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Exchange Blood Transfusions in a Case of Sickle Cell Anaemia (SCA) with Multi Organ Failure

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Abstract

Sickle Cell Anaemia (SCA) is an uncommon haemoglobin disorder in Pakistan. In North of Pakistan Kohat and adjacent tribal areas witness families with SCA. Here we present a young male, known case of SCA .He presented with high grade fever and multi organ failure.He had haemolytic crisis along with hepatic crisis and renal failure. Along with that he had chest crisis. His condition worsened. At that juncture red cell concentrates exchange transfusions were performed, which showed significant improvement

Key Words: Sickle Cell Anaemia, Multi Organ Failure, Exchange Blood Transfusion, Plamodium Viax

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Introduction

Sickle cell anaemia (SCA) is an inherited haemoglobinopathy ,characterized by chronic haemolytic anaemia ,vaso occlusive crisis (VAC) and multi organ complications.[1] The hall mark of SCA lies in the production of abnormal haemoglobin S (HbS), which results from a single point mutation in β –globin gene, leading to substitution of valine for glutamic acid at position-6.[2,3] Under condition of low oxygen tension HbS polymerizes causing red blood cells to assume a sickled shape. These sickled cells have reduced deformability, leading to vaso-occlusion and haemolysis , which in turn contributes to chronic anaemia, organ damage and episodic crisis. Inherent complications of SCA result in increased morbidity and mortality .[1,4]

SCA is a multi-system disorder. Patients with SCA suffer for chronic variable intravascular haemolysis, microvascular ischemia and organ damage. Vaso-occlusion results from a dynamic combination of abnormalities in HbS structure and function,red blood cells membrane integrity, erythrocytes density ,endothelial activation, microvascular tone, inflammatory mediators and coagulation.[5] SCA patients' blood is replete with inflammatory mediators, cytokines, chemokines, antibodies, procoagulants and many other deleterious molecules. These components mediate direct pro-inflammatory, proliferative and pro-oxidant effects on micro vessels and endothelial cells. [6]

Patients of SCA can develop multi-organ failure (MOF), which is defined as rapid dysfunction of approximately 2-3 organ system. The decline in organ function in this setting is proposed to be secondary to occlusion of microvasculature leading to ischemia of tissue .[7,8]

In addition to hydration, pain medication, disease modifying drug therapy and red blood cells (RCC) transfusion is the main stay of treatment.[3] Blood transfusions play a critical role in the management of both acute and chronic complications of SCA. In addition, there are situations where exchange blood transfusions are required.[1] Transfusion therapy aims to reduce the proportion of sickled erythrocytes, improving oxygen delivery and reducing the risk of vaso- occlusive- crisis (VOC) and other complications.[1,9]

Methodology

A 14 years old male, resident of Dera Ismail Khan(Bhittani tribe)presented with high grade continuous fever (associated with rigors and chills) for one week. He was a known case of Sickle Cell Anaemia (SCA). There was associated joint pains. He also gave history of darkening of urine and associated backache. On examination patient had pallor with yellowish coloured sclera. He was dehydrated. There was no organomegaly. Patient had toxic look and had severe breathlessness. He required oxygen support. On work up peripheral blood film revealed severe anaemia with reticulocytosis. Sickle cells were demonstrated on his peripheral film examination. Immuno- Chromographic -Test (ICT) for malaria revealed presence of plasmodium vivax. Repeat haemoglobin electrophoresis revealed 85% HbS. Anti-malarial management was initiated with intravenous artesurate (120 mg at 0,12 and 24 hours). Primaquine was started afterword. Liver function tests showed jaundice with

cholestastic pattern (elevated bilirubin with alkaline phosphatase). Renal function tests were consistent with renal failure. Bilirubin levels reached upto 14.0 mg/dl and creatinine level showed high level (9.0 mg/dl). Bilateral infiltrates were present on X-ray Chest (PA view) (Figure 01).

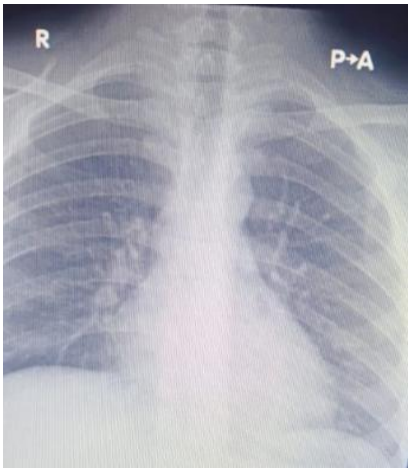


Figure 1: X ray Chest PA View: Bilateral bronchovascular and perihilar prominences. Increased interstitial / reticular markings in lower zones bilaterally. Suggestive of pulmonary infiltrates

