Chronic blood transfusion in a long-survivor sickle cell anaemia patient

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Case report

Abstract

Background: Multiple blood transfusions, with consequent iron overload, are inevitable in Sickle Cell Anaemia (SCA) patients who suffer from chronic haemolytic process that is frequently complicated by hyper-haemolytic crisis.
Objective: This paper reports the long term effects of blood transfusion in a long surviving SCA patient and to emphasize the need for exchange blood transfusions, regular iron studies and the need for chelation therapy in order to avoid organ failures.
Materials & Method: The hospital record of the patient was reviewed.
Results: This case typifies one of the extremes of transfusion requirement in a sickle cell anaemia patient. She survived multiple crises and complications of the disease up to the age of sixty one years, but in the course of the disease, she developed chronic kidney disease that warranted multiple episodic and chronic blood transfusions. The associated hypertension and subsequent heart failure led to her sudden death. Altogether, she received 40 units of blood, amounting to about 8,800 mg of exogenous iron. Iron overload was therefore a possible contributory factor to organ failures and death. However, patient's family refused post mortem examination which could have been helpful to determine iron load in the liver, heart and the bone marrow retrospectively.
Conclusion: In view of the complications of multiple blood transfusions with consequent iron overload in SCA patients, the use of artificial blood, regular use of hydroxyurea, iron chelation therapy when indicated will go a long way in improving survival in SCA patients.

Key words: Sickle Cell Anaemia, chronic blood transfusion, iron overload, organ failure.

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Chronique la transfusion sanguine dans une longue survivant anémie falciforme patient

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Rapport de cas

Résumé

Arrière-plan : Plusieurs transfusions sanguines , avec pour conséquence une surcharge en fer, sont inévitables dans la drépanocytose (SCA) les patients qui souffrent de maladies chroniques processus hémolytique qui est souvent compliquée par hyper- crise hémolytique.
Objectif : Le présent document expose les effets à long terme de la transfusion sanguine dans une longue survie à un arrêt cardio-respiratoire du patient et d'insister sur la nécessité d'échanger les transfusions sanguines, fer ordinaire des études et la nécessité de chélation thérapies afin d'éviter les défaillances organe.
Méthode : L'enregistrement de l'hôpital du patient a été examiné.
Résultats : Ce cas illustre bien l'un des extrêmes de transfusion prescription dans une anémie falciforme patient. Elle a survécu à de multiples crises et les complications de la maladie jusqu'à l'âge de soixante et un ans, mais dans le cours de la maladie, elle a développé maladie chronique des reins qui justifiaient plusieurs épisodiques et chroniques des transfusions sanguines. L'hypertension artérielle lié ultérieures et défaillance cardiaque conduit à sa mort subite. Au total, elle a reçu 40 unités de sang, s'élevant à environ 8 800 mg de fer exogènes. Surcharge en fer était donc un possible facteur d'orgue les défaillances et de la mort. Toutefois, patient rapport refusé examen post mortem qui aurait pu être utile de déterminer charge en fer dans le foie, le coeur et la moelle osseuse a posteriori.
Conclusion: Compte tenu des complications de plusieurs transfusions sanguines avec pour conséquence une surcharge en fer SCA les patients, l'utilisation de sang artificiel, l'usage ordinaire de hydroxyurée, fer traitement chélateur lorsque indiqué ira un long chemin en amélioration de la survie dans SCA les patients.

Mots-clés: anémie falciforme , chronique de transfusion sanguine, surcharge en fer, défaillance des organes.

