Role of Emergency Automated Red Cell Exchange in Sickle Cell Crisis: A Case Report

Clinical Medicine Insights: Case Reports
Volume 13: 1–5

DOI: 10.1177/1179547620970200
SAGE

Anubhav Gupta[1], Kiran Chaudhary[1] and Rajnish Kaushik[2]

[1]Department of Transfusion Medicine, Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital Delhi, India. [2]Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital Delhi, India.

ABSTRACT: For many years main stay of treatment for sickle cell anaemia was transfusion therapy. But repeated transfusions put the patient at risk of iron overload. Automated red cell exchange is an evolving and newer technique which rapidly removes the sickle cells and has benefit in decreasing sickle cell load and related complications. Red cell exchange is a therapeutic procedure in which the patient's whole blood is processed centrifugally in cell separator. Patient's red cells are separated from other blood components and removed and replaced with donor red cells and colloids. We report our first experience of automated red cell exchange in 24-year-old female diagnosed case of sickle cell anaemia presented to us with acute chest syndrome with septic shock. Red cell exchange was planned to tide over the acute sickle cell crisis and provide symptomatic improvement. We also highlight that compound heterozygous thalassaemia could be associated with sickle cell disease which could make the diagnosis difficult. New generation automated Apheresis equipment's provides better monitoring of the procedure that can be useful in severely ill patients also.

KEYWORDS: Automated Red cell Exchange, sickle cell crisis, apheresis

RECEIVED: September 25, 2020. **ACCEPTED:** October 4, 2020.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

CORRESPONDING AUTHOR: Anubhav Gupta, Department of Transfusion Medicine, Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital Delhi, Baba Kharak Singh Marg, Near Gurudwara Bangla Sahib, Connaught Place, New Delhi 110001, India. Email: dr.anubhavgupta@yahoo.com

Introduction

India has a significant burden of sickle cell disease[1] with varying prevalence in different regions ranging from 0% to 18% in north eastern India, 0% to 33.5% in western India, 22.5% to 44.4% in central India and 1% to 40% in southern India, and the gene frequency of sickle haemoglobin (Hb-S) varies between 0.031 and 0.41.[2,3]

Sickle cell disease (SCD) is an inherited autosomal recessive blood disorder. Sickle cell anaemia (SCA), the most common type of SCD, is a chronic disorder having qualitative defect in globin chain. It is caused by a single mutation and substitution of valine with glutamic acid at sixth position in beta globin gene resulting in abnormal haemoglobin Hb-S.[4] Hb-S has the tendency to polymerise on deoxygenation and causes red blood cell (RBC) to become sickle shaped. Sickle cell RBC tend to adhere with each other and causes increase in RBC transit time in already inflamed tissues leading to microvascular occlusion and infarction. These sickle shaped RBC's get sequestered in the spleen leading to haemolysis and congestion followed by infarction of the organ, known as hyposplenism and phenomena known as autophagy. Hyposplenic individuals are at higher risk for developing infections. Pneumococcal polysaccharide vaccine is ineffective in asplenic or hyposplenic individuals because they require IgM memory B cells for functioning. During this period, patient may present with anaemia, jaundice and complain of episodic pain varying in intensity and duration, frequent infection, delayed growth in children and ulcers mainly over the limbs. Immediate and delayed complications attributed to Hb-S may also include acute stroke, acute chest syndrome, vaso-occlusion, micro infarcts, painful crisis, haemolysis, hepatic sequestration, splenic sequestration, intrahepatic cholestasis and multi organ failure.[5]

For many years, the main stay of treatment for SCA was transfusion therapy to keep haemoglobin (Hb) threshold above 8 g/dl.[6] But repeated transfusions put the patient at risk of iron overload. Automated red cell exchange is an evolving technique which rapidly removes the sickle cells and replace with allogenic donor cells. It provides immediate symptomatic relief to patient presenting with acute chest syndrome, bone pain, priapism, improves the oxygen carrying capacity and ongoing haemolysis. It also prevents associated complications of SCA like iron overload, damage to renal tubules, pre-existing vaso-occlusion leading to stroke, multi organ dysfunction, etc.