Small, vestigial spleen was found on CT scan, reflecting hyposplenism. The condition of patient deteriorated further. Haemoglibn levels did not improve even after multiple transfusions. Haemodylasis was performed and patient was shifted to Medical Intensive Care Unit. It was decided to perform red cells exchange transfusions. Three sessions were performed. In each session three hundred and fifty ml of patient's blood was removed. Followed by administration of one unit of 5% dextrose normal saline and replacement by one unit of blood group compatible red cells concentrate. This led to a significant improvement in patient's condition and relevant lab results (Table I)

Discussion

In Pakistan Hb-S is mostly distributed in Baloch, Pathan and immigrant population from north part of India. Clustering of Hb-S has been seen in the Bhittani tribe from South Waziristan and adjacent Dara Ismail Khan. Patient reported in this case report also belonged to Bhittani tribe. [10]

SCA is a multisystem disorder. Sickled red cells interact

Table I: Lab variables in sickle cell anaemia ,before and after exchange transfusions

	Before Exchange Transfusion		After Exchange Transfusion		
	1st Week	2nd Week	1st Week	2nd Week	3rd Week
Haemoglobin (Ref Range:13.5-17.0G/dl)	5.1	5.9	8.9	9.0	9.9
Bilirubin (Ref Range:0.2-1.0 mg/dl)	11.5	14.34	6.52	3.27	2.09
Alkaline Phosphatase (Ref Range:50-200 ul/L)	4050	4070	2410	1300	970
ALT (Ref Range:5-50U/L)	90	80	70	50	50
Urea (Ref Range:	144	254	212	146	56
Creatinine (Ref Range:Upto 1.2 mg/dl)	2.5	8.9	5.5	2.0	0.96
pH (Ref Range:7.35)	7.9	8.3	7.47	7.3	7.3
pCO2 (Ref Range:35-45)	26.4	27.0	40	42	41
pO2 (Ref Range:80-100)	50	56	92	95	101
HCO3 (Ref Range:22-26)	12.4		23		
Sodium (Ref Range:135-150)	130	119	139	142	149
Potassium (Ref Range:3.5-5.4)	6.3	7.7	5.0	4.3	3.5
Chloride (Ref Range: 95-108)	90	82	99	101	107

and disturb the rheology and physiological functions of different organs In SCA patients hypoxia, acidotic and hypertonic renal medulla favours vaso-occlusion, leading to destruction of vasa recta and hyposthenuria.[2]Even in the absence of clinically apparent renal disease, small cortical infarcts of varying ages are evident in SCA. [11]

Intra-renal vaso-occlusion or renal infarction in SCA, can lead to acute renal failure. In rare and severe cases of renal meduallry/cortical infarction or multi-organ failure during a vaso-occlusive crisis, early recognition and prompt initiation of exchange transfusions, frequently paired with renal replacement therapy (such as continuous haemodylasis) can arrest kidney destruction or promote substantial or complete renal recovery.[11]

Acute Chest Syndrome (ACS) can be caused by sickling of erythrocytes in pulmonary circulation, pneumonias or due to pulmonary edema.[4] It is characterized by fever and respiratory symptoms/signs (e.g. oxygen desaturation, chest pain, tachypnea, dyspnea), accompanied with a new pulmonary infiltrate.[11] If arterial PO2 value becomes less than 75 mm Hg then clinician should consider prompt simple transfusion, or exchange transfusion.[11]

Hyperbilirubinemia in SCA can lead to increase in both direct and indirect bilirubin. Intrahepatic sickling referred as “Sickle hepatopathy” or “hepatic crisis” refers to an intrahepatic cholestasis or may be defined by a total serum bilirubin concentration more than 13 mg/dl, not explained by severe acute haemolysis, viral hepatitis, extrahepatic obstruction or hepatic sequestration.[11,12]

Plasmodium vivax infestation, in present case, further worsened the condition. Hb-S supposed to confer protection against plasmodium falciparum, but the protective effect of Hb-S is not universal against all species of plasmodium. Plasmodium falciparum infected RBCs express a surface protein called PfEMP1 (Plasmodium falciparum Erthrocytes Membrane Protein 1). PfEMP1 allows infected RBCs to adhere to vascular endothelial cells. This causes sequestration of infected RBCs in small blood vessels and contribute to severe malaria in normal persons. While Hb-S containing RBCs have reduced expression or display of PfEMP1 and reduced adhesive properties. That confers protection against p.falciparum to sickle red cells. Plasmodium vivax invades reticulocytes. In reticulocytes a major pathway involves the interaction between the parasite’s Duffy – binding protein (PvDBP) and the Buffy antigen receptor for cheomokines (DARC) on reticulocytes. The sickle haemoglobin mutations does not eliminate these receptors. Therefore p.vivax can still invade susceptible reticulocytes on individuals with sickle cells disease.[4,13]

Plasmodium vivax malaria in SCA needs complete eradication, due to its relapsing nature. In this regard primaquine is the treatment of choice.[4,13] Exchange transfusion has a dual indication in these patients of SCA with malaria. It permits simultaneous parasitic clearance and removal of sickled cells.[4,14]

Early recognition of severe cases and aggressive exchange transfusion is critical for the patients with severe SCA and having evidence of multi organ failure (MOF). [2]Majority of patients (70%) with SCA require blood transfusions in their clinical course. Approximately thirty percent require exchange transfusion for varied indications. [1] The goal of RBC transfusion is to decrease HbS levels less than 30% and maintain the patient’s haematocrit at less than 30%.[3] In SCA transfusion can be administered through three methods, depending on clinical consideration and feasibility. Simple transfusion (transfusion of allogenic packed red blood cells), manual red cell exchange (autologous whole blood phlebotomy, alternating with allogenic red blood cells and fluid infusion), or automated red cells exchange (removal of autologous red blood cells and with allogenic red blood cells replacement in an apheresis device). [3]In a cohort of patients, studied by Alsharai E, most patients undergoing transfusion in acute settings were treated with exchange transfusions, while simple transfusions were primarily reserved for cases on prophylactic regimens with low haemoglobin. [1]

The choice of performing exchange transfusion is partly dependent on the indication. Acute indications include acute stroke,acute chest syndrome(ACS) ,acute multi-organ failure (MOF),intrahepatic cholestasis, heptic/splenic sequestration and priapism. Chronic indications include stroke prophylaxis, silent infarcts, recurrent ACS, recurrent painful episodes and complicated pregnancy. Elective transfusions are also required pre-operatively.[3]

Although automated and manual red cell exchange (RCE) requires more red cells units than simple transfusion (ST), their advantage is the ability to more rapidly achieve a low HbS level without an increase in

haematocrit or total blood volume. Simple top-up transfusions can lead to a substantial rise in haematocrit and whole blood viscosity, an exchange transfusion reduces the concentration of rigid sickle cells while maintaining a controlled overall haematocrit. Iron loading, hyperviscosity and transfusion associated cardiac overload can thus be minimized. RCE has also been shown to result in an increase in arterial oxygen pressure.[1,3,11]

In recent years, the approach to transfusion management has evolved, with a growing emphasis on exchange transfusion. [1,3,15,16] Studies revealed prompt favourable results in patients of SCA with MOF.[5] Bhatwadekar SS, et al (2020) reported manual exchange transfusion in 32% patients of SCA. All of them recovered completely with less than five sessions.[17] Sahoo D, et al (2015) reported favourable outcome, of red cells exchange therapy, in patients of SCA, with VOC. These patients were not responding to standard pain management. [18] In addition to red cell exchange, plasma exchange is in another synergistic potion in SCA. It has shown to decrease the risk of refractory vaso occlusion and MOF. [9]

In present case small vestigial spleen was noted on abdominal scan. Hyposplenism is an important complication of SCA). It develops because of repeated sickling and vaso-occlusion within the splenic microcirculation, resulting in progressive splenic infarction, fibrosis and eventual loss of splenic function (Auto-splenectomy). This leads to repeated infections (most importantly by capsulated organisms) and impaired immunity.[21,22]

In conclusion, the management of SCD continues to be supportive and includes hydration, pain relief, blood transfusion and psychological support. However, transfused red cell are liable to increase blood viscosity, potentially reducing blood flow, if the haemoglobin level rises above 10 g/dl. Therefore, if the goal is an acute reduction in the proportion of sickled red cells, in addition to an increased in oxygen-carrying capacity, exchange transfusion is the therapy of choice.[5]

Manual exchange transfusions is a cost effective intervention to decrease morbidity and mortality in SCA cases. But, perhaps, it is an underutilized therapy.[17,19] It seems that exchange transfusion is mostly delayed for clinical reasons, trying to rule out other disorders or contributing factors and when the exchange therapy is initiated the patient is already in the intensive care setting.[5]

Clinical management of patients of SCA should be centered in rapid clearance of triggering factors, blood/exchange transfusions, careful parenteral hydration, broad spectrum antibiotics and general support measures.[4,15,20] In patients of SCA, with multi-organ failure, red cells exchange transfusion is effective modality and should be initiated as soon as possible.[5]

There are variabilities in transfusion practices, particularly concerning decisions to use simple versus exchange transfusions. Minimal exposure to SCA led to inadequate management protocols in our set up. It is required to establish standardized algorithms in the management of SCA

Conclusion

AOCD was the predominant subtype of normochromic normocytic anemia in adults and was concentrated in the middle-aged, whereas MDA predominated among adolescents and young adults of both genders and was associated with more severe anemia. Age is therefore a useful guide in the evaluation of NNA: a normocytic blood picture in a young patient should prompt peripheral smear examination and assessment of iron, vitamin B12 and folate status, while NNA in middle-aged adults should prompt a search for underlying chronic disease. Larger community-based studies including older adults and advanced iron markers are recommended.

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