Suspecting a delayed hemolytic transfusion reaction, immunohematological work up was done. DAT was negative but IAT (antibody screening) turned to be positive. New antibody detected was "anti-E" on post transfusion sample.

Table 2. Day 3 laboratory parameters after one unit of crossmatch compatible transfusion.

Hemoglobin	5.7g/dl
Total Bilirubin	19.8mg/dl
Unconjugated Bilirubin	17.8mg/dl
LDH	2098 U/L
DAT	Negative
IAT (antibody screening)	Positive
Antibody detected	Anti-E

In view of severity of symptoms and anemia, decision was made to transfuse two units of E- antigen negative cross match compatible unit along with intensive care support.

Hb improved from 5.7 to 9.2 g/dL after the transfusion of two units of E-antigen negative PRBC.

On Day 10, her Hb levels dropped even further reaching to 4.7g/dl , hct-12.8%, WBC – 4000 cells/cumm, platelet count 1.2 lakhs/cumm , reticulocyte count of 8.5%, LDH- 3126 U/L. Considering the hypothesis of hyperhemolytic syndrome as patient's Hb continued to drop despite E-antigen negative cross match compatible blood transfusion, prednisolone 40 mg/ day was started and further transfusions were restricted to avoid life threatening complication.

The patient improved over the next few days and was discharged on Hb- 7.7, Hct-22.8, platelet count 2.5 lakhs/cumm, LDH of 568 U/L, bilirubin level of 4.8 mg/dl.

On follow up after one and two weeks, patient was stable with no fall in Hemoglobin and hemolytic indices normalized over time.

DISCUSSION

RBC transfusion is a cornerstone of therapy for SCD. However, one of the major complications of transfusion is alloimmunization in the recipient to antigens present in the transfused blood[1].

Among SCD patients transfused with RBCs matched only for ABO and D antigens, the rate of alloimmunization to non-ABO RBC antigens is much higher than for other transfused patient populations, ranging from 18 to 36%.[2,3]

The most life-threatening consequence of alloimmunization in SCD is the development of DHTR with hyperhemolysis. HS is mainly caused by destruction of both donor and recipient RBCs. HS is characterized by severe anemia, with Hb lower than pre-transfusional levels, pain, fever and signs of hemolysis This type of hemolytic reaction is unpredictable and potentially under-recognized because its clinical presentation may resemble a Vasoocclusive crisis (VOC) or other complications of SCD itself [4,5].

The patient described here also presented with symptoms like VOC and developed DHTR after receiving one unit of crossmatch compatible PRBC. In this patient pretransfusion antibody screening was negative. However in post transfusion sample new antibody was detected i.e anti-E.

As this patient had received more than 10 transfusions, she had a high risk of developing alloantibodies. Over time, 30 to 40% of alloantibodies decrease in titer and become undetectable by routine pre-transfusion serological tests[6,7]. Once those antibodies are not detected, ABO/Rh compatible units seem to be phenotypically compatible and are released for transfusion. However, subsequent re-exposure to the antigens that triggered the antibody production stimulates an anamnestic response leading to hemolysis[8,9].

Generally, the antibody is detectable 2 to 14 days after the patient is re-exposed to the antigen. Blood group antibodies in the Rh, Kell, Kidd and Duffy systems are notorious for exhibiting this behavior. The rapidity of antibody development and characteristics of the antibody specificity influence the potential for red cell destruction. For most delayed hemolytic transfusion reactions, red cell destruction occurs through extravascular hemolysis when sensitized RBCs are removed from the circulation by the reticuloendothelial system (RES)[7,10] .

In view of severity of symptoms and anemia in this patient, decision was made to transfuse E antigen negative PRBC unit. This patient's Hb continued to drop despite E-antigen negative blood transfusion. If E antigen incompatibility would have been the only cause of hemolysis, then her Hb should have remained stable at that time. The fact that the patient continued to hemolyze RBCs even with E-negative blood transfusion raised the possibility of hyperhemolytic syndrome, when not only transfused but host's own RBCs are attacked by the host's immune system. Both the times her Hb after transfusion was lower than pre-transfusion level. Continuing to transfuse in the face of falling hemoglobin during an immune-mediated hyperhemolytic transfusion reaction can exacerbate the hemolysis leading to life-threatening anemia.