In the absence of preventative therapies, ischaemic stroke can occur in up to 10% (overt stroke) or 20% to 35% (silent stroke) of patients, with a recurrence rate of 46% to 90%.[5] In paediatric patients presenting with vaso-occlusive stroke, red cell exchange (RCEx) is recommended as initial treatment performed soon after diagnosis is made.[7] Here we reported a case of sickle cell disease successfully managed with emergency automated red cell exchange.

Case Report

A 24-year female, resident of Odisha, presented with complaints of chest pain, fever, cough with yellowish sputum, breathlessness at rest, pain in all limbs more in upper limb compared with lower limb. She also complaint of headache, pain in abdomen often at right hypochondrium associated with

vomiting. Patient had similar episodes in the past with frequent history of easy fatigue, anaemia, jaundice, skin ulcerations, upper respiratory infections and gall bladder stones. She had received only 1 unit of blood transfusion in her childhood.

On examination patient was dyspnoeic with severe pallor, yellowish discoloration of eyes and a small ulcer on the lateral side of her right thigh. She had sinus tachycardia with pulse rate of 131 beats/minute, SPO_2 of 78% on room air and blood pressure (BP) of 100/60 mmHg. On auscultation crepitations were present on the right infrascapular and infraaxillary region. Abdominal palpation revealed an enlarged liver measuring 7 cm below the right costal margin and an enlarged spleen measuring 12 cm in its largest dimension. Chest X ray at mid inspiration revealed right anterior rotation with ill-defined radio opacity, and right lower zone consolidation. Abdominal ultrasound revealed splenomegaly of 13.5 cm with obliteration of medullary pyramids.

Laboratory findings as in Table 1, showed severe anaemia, increase in total leucocyte count predominant with neutrophils, with sickle cells on peripheral smear. Additional test showed positive sickling test and total bilirubin of 5.90 mg/dl. High performance liquid chromatography (HPLC) showed Hb-S = 76 area%, Hb-F = 19 area%, Hb-A1 = 1.7 area%, Hb-A2 = 2 area%. A provisional diagnosis of sickle cell anaemia with hereditary persistence of foetal haemoglobin (Hb-F) or compound heterozygous thalassaemia was made. Patient was second order female child with no similar complaint in other family members. Her father and mother were screened for sickle cell disease by HPLC and were found to be sickle cell trait with Hb-S, 36.2 area% and 33.9 area%, respectively.

In view of persisting symptoms and discussion with clinician, automated red cell exchange was planned. On day 3 of admission, an internal jugular line was secured and red cell exchange was started on automated cell separator (RCEx). Before the start of procedure, patient's condition deteriorated with sudden fall in SPO_2, severe breathlessness, chest pain, fall in blood pressure, feeble pulse and bradycardia. Procedure was postponed and the patient was shifted to intensive care unit (ICU) where she was immediately intubated and given normal saline as bolus with adrenaline in 1 in 10 000 dilution intravenously. Her chest X ray was repeated which showed new pulmonary opacities, and bilateral pulmonary effusion (Figure 1), suggestive of deterioration in condition. Electrocardiography (ECG) was within normal limits and 2D-ECHO shows left ventricular ejection fraction (LVEF) of 60%, normal cardiac dimensions, and valves with no features of pulmonary embolism. Non-contrast CT scan (NCCT) head was normal. On day 8 of admission, in view of persisting and severe symptoms, clinical team requested for RCEx. RCEx was done on patient on ventilator support with blood pressure of 96/58 mmHg on noradrenaline and pulse 122 beats/minutes. Target haematocrit was kept at 30% and fraction of cell remaining (FCR) at 30%, cell separator processed a total of 3178 ml of the whole blood and removed 1929 ml of red cell volume. The blood volume was replaced with 1696 ml (8 units of packed red cell) of leucoreduced Rh and Kell matched and cross match compatible packed red cell having a haematocrit of 55%. During the procedure, patient received 122 ml of acid citrate dextrose as anticoagulant and 40 ml of 0.93% of calcium gluconate in 400 ml normal saline at 1 ml/min to prevent calcium chelation. Whole procedure was completed in 193 minutes and patient was comfortable and did not show any signs of further deterioration. Complete blood count, liver function test, renal function test, ionised calcium and HPLC were repeated after 12 hours as shown in Table 1, showing dramatic improvement in laboratory values. Patient was relieved of chest pain and bone pain immediately after the procedure. Oxygen saturation improved to above 90% on room air. On day 13, patient was asymptomatic, comfortable and was discharged on hydroxyurea 500 mg twice daily, folic acid supplement and advised for influenza and pneumococcal vaccinations. She was followed up monthly for next 3 months with Hb-S load and planned for prophylactic RCEx if Hb-S greater than 50% or if she becomes symptomatic, that is in crisis.

She was given instructions to seek medical help in case of fever, new ulcers on limbs, bone pain that does not get away with treatment, abnormal speech, weakness and to prevent herself from infection and dehydration. During her stay in the hospital, genetic analysis of the patient and her parents could not be done but were advised for the confirmation and characterisation of compound heterozygous thalassaemic state with sickle cell disease.

Discussion

Sickle cell disease (SCD) is an autosomal recessive inherited blood disorder. Sickle cell anaemia (SCA) is the most common type of SCD in which red blood cell (RBC) are rigid and sickle shaped upon deoxygenation which hamper the transport of oxygen to the tissues. These rigid cells loss their property of deformation and stuck up at micro-vasculature and precipitate symptoms. Transfusion support in SCA is expected to provide normal RBC to the patient to alleviate anaemia, reduce the blood viscosity for permitting it to stream more unreservedly and forestall the complications. Simple transfusion remains an essential technique in SCA in which red blood cells are transfused to the patient. Simple transfusion is simple and particularly required in intense stages or acute phases in which there is a rapid need to increase oxygen-carrying capacity.[8] Chronic transfusions limits increment in oxygen carrying capacity as well as keep up a lower level of HbS.[8] Yet simple transfusion can cause volume overburden, increased blood viscosity and iron deposition. To overcome the limitations of simple transfusion, exchange transfusion is the technique in which the patient red cells are removed either manually or by an automated apheresis equipment and replaced with donor (allogenic) red cells. Manual exchange transfusion uses a 3-way stopcock for

Table 1. Comparison of laboratory parameters at the time of admission, before red cell exchange and after red cell exchange.

PARAMETERS	AT THE TIME OF ADMISSION	BEFORE RBEX	AFTER RBEX
Hb (g/dl)	6	8.8	10.7
M = 13-17.5 g/dl			
F = 11-16.5 g/dl			
TLC (cumm) (4000-11 000/cumm)	13 000	12 200	10 900
DLC (cell%)	N = 78	N = 92	N = 63
	L = 20	L = 06	L = 30
	E = 02	E = 01	E = 03
	B = 00	B = 00	B = 00
	M = 00	M = 01	M = 04
Platelet (cumm) (1.5-4.5 lakhs/cumm)	1.6	3	1.75
PCV (%)	15.4	29.1	31
M = 40%-50%			
F = 33%-44%			
Total RBC (million cells/µl)	1.93	3.1	3.28
M = 4.7-6.1 million cells/µl			
F = 4.2-5.4 million cells/µl			
MCV (fl) (80-94 fl)	79.8	92.7	87.5
MCH (pg) (27-33 pg)	24	28	30.6
MCHC (g/dl) (32-36 g/dl)	30	30.2	34.9
Reticulocyte count (%) (0.5%-2%)	2.6	2	1.8
Urea (mg/dl) (20-40 mg/dl)	16	23	17
Creatinine (mg/dl) (0.3-1.1 mg/dl)	0.41	0.36	0.3
Uric acid (mg/dl) (2-6 mg/dl)	2.16	2.79	1.9
Total bilirubin (mg/dl) (0.1-1 mg/dl)	5.90	7.46	3.1
Direct bilirubin (mg/dl)	0.75	1.30	0.7
AST (u/l) (15-33 u/l))	39	23	15
ALT (u/l) (20-40 u/l)	29	19	19
ALP (u/l) (44-147 u/l)	68	51	91
Na+ (meq/l) (135-145 meq/l)	139	130	136
K+ (meq/l) (3.5-4.5 meq/l)	3.20	3.11	4
Cl- (meq/l) (96-106 meq/l)	112	110	113
Total protein (g/dl) (6-8 g/dl)	6.18	5.55	5.33
Albumin (g/dl) (3.4-5.4 g/dl)	3.24	3.16	3.21
LDH (u/l) (140-250 u/l)	629	893	666
pH (7.35-7.45)	7.423	7.479	7.461
iCa+ (mmol/l) (1.3-1.5 mmol/l)	0.9	0.8	0.7
Hb-S (area%)	76	76	9.2
Hb-F (area%)	19	19	3.4
D- dimer µg FEU/ml (<0.05)	0.70	ND	ND

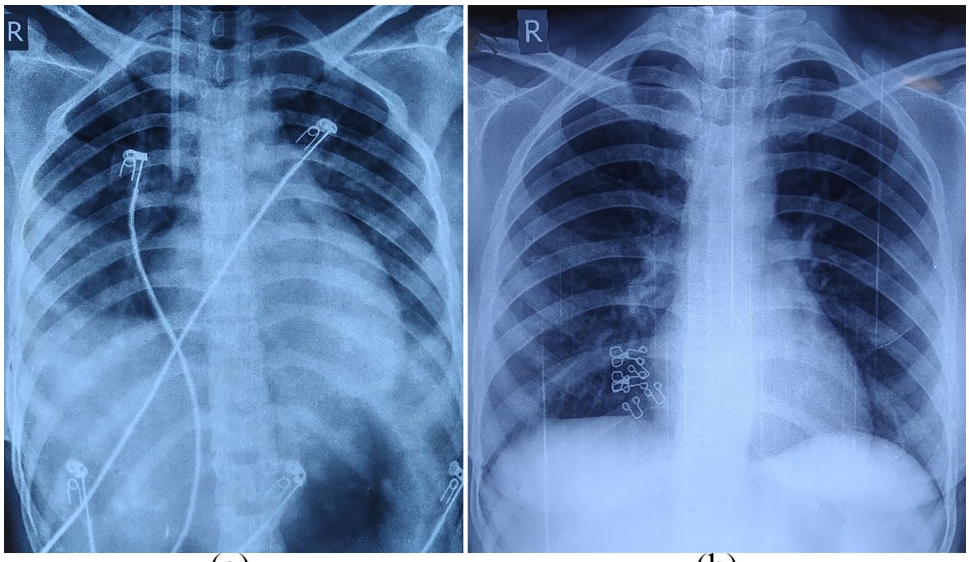

Figure 1. Comparison of chest x-ray before and after red cell exchange (a) shows consolidation of right lower lobe and obliteration of CP angle, (b) shows clearance of lung and prominent CP angle.

removal of blood and infusion of red cells in saline or plasma whereas automated exchange transfusion uses an apheresis equipment with a dedicated venous access. Advantage of automated exchange transfusion is more rapid increment in haematocrit (Hct) and abatement in sickle cell haemoglobin (Hb-S) level and a lower risk of iron and fluid overburden. Regardless, all transfusion episodes in SCA should focus on final Hct of 30% or less so as to avoid an unsafe increment in blood viscosity.

Autoantibodies, alloantibodies and hyperhaemolysis syndrome are important adverse effects associated with the transfusion. These multi-transfused patients are more prone for autoantibodies formations with the presence of multiple alloantibodies.[9,10] Studies reported the rate of alloimmunisation ranging 2% to 6% of all patients who receive RBC transfusions but in multi-transfused SCD patients rate may be as high as 36%.[11] Moreover, more serious complication of RBC transfusion in SCD patients is the hyperhaemolytic transfusion reaction in which transfused red cells are destroyed and reticulocytopenia may occur.[12] American Society For Apheresis (ASFA) guidelines 2019 have recommended red cell exchange in acute and chronic complications of sickle cell anaemia.[5] Our patient presented with features of acute chest syndrome and vaso-occlusive crisis which needed rapid removal of sickle cells and replacement with allogenic donor cells. Automated red cell exchange was done to decrease sickle cell load by removing and replacing sickle cells will allogenic donor red cells. Choice for automated red cell exchange relies on the accessibility of apheresis services, adequate intravenous access, leucoreduced Rh and Kell matched and crossmatch compatible blood products. RCEx allows continuous monitoring of the patient in addition to patient comfort and safety. For acute stroke and stroke prophylaxis RCEx is ASFA category I. Hulbert 2006, observed that in patients with first stroke, RCEx appears to lower the stroke recurrence rate when compared with patients treated with simple RBC transfusion 21% (8/38) versus 57% (8/14), respectively.[13] Aneke et al, reported that after RCEx in acute chest syndrome SPO_2 recovery time on room air was shorter ranging from 6 to 96 hours.[14] RCEx is relatively safe procedure still the patient is at risk for transfusion-associated adverse events, in addition to apheresis risks. Risk may include but not limited to central venous catheter thrombosis, haemorrhage, mitigation of catheter at internal jugular site, etc.[15]

Conclusion

Automated red cell exchange done in our patient proved to be a lifesaving modality with rapid reversal of symptoms, and near normalisation of laboratory parameters. Our patient was 24 years old female who had splenomegaly and had received only 1 packed red blood cell in her lifetime which was very unusual in sickle cell disease patients in whom spleen autophagy is seen up to age of 5 years. This case report also demonstrated that compound heterozygous thalassaemia could be associated with sickle cell disease which could make the diagnosis difficult. New generation automated Apheresis equipment's provides better monitoring of the procedure that can be useful in severely ill patients also.

Acknowledgements

We would express our thanks of gratitude to Dr Swati Asati, Dr Anupa Pokhrel, Dr Prerna Sachdeva, Dr Shilpi Varshney, Dr Harkiran Arora in completing the manuscript and in

patient support care. We are thankful to the patient and her family being so co-operative.

Authors' Contributions

All authors were involved in drafting, reviewing and revising the manuscript and gave intellectual inputs.

Patient Consent Confirmation Statement

Patient consent was secured to publish the findings of this case study.

REFERENCES

1. Hockham C, Bhatt S, Colah R, et al. The spatial epidemiology of sickle-cell anaemia in India. *Sci Rep*. 2018;8.
2. Serjeant GR, Ghosh K, Patel J. Sickle cell disease in India: a perspective. *Indian J Med Res*. 2016;143:21-24.
3. Gorakshakar AC. Epidemiology of sickle hemoglobin in India. *Res.in*. Accessed September 20, 2020. https://nirth.res.in/publications/nsth/14.AC.Gorakshakar.pdf
4. Ashley-Koch A, Yang Q, Olney RS. Sickle hemoglobin (HbS) allele and sickle cell disease: a HuGE review. *Am J Epidemiol*. 2000;151:839-845.
5. Szczepiorkowski ZM, Shaz BH, eds. Erratum: Special issue: Clinical applications of therapeutic apheresis: an evidence based approach. 5th edition. *J Clin Apher*. 2010;25:237-237.
6. Liumbruno G, Bennardello F, Lattanzio A, Piccoli P, Rossetti G. Recommendations for the transfusion of red blood cells. *Blood Transfus*. 2009;7:49-64.
7. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *N Engl J Med*. 1998;339:5-11.
8. Swerdlow PS. Red cell exchange in sickle cell disease. *Hematology Am Soc Hematol Educ Program*. 2006;2006:48-53.
9. Castellino SM, Combs MR, Zimmerman SA, Issitt PD, Ware RE. Erythrocyte autoantibodies in paediatric patients with sickle cell disease receiving transfusion therapy: frequency, characteristics and significance. *Br J Haematol*. 1999;104:189-194.
10. 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.
11. Shaz BH, Zimring JC, Demmons DG, Hillyer CD. Blood donation and blood transfusion: special considerations for African Americans. *Transfus Med Rev*. 2008;22:202-214.
12. Win N, Doughty H, Telfer P, Wild BJ, Pearson TC. Hyperhemolytic transfusion reaction in sickle cell disease. *Transfusion*. 2001;41:323-328.
13. Hulbert ML, Scothorn DJ, Panepinto JA, et al. Exchange blood transfusion compared with simple transfusion for first overt stroke is associated with a lower risk of subsequent stroke: a retrospective cohort study of 137 children with sickle cell anemia. *J Pediatr*. 2006;149:710-712.
14. Aneke JC, Huntley N, Porter J, Eleftheriou P. Effect of automated red cell exchanges on oxygen saturation on-air, blood parameters and length of hospitalization in sickle cell disease patients with acute chest syndrome. *Niger Med J*. 2016;57:190-193.
15. Yeral M, Boga C, Oguzkurt L, Asma S, Kasar M, Kozanoglu I. Short-term central venous catheter complications in patients with sickle cell disease who undergo apheresis. *J Thromb Thrombolysis*. 2014;37:97-101.