Case Report

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Hepatic Encephalopathy Precipitated by Sickle Cell Crisis in a Patient with Chronic Hepatitis C Undergoing Automated Exchange Transfusion: A Rare Case Report

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ABSTRACT

Hepatic involvement in Sickle Cell Disease (SCD) encompasses a broad spectrum known as sickle cell hepatopathy, ranging from self-limiting acute hepatic crisis to fatal Sickle Cell Intrahepatic Cholestasis (SCIC). In patients with co-existing Hepatitis C (HCV), chronic liver damage significantly reduces hepatic reserve, predisposing them to Acute-on-Chronic Liver Failure (ACLF) during a Vaso-Occlusive Crisis (VOC). This case highlights a scarcely reported and an exceptionally rare presentation of Hepatic Encephalopathy (HE) triggered by sickle cell crisis in patient with known HCV, requiring emergent intervention. An 18-year-old male patient with known history of Homozygous Sickle Cell Anaemia (HbSS) and chronic Hepatitis C presented with severe VOC, progressive jaundice and altered mental status. Clinical evaluation revealed features of overt HE, acute liver decompensation and sickle cell crisis. Laboratory findings revealed marked hyperbilirubinaemia, elevated transaminases, prolonged Prothrombin Time /International Normalised Ratio (PT/INR). Imaging confirmed hepatomegaly without biliary obstruction, while the high Haemoglobin (Hb) S pointed toward sinusoidal sickling as acute driver of hepatic failure. Due to severity of hepatic failure and life-threatening nature of illness, the patient underwent Automated Red Cell Exchange (A-RCE) which rapidly reduced HbS, alleviating sinusoidal obstruction and improving hepatic perfusion. Standard medical management for encephalopathy was concurrently administered. Following A-RCE, the patient showed dramatic clinical and neurological improvement within 48 hours and liver enzymes showed a steady downtrend. This case underscores that A-RCE is a critical, life-saving modality for managing acute hepatic failure in SCD, particularly when compounded by chronic viral hepatitis and thus should be considered first-line to prevent irreversible multi-organ failure.

Keywords: Sickle cell anaemia, Sickle hepatopathy, Sinusoidal obstruction

CASE REPORT

An 18-year-old male presented to the emergency department with altered sensorium, progressive jaundice and generalised body pain for three days. He was a diagnosed case of Homozygous Sickle Cell Anaemia (HbSS) (diagnosed 12 years back but not on any treatment) and chronic hepatitis C infection {HCV Ribonucleic Acid (RNA) positive} (diagnosed 7 years back). Fibroscan done at the time of diagnosing HCV showed Liver stiffness measurement of 15.1 kPa for which he was advised tablet Sofosbuvir 400 mg and tablet Daclatasvir 60 mg but patient did not start the treatment due to financial restraints. Past history of recurrent VOC since childhood along with multiple prior blood transfusions. Personal history of alcohol intake or hepatotoxic drug use was negative. On examination, pulse was 110/min, BP 110/70 mmHg, Icterus and pallor were present, Glasgow Coma Scale (GCS) E2V3M4, Asterixis positive, Hepatomegaly with right upper quadrant tenderness present. His investigations were as tabulated in [Table/