Steroid therapy was started in our patient as soon as the diagnosis of hyperhemolysis after transfusion was made. The patient did not require transfusions on prednisolone therapy, and her Hb improved, this suggests that the production of the offending anti-E antibody by the immune system was effectively shut down, and no further hemolysis of the patient's native RBCs occurred without further PRBC transfusion needed.

The pathophysiology of this phenomenon is poorly understood. The possible mechanisms include "bystander hemolysis" whereby sickled RBCs are destroyed by antibodies without expressing the specific antigen against which this antibody is directed, suppression of erythropoiesis and RBC's being destroyed by activated macrophages[9] .

Management of HS depends upon the severity of anemia and the speed of hemolysis. In the mild form, additional transfusion should be avoided, and oral prednisolone (1–2 mg/kg/day) should be tried and the Hb level monitored closely. If presenting with rapid severe hemolysis, the patient may require transfusion. As additional transfusion may exacerbate hemolysis, IVIG–steroid cover should be given at the same time[11,12].

Our patient responded well to 4 weeks of steroid therapy which was slowly tapered over a period of further 4 weeks. On regular follow up she was found to be stable with normal hemolytic indices.

The presence of this syndrome should be recognized promptly to allow for abrupt cessation of exacerbating transfusions and to commence steroids and IVIG administration for quicker resolution.

CONCLUSION

Awareness and recognition of HS is important. Further transfusion may exacerbate ongoing hemolysis, worsen the degree of anemia and lead to a protracted course or even death. Early diagnosis is crucial to prevent this life-threatening complication. Special attention should be given to those patients who are submitted to multiple transfusions during their lives as they are at high risk for DHTR and hyperhemolytic syndrome.

REFERENCES

1. Rosse WF, Gallagher D, Kinney T, Castro O, Dosik H, Moohr J, Wang W, Levy PS. Transfusions and alloimmunization in sickle cell disease. The cooperative study of sickle cell disease. Blood 1990 Oct 1;76(7):1431–7.
2. Castro O, Sandler SG, Houston-Yu P, Rana S. Predicting the effect of transfusion only phenotype-matched RBCs to patients with SCD; theoretical and practical implications. Transfusion 2002;42:684–690.
3. Aygun B, Padmanabhan S, Paley C, Chandrasekaran V. Clinical significance of RBC alloantibodies and autoantibodies in sickle cell patients who received transfusions. Transfusion 2002;42:37–43.
4. Fabron A, Jr, Moreira G, Jr, Bordin JO. Delayed hemolytic transfusion reaction presenting as a painful crisis in a patient with sickle cell anemia. Sao Paulo Med J 1999;117(1):38–39.
5. Kalyanaraman M, Heidemann SM, Sarnaik AP, Meert KL, Sarnaik SA. Anti-s antibody-associated delayed hemolytic transfusion reaction in patients with sickle cell anemia. J Pediatr Hematol Oncol 1999;21(1):70–73.
6. Talano JA, Hillery CA, Gottschall JL, et al. Delayed hemolytic transfusion reaction/hyperhemolysis syndrome in children with sickle cell disease. Pediatrics 2003; 111 (6 Pt 1): e661-e665.
7. Garratty G. Severe reactions associated with transfusion of patients with sickle cell disease. Transfusion 1997; 37: 357–61.
8. Petz LD, Calhoun L, Shulman IA, Johnson C, Herron RM. The sickle cell hemolytic transfusion reaction syndrome. Transfusion 1997;37(4):382-392.
9. Win N. Hyperhemolysis syndrome in sickle cell disease. Expert Rev Hematol 2009;2(2):111–115.
10. Cox J, Steane E, Cunningham G, Frenkle E. Risk of alloimmunization and delayed hemolytic transfusion reactions in patients with sickle cell disease. Arch Intern Med 1988;148:2485–2489.
11. Win N., Yeghen T., Needs M., Chen F.E., Okpala I. Use of intravenous immunoglobulin and intravenous methylprednisolone in hyperhaemolysis syndrome in sickle cell disease. Hematology 2004;9(5/6):433–436.
12. Win N., Doughty H., Telfer P., Wild B.J., Pearson T.C. Hyperhemolytic transfusion reaction in sickle cell disease. Transfusion 2001;41(3):323–328.

How to cite this article : Neha H. Sickle Hyper-hemolytic Transfusion Reaction Syndrome. Perspectives in Medical Research 2018; 6(3):87-89.

Sources of Support: Nil,Conflict of interest:None declared