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Introduction

Sickle cell Anaemia (SCA) is a wide-spread genetic disorder characterized by red blood cells (RBCs) deformity to abnormal rigid and sickle shaped forms that result in a risk of serious complications. It occurs in high frequency in many tropical countries. In Nigeria, the prevalence of SCA is 2–3% and the trait (HbAS) is 23% (1, 2). In SCA, appropriate blood transfusion improves blood flow by reducing the proportions of red cells capable of forming sickle haemoglobin polymer (3). The clinical manifestations of the disease are due to chronic haemolysis and intermittent micro-vascular occlusion characterized by repeated painful vaso-occlusive crises and eventual end-organ damage consequent to repeated bouts of ischemia-reperfusion injury resulting in significant disabilities and early mortality (3). The life expectancy of patients with sickle cell anaemia (SCA) has improved with modern medical care, and this has led to frequent observation of various chronic complications of the disease including abnormalities in renal function especially in the long survivors (4).

We present a case report of a 61 year old, late SCA patient, diagnosed in childhood and followed up to over six decades of life. She received multiple episodic blood transfusions due to hyper-haemolytic crisis secondary to infections and aplastic crisis, and also was subjected to chronic blood transfusions when she developed CKD. Altogether, she was transfused with 40 units of blood, equivalent to about 8,800mg of exogenous iron. She was unable to benefit from hydroxyurea therapy because it was neither available nor affordable and she was unable to afford erythropoietin therapy.

Case Report

A 61 year old female, was diagnosed HbS at the age of 3 years and 4 months in the University College Hospital (UCH), Ibadan when she presented with hand and foot syndrome. However, further management was continued at a secondary healthcare facility. Hospital records showed that she was successfully treated for osteomyelitis of the right radius before she was eventually referred back to the UCH at age 13 years where she received treatment until her demise.

Vaso-occlusive crises (VOC) and hyper-haemolytic crises [HHC] dominated the clinical picture. The frequency of VOC was about 1-2 per year from the time of diagnosis. There were however some years when she was crisis-free. She was never admitted on account of VOC alone. The rate at which she presented with VOC declined with age, especially when she was diagnosed with chronic kidney disease (CKD), seven years prior to death. She did not develop any bony deformity.

About six episodes of HHC, characterized by sharp decline in the packed cell volume (PCV) and passage of dark urine were documented. The first was at age 18 years and it was precipitated by acute pyelonephritis. This necessitated hospital admission for a period of forty days and transfusion with 10 units of packed red cells. The other five episodes of HHC crises required transfusion of a unit of blood each, adding up to additional 5 units of blood transfused.

The first confinement was in 1977 which resulted in fresh still birth (post-date). Five years later she was delivered of a life male child although it was complicated by postpartum haemorrhage due to retained products of conception which warranted 2 units of blood transfusion. The third confinement was uneventful. The last was complicated with VOC, hyper-haemolysis (for which she received 2 units of blood) and puerperal sepsis which necessitated 12 days of hospital admission.

Hospital records showed that she was managed for many episodes of malaria. There was significant history of recurrent urinary tract infection (acute pyelonephritis) and lobar pneumonia. Repeated culture of the mid-stream urine (MSU) yielded no growth and intravenous pyelography showed no abnormality of the urinary system. Acute pyelonephritis was the cause of HHC in most cases. There were no records of viral studies in this patient.

The steady state packed cell volume (PCV) ranged from 22-25% at diagnosis and this reduced to 15-16% during hyper-haemolytic crisis. It also sharply reduced to 13-15% after diagnosis of CKD. This declined further to 9%

as chronic anaemia progressed. The steady state white blood cell ranged between 8.5-9.200/mm^3. It however increased to 18,000/mm^3 with left shift during crisis. There was no significant change in white blood count with the onset of CKD. Platelet count ranged between 240,000-430,000/mm^3 throughout the course of the disease. Eleven years prior to her demise she was diagnosed of hypertensive heart disease, chest x-ray confirmed cardiomegaly and aortic unfolding while progressive renal insufficiency and worsening of anaemia was diagnosed 6 years before her demise. Ultrasound confirmed bilateral grade one renal parenchymal disease and serum creatinine was 5.4mg/dl. The PCV declined to 9.6%.

Subcutaneous erythropoietin 4,000IU thrice weekly was advised but this could not be sustained due to financial constraints. Consequently, the PCV ranged between 9-11% thus requiring blood transfusions almost on a monthly basis.

