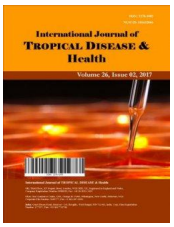

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A Case Report of Alloimmunization with Hyperhaemolysis in a Multiple Transfused Known SCD Patient at a Tertiary Hospital South Nigeria: A Challenge in Developing Countries

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Authors' contributions

This work was carried out in collaboration between all authors. Authors KA and EC designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors NA and HI managed the analyses of the study. Authors BOB and OF managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Hyperhaemolysis is a fatal life threatening haemolytic transfusion reaction which is common among sickle cell disease patient.
Aim: The aim is to create the awareness of the increasing trend of hyperhaemolysis among chronic transfused sickle cell patients and to educate medical practitioners on the means of ameliorating this menace.
Presentation of Case: The patient was a 14 years, old male; known sickle cell anaemia (Hbss) diagnosed 13 years ago with Haemoglobin electrophoresis. Patient's present condition was said to

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have worsen 4 years ago when patient crisis became so frequent with about 6-8 episode per year, which is so severe that at each episode patient is said to have received between 2-5 unit of whole blood. Further work up revealed a negative direct antiglobulin test (DAT) but Indirect antiglobulin test (IAT) was positive demonstrating the presence of anti-Jka alloantibodies. Patient RBC were phenotyped and was found to be JKa negative, whereas patient blood group is O^+ and had received several blood transfusion in our centre where extended phenotyping is not done for the past 3 decades. Each transfusion precipitated a drop in Hb and Hct to levels lower than before transfusion; once transfusions were withheld, the patient slowly recovered.

Summary: Hyperhaemolysis in the setting of alloimmunization is a common complication among multiple transfused SCD which is life threatening requires prompt intervention if taking into consideration among managing physician and also ensure measure to prevent it from occurring.

Conclusion: Transfusions worsens features of hyperhaemolysis in SCD patients. Extended red cell phenotyping may reduce associated risk.

Keywords: Alloimmunization; hyperhaemolysis; sickle cell disease; multiple blood transfusion.

1. INTRODUCTION

Alloimmunization of red cell is the process of immunogenic response of an individual to foreign red cell antigen from transfuse red cell. Chronic transfusion has remained one of the mainstays of management of sickle cell subject in developing countries. Alloimmunization to red blood cell antigen occur at a rate of 2-5% among all transfusion recepients [1]. SCD patient receive RBC transfusion for correction of anaemia, reduce the burden of sickling cells [2]. Hyperhaemolysis is a sequel of alloimmunization that is fatal in a multiple transfused patient which can be easily missed by most clinicians.

There is a paucity of information on alloimmunization in SCD patient in our environment. Thus a study by Ugwu reported a prevalence of 9.3% of red cell alloantibody in SCD patient in Benin with Rhesus antigen contributing 87.5% (anti E 37.5%, anti C 25%, anti D 12.5%, anti E 12.5%) while Kell and Lutherance blood group makes up the remaining [3]. Thus the prevalence varies from one region to another [4,5].

Hyperhaemolysis is a life threatening condition that is characterise with a drop in Haemoglobin (Hb) and hematocrit (HCT) to level lower than those present before transfusion [6-9]. This condition is commonly found in sickle cell disease and β-thalassaemia [10].

2. CASE REPORT

The patient was 14 years old, male, known sickle cell anaemia (HbSS) diagnosed 13 years ago with Haemoglobin electrophoresis. Patient's crisis became intensified 4 years ago when patient crisis became so frequent with about 6-8 episode per year, which is so severe that at each episode patient is said to have received between 2-5 unit of whole blood. Patient steady state HCT was said to be 24%. A year ago patient presented with multiple complication (Acute chest crisis, Avascular necrosis of the head of femur, Gallstone delayed cholecystectomy) on account of this patient was admitted on examination, the patient was in respiratory distress, febrile (37.8°C), pale deeply icteric acyanose, dehydrated. Laboratory evaluation showed Hb and HCT at 4.2 g/dl and 12% respectively and evidence of haemolysis with lactate dehydrogenase at 1950 iu/L (normal range <125) from the fifth day after transfusion, total bilirubin 155 umol/L normal range (0.3-1.2 mg/dl) with direct bilirubin 17 umol/L (2-7 umol/L), haptoglobin 14.3 mg/dl (normal range 0.5-5mg/dl), Full blood count showed WBC= $13.1x10^9$/L, Neutrophil 53%, Eosinophil 61%, Lymphocyte 46%, platelet $302x10^9$/L, with mild left shift of Neutrophils. There was also a history of passage dark coloured urine and urine analysis confirmed presence of Haemoglobin. Further work up revealed a negative direct antiglobulin test (DAT) but Indirect antiglobulin test (IAT) was positive demonstrating the presence of anti-Jka alloantibodies. Patient RBC were phenotyped and was found to be JKa negative with blood group O^+ whereas patient had received several blood transfusion in our centre were extended phenotyping is not done for the past 3 decades.

