Case Report

Hemoglobinuria in a child with Sickle/β-Thalassemia trait

Srinivasan Thiagarajan[1], Delhi kumar CG[1], Ashritha Avalareddy[1]

Author's Affiliation:
1- Department of Pediatrics,Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India.

Correspondence:
Dr. Delhi Kumar CG, Assistant professor, Department of Pediatrics, JIPMER, Puducherry-605006, India. Email:dillikumar14@gmail.com

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Abstract:

A 7 year old male child who is a known case of sickle β-thalassemia presented with hemoglobinuria following packed red blood cell transfusion one week prior to the clinical presentation.He was diagnosed as a case of delayed haemolytic transfusion reaction(DHTR) which is extremely rare. The child responded to intravenous immunoglobin and steroid therapy. Early recognition is of paramount importance as transfusions would only further aggravate allo-antibody mediated hemolysis and this crisis is mitigated only by early institution of immunosuppressive therapy.

Key words: Hemoglobinuria, Sickle β-Thalassemia, Delayed haemolytic transfusion reaction.

Introduction

Sickle beta thalassemia is agenetically inherited autosomal recessive compound heterozygous hemoglobinopathy. Commonacute complications of sickle cell disease includevaso-occlusive crises like dactylitis, acute chest syndrome, splenicsequestration, osteonecrosis etc[1].Hemoglobinuria due to intravascular hemolysis is a rare phenomenon in sickle β-thalassemia [2].Here, we report a 7 year old male child who is a known case of sickle β-thalassemia presented with hemoglobinuria.

Casereport:

A 7 year old male child known case of sickle β-thalassemia presented with complaints of fever for 3 days associated with leg pain. The diagnosis was made 3 years earlier by electrophoresis (HbS-71 %, HbF-23%, HbA-1.8%,HbA_2-2.6%) and the child required only 2 transfusions after the diagnosis. First transfusion was given one year before and the second transfusion was one week prior to the presentation. On the first day of hospital stay child started passing blackish urine with concurrent progressive pallor. General examination revealed pallor and icterus. Spleen was palpable10 cm below left costal margin and no hepatomegaly. Hydrogen peroxide test for haemoglobin in urine was positive. However, urine microscopy showed no red blood corpuscles. Hence, intravascular haemolysis was considered. The baseline investigations are given in table no.1.In view of pyrexia(100.2 degree F), ceftriaxone was started. Due to on-going haemolysis and progressive pallor (haemoglobin dropped to 5.0 gm/dl from admission haemoglobin of 7.8gm/dl), packed red blood cell transfusion was given and child was started on 1.5 times maintenance intravenous fluids for renal protection in view of acute kidney injury secondary to hemoglobinuria (urea-71, creatinine-1.03). Peripheral smear showed no malarial parasite and immunochromatography for malaria was negative. Indirect and direct coomb's tests were negative. A total of three packed cell transfusions were given due to progressive hemolysisas evidenced by

increasing hemoglobinuria and worsening anemia. Hence, the possibility of delayed haemolytic transfusion reaction (DHTR) was considered. Therefore, further transfusions were withheld and the child was given intravenous immunoglobulin at 1gm/kg and pulses of methyl prednisolone 30mg/kg for three days. Following immunosuppressive therapy, hemoglobinuria resolved gradually over the next two days, and renal function tests normalized(urea-18mg/dl, creatinine-0.6mg/dl).The mildthrombocytopenia ($121x10^6$/L) noticed during hemolysis also resolved ($262x10^6$/L) after treatment. As the hemolysis resolved, his haematocrit stabilized and the patient was discharged.

Table 1. Baseline investigations

Investigation	Value
Hemoglobin	7.8 g/dl
Total count	5.48 x109/L
Differential count	Neutrophils 58% Lymphocytes35% Monocytes 7%
Platelet count	121 x109/ L
Corrected Reticulocyte count	1.3 %
Peripheral Smear	Normocytic normochromic RBCS Occasional sickle cells Few polychromatophils Slightly reduced platelets
LDH	5199 iu/dl
Total Bilirubin	7.3 mg/dl
Direct Bilirubin	1.3 mg/dl
Ferritin	307.8 ng/ml
Urea	71 mg/dl
Creatinine	1.03 mg/dl
Sodium	132 meq/L
Potassium	4.12 meq/L
Urine Hemoglobin	Positive
Indirect coombs test	Negative
Direct coombs test	Negative