Overall, the patient was transfused with a total of about 40 units of packed red cells. Twenty units were transfused in the last seven years as a result of chronic renal failure. Since a unit of packed red cells is 220mls and each milliliter contains 1mg of iron, therefore, the patient received about 8,800 mg of exogenous iron. The only iron study found in the record (which was as a result of a research study) was in 1970 which showed serum iron of 15ug/100ml, unsaturated iron binding of 318ug/100mls, TIBC of 468ug/100ml and saturation of 32%. This was so because iron study is yet to be a routine investigation in the institution.

Discussion

In SCD, simple transfusion is not an effective intervention for the management of acute painful episodes. Instead, exchange blood transfusion has been adopted for various indications warranting chronic blood transfusion e.g. the alleviation of bouts of severe, intractable pain (5). In addition, chronic/long term transfusion therapy has been used to decrease the frequency of pain in patients with recurrent debilitating painful crises (6). Although chronic (repeated) blood transfusions have a number of associated problems, iron overload is usually prevented by exchange blood transfusion. These problems are well highlighted by this case presentation.

In contrast with thalassemia major where effects of long term transfusion and iron overload have been studied extensively and end organ damages well characterized, similar studies are lacking in SCD simply because blood transfusion requirement in SCA is comparatively lower than that of thalassaemia. Available results however suggest that SCD patients are relatively protected from iron induced cardiac and endocrine organ damage as compared with thalassemia major patients although the reason for this is yet to be established.

The case in view was offered simple [not an exchange] blood transfusion for both the sporadic and the chronic blood transfusion offered. While sporadic transfusions were given as part of treatment of hyper-haemolytic crisis, the chronic blood transfusion was indicated during the event of CKD. However, rather than simple blood transfusion, this patient would have benefited better from exchange blood transfusion which will prevent not only iron overload but effectively reduce the percentage of sickled red cells to a large extent.

Aside CKD in this patient, there are many established use of chronic transfusion therapy in patients with SCD and the most common indication is associated stroke. Other indications include, treating recurrent severe episodes of sickle cell pain, and as a prophylactic measure in pregnant patients.

Studies had shown that the utility of transfusion therapy is limited by complications, most notably allo-immunization and iron overload (7). Clinically significant iron overload can occur after as few as 30 units of packed red cell transfusions. In this index case, iron overload requiring chelation therapy is clearly indicated since the patient received 40 units of blood, amounting to 8,800 mg of exogenous iron.

Renal complications, which incidentally were the major indications for chronic blood transfusion in the index case, are well-known causes of morbidity and mortality in SCD and the incidence of renal failure increases as patient survival improves. A Jamaican study showed an increase in the prevalence of end-stage renal

disease in SCD (4). As renal function declines, the ability of the kidney to synthesize erythropoietin also declines. This was indirectly demonstrated in our patient. SCD patients with normal kidney function invariably have erythropoietin levels above the normal range.

Infections, especially pyelonephritis, were prominent in this case. It is well established that patients with SCD are susceptible to overwhelming infections (8, 9, 10).The most significant factor is splenic auto-infarction during childhood (11). The resultant functional asplenia makes such patients vulnerable to infections with encapsulated organisms such as *Streptococcus pneumoniae* and *Hemophilus influenzae*. Other factors include lazy leucocyte syndrome and poor opsonization (12).

In conclusion, this case, apart from demonstrating that our SCD patients can live long, equally highlighted various possible complications. The case report also demonstrated the indications for episodic and chronic blood transfusion, precipitation of iron overload with consequent organ failure following infusion of a total of 40 units of blood to the patient.

Therefore, stepping up of facilities that enable better therapy of SCD patients to include provision of apharesis machine for exchange blood transfusion, adoption of hydroxyurea therapy, stem cell transplant, iron studies at minimal cost and initiation of chelation therapy at assisted cost, will go a long way to improve survival and quality of life in SCD patients.

Conflict of interest: The authors declare no conflict of interest.

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