On the first day of admission, patient was transfused with 2 unit of Jka negative RBC, his haemoglobin and heamatocrit initially rose to 5.1 g/dl and 15% directly after transfusion. On day two patients haemoglobin had drop to 4.4 g/dl

(HCT 13%) and he was transfused again with 2unit of JKa negative blood. Again his blood Hb and HCT rose to 5.5 g/dl (16.3%), 24hrs after the Hb (4.5 g/dl) and HCT (14%). A new blood sample was taken for Direct antiglobin test which was negative while Indirect antiglobin test remained positive due to anti-JKa alloantibody.

Further investigation showed a poor reticulocyte response of 4.0% (normal range 0.5-2.5%) Ferritin was elevated 4250 ug/L (normal range 8-252 ug/L). B_{12} and Folate level were normal, as were coagulation studies peripheral smear showed nucleated Red blood cell and spherocyte.

Transfusion was withheld due to the continuous dropping Hb and HCT with each subsequent transfusion, Hydroxyurea was also prescribed but the patient could not tolerate it and hence it was discontinued because of the gastrointestinal side effect. A consult was sent to the Haematologist and patient was placed on steroid and iron supplementation and 2 weeks later it was noticed that the Hb and HCT was gradually increasing towards the patients steady state (7.4 g/dl and 22%) and reticulocyte appreciated.

3. DISCUSSION

Red blood cell transfusion is a major component of successful management of sickle cell disease in developing country. Transfusion helps to correct anaemia, improve oxygenation, reduced the propensity for sickling by diluting patient cells and temporarily suppresses the production of HbSS red cell [1]. Despite the importance of transfusion therapy in sickle cell disease, it is associated with several adverse short and long term complications which include transmission of infections, transfusion haemosiderosis, alloimmunization among others [2].

Hyperhemolysis which is a sequel of alloimmunization is charecterised by destruction of both transfused and autologous RBCs, which leads to a consequent fall in post transfusion haemoglobin lower than the level present before transfusion [7,8,9]. Hyperhaemolysis are of two type, an acute and delayed form of hyperhaemolysis. The acute form can be easy distinguish from acute haemolytic transfusion reaction, while the delay form can be distinguish from the delay haemolytic transfusion reaction (DHTR), with presence of alloantibody in the later and also involves the destruction of transfused red blood cells only, while the former involves the destruction of both the transfused and autologous red cells [11,12].

The index patient was thought to have developed DHTR but the post-transfusion Hb and HCT level was consistently lower than those of pre-transfusion which is more consistent with hyperhaemolysis. Furthermore transfusion in hyperhaemolytic episode can exaggerate haemolysis causing a life threatening anaemia [13], which was seen in our index patient, a JKa negative blood products further causes a drop in Hb and HCT in our patient, indicating that autologous RBC destruction was occurring.

Reticulopenia is a documented finding of hyperhaemolysis while haemolytic reaction is characterised by reticulocytosis. The Reticulopenia was previously attributed to secondary suppression of erythroporesis from multiple transfusion. It is now hypothesised to be likely from peripheral consumption and destruction by hyperactivated macrophages in the reticuloendothelial system [12-14].

The concept of bystander haemolysis has also been suggested. It is a phenomenon where antibodies reacting with foreign antigen in transfused red cells causing activation of complement system [14]. This can be supported by the fact that IVIG and steroid can increase blood reticulocyte. Furthermore, there is room for prophylactic immunosuppressive agent (rituximab, eculizummab) [15]. Hyperhaemolysis is further suggested by gradual appreciation of the reticulocyte count [16].

This case is important to clinicians, to emphasise the complication of multiple transfusion in SCD patient especially hyperhaemolysis syndrome which is a sequel of alloimmunization. Early detection allows for abrupt intervention in order to minimise the adverse effects of red cell transfusion. Steroid and immunoglobulin administration has been found to be useful in ameliorating this condition.

4. CONCLUSION

Hyperhaemolysis in the background of alloimmunization is a common complication in multiple transfused SCD and should be looked out for, with prompt intervention. Also health practitioners should minimise the rate of transfusion among sickle cell patients and if transfusion is to be encouraged he should ensure the use of leuco-depleted red cell and extended red cell phenotyping should be encouraged.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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