Discussion

DHTRis an acute life threatening complication observed in patients receiving multiple blood transfusions[2].Common reported associations are sickle cell disease and thalassemia[3].The mechanism of the worsening anemia that occurs following RBC transfusion remains controversial. The "bystander hemolysis" is a possible mechanism in DHTR in sickle cell disease wherein the sickled RBCs are destroyed by antibodies, though they do not express the specific antigen against which these antibodies are directed. Bystander hemolysis during DHTR may occur following activation of complement as a result of the reaction of alloantibodies with transfused RBCs or other antibody reactions with transfused foreign antigens, leading to the attachment of activated complement components to the autologous RBCs[2].Patients typically present with fever, jaundice, back pain, abdominal pain, leg pain, hemoglobinuria, and laboratory evidence of severe hemolysis including hyperbilirubinemia and elevated lactate dehydrogenase (LDH).Standard treatment regimen include avoiding further transfusions unless absolutely necessary, and initiating intravenous immunoglobulin and/or steroids[4].

DHTR usually occurs approximately 6 to 10 days following packed red blood cell transfusion[4].This child developed the characteristic clinical symptoms one week after a packed red blood cell transfusion supporting the

diagnosis of DHTR .Negative coombs test does notpreclude the diagnosis of a DHTR[2]and may remain negative in as many as 50 to 75% of the patients[4,5].The presence of mild thrombocytopenia which improved after two days of immunosuppressive therapy is probably due to the alloantibody mediated destruction of platelets similar to the mechanism of post transfusion purpura[6]. Relative reticulocytopenia (1.3%) against his baseline count (5%) is explained by the peripheral destruction of immature red blood corpuscles which is commonly seen in DHTR due to hyperactivity of macrophages rather than suppression of erythropoiesis[2].All these features confirm the possibility of alloantibody mediated DHTR.

Other causes of hemoglobinuria in hemoglobinopathies include malarial infection[7], glucose -6-phosphate dehydrogenase(G6PD) deficiency[8], and drug induced hemolysis[9].Malaria was ruled out by peripheral smear and immunochromatography. There was no history of any drug intake other than hydroxyurea and folate.G6PD deficiency is very unlikely in this case because of worsening hemoglobinuria after transfusion and cessation of hemolysis following immunosuppressive therapy.

DHTR is a life threatening complication in children with sickle cell hemoglobinopathy. Early clinical suspicion and diagnosis is of paramount importance as the immediate management requires immunosuppressive therapy and withholding transfusion which is quite far removed from other sickle cell crises.

Compliance with Ethical Standards:

Funding: None

Conflict of interest: None

Ethical approval: All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Written Informed Consent: Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images.

REFERENCES:

1. Sebastiani P, Steinberg MH.Genetic modifiers of sickle cell disease.Am J Hematol.2012;87:795– 803.

2. ScheunemannLP , AtagaKI.Delayedhemolytic transfusion reaction in sickle cell disease. Am J Med Sci. 2010;March ; 339(3): 266–269.

3.Dogra A, Sidhu M.A case of delayed hemolytic transfusion reaction in sickle cell disease patient. Asian J Transfus Sci.2016;10(2):150-151.

4.BrandowAM,Liem RI. Sickle Cell Disease in the Emergency Department: Atypical Complications and Management.ClinPediatrEmerg Med. 2011; 12(3): 202–212.

5. De MontalembertM,Dumont MD et al.Delayedhemolytic transfusion reaction in children with sickle cell disease.Haematologica; 2011;96(6):801-807.

6. Gonzalez CE, Pengetze YM. Post-transfusion purpura.CurrHematolRep.2005 ;Mar;4(2):154-9.

7. Boringa JB, de Jong GM. Tropical malaria and sickle-cell anemia: a tropical surprise.Tijdschr Kindergeneeskd.1992 ;60(4):120-2.

8.Al-Nood HAet al. Thalassaemia and glucose-6-phosphate dehydrogenase deficiency in sickle-cell disorder patients in Taiz, Yemen. East Mediterr Health J. 2011; May;17(5):404-8.

9. Bernini JC, Mustafa MM, Sutor LJ, Buchanan GR. Fatal hemolysis induced by ceftriaxone in a child with sickle cell anemia. J Pediatr. 1995 ; 126:813-5.