Case Report

Alloimmunisation in Sickle Cell Disease Presenting As Haemolytic Crisis

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ABSTRACT:
Bystander haemolysis is a devastating consequence of delayed haemolytic transfusion reaction (DHTR) in cases of sickle cell disease receiving multiple transfusions. This can be potentially a life-threatening complication, which should be kept in mind while treating patients of sickle cell disease with haemolytic crisis. We present a case of a 22-year-old male who presented to us with symptoms of severe anaemia; later, diagnosed as DHTR and managed accordingly.

Key Words: DHTR, sickle cell disease, anaemia, transfusion.

INTRODUCTION:
Sickle cell disease is a chronic haemolytic anaemia with various compound heterozygote genotypes. The clinical manifestations range between haemolytic and vaso occlusive sub phenotypes.¹ Patients of SCD frequently require RBC transfusions because it is an important treatment modality. Basically, it increases oxygen carrying capacity and improves the physiologic property of blood in these patients.

Absolute indications for transfusion are: Aplastic crisis, severe anaemia causing haemodynamic compromise, cardiac failure and splenic sequestration.

Exposure to multiple RBC transfusions, may put the patient for the risk of infections, iron overload, and DHTR because of alloimmunisation. DHTR can be potentially serious and should be identified at an early stage because it can masquerade hyper haemolytic crisis.

CASE REPORT:
A 22-year-old male, known case of sickle cell disease for 15 years, presented to us with chief complaints of increasing fatigue, lassitude, palpitations, pre-syncope and chest pain of 10 days’ duration. 1 month back he was admitted for painful crisis in another hospital and was transfused 2 units of packed red cell. There was no history of fever, bone pains, cough, haemoptysis, urinary complaints. Examination revealed pulse of 115/min regular high volume, blood pressure 100/70 mmhg, severe pallor was present, icterus was present. JVP was normal. There was no Petechiae, gum bleeding, oral ulcers, leg ulcers. Per abdomen, CVS, RS were within normal limit.

INVESTIGATIONS: Hb-3.2 gm/dl, bilirubin 12 mg/dl unconjugated 8 mg/dl, LDH-4000 U/L, direct and indirect coombs test were positive. Haemoglobin electrophoresis revealed HBA – 0%, HBF-30%, HBA2-3.1% AND HBS-66.9% suggestive of sickle cell disease pattern. Reticulocyte count was 6%.

The discharge document of the hospital where he received blood transfusions, showed initial haemoglobin (pre-treatment was 5 gm/dl and after two transfusions was 8.2 gm/dl) Reticulocyte count (Pre-treatment 25 % and Post treatment was 18%). In view of severe decrease in the haemoglobin level along with reticulocyte count, a probable diagnosis of DHTR was kept and antibody study was done which revealed ANTI JK ANTIBODIES BY AHG GEL CARDS. The patient was treated with corticosteroids, antigen negative blood units by antigen typing. After 5 days, his haemoglobin was stable at 7 gm/dl. Patient was discharged and 2 weeks follow up haemoglobin level was 8.1 gm/dl.

DISCUSSION: DHTR is a dangerous complication especially in patients of sickle cell disease. It typically occurs around 1-2 weeks’ post transfusion and presents with fever, abdominal and back pain. Severe anaemia deepening icterus and haemoglobinuria.² It occurs due to stimulation of alloantibody to a foreign surface antigen on the transfused RBCs. It is sometimes confused with hyper haemolytic crisis which is another manifestation of sickle cell disease patients.

Prevalence and risk factors: Alloimmunisation rate in SCD...
has been reported to be around 19-47 % in adult patients.\(^2\) Ironically these antibodies may become undetectable in a substantial number of cases.\(^9\)

Table 1 shows risk factors FOR DHTTR in SCD patients.

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<thead>
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<tbody>
<tr>
<td>1</td>
<td>Old age at time of 1st transfusion</td>
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<tr>
<td>2</td>
<td>Female sex</td>
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<tr>
<td>3</td>
<td>Racial difference (Afro-American recipients/Caucasian donors)</td>
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<td>4</td>
<td>RBC antigens E, C, Kell, Fy(^a), Fy(^b) AND JK(^r) (^9)</td>
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<td>5</td>
<td>HLA DRB1 1503 is associated with worst prognosis and HLA DRB1 0901 is protective</td>
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<td>6</td>
<td>? Inflammation</td>
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Decreased haemoglobin levels with reticulocytopenia indicates DHTTR.

PATHOPHYSIOLOGY: Bystander haemolysis mechanism is the cornerstone for DHTTR in SCD. Immune haemolysis of RBCs that are negative for the antigen against which the culprit antibody is directed and destroys patients own cells and the transfused red cells by activating complement. Suppression of erythropoiesis that accompanies transfusion also contributes to the anaemia which follows DHTTR.\(^7,\,8,\,9,\,10,\,11\) The situation is further aggravated because patients of SCD already have shortened RBC survival. Some case reports also suggest that rather than suppression of erythropoiesis increased peripheral consumption of RBCs may be another mechanism.\(^12\)

DIAGNOSIS: DHTTR is diagnosed based on appropriate history and laboratory testing. New onset painful crisis, decreasing haemoglobin levels approximately 1-2 weeks following transfusion of RBC, reticulocytopenia, jaundice, positive coombs test (direct and indirect) and increased LDH are the indicators of DHTTR. Urine examination may show haemoglobinuria suggestive of intravascular haemolysis. In many cases antibody screening remains negative.\(^13\)

TREATMENT: Whenever DHTTR is encountered RBC transfusion should be withheld temporarily because it may precipitate acceleration of haemolytic reaction. High dose corticosteroids appear to improve the situation. Resistant cases may benefit from IVIG therapy. Rituximab a monoclonal antibody that targets B cells by binding CD20 allows successful transfusion.\(^14\) Post transfusion haemoglobin levels should be kept below 10 gm/dl because more RBC transfusion increases blood viscosity thereby paradoxically decreasing the oxygen carrying capacity.

CONCLUSION: DHTTR is an important complication of transfusion in SCD. A high index of suspicion should be kept while treating SCD patients who deteriorate with severe anaemia and features of haemolysis usually after transfusions. Once DHTTR is detected further transfusions should be withheld unless necessary. Treatment is with high dose steroids with or without immunoglobulin.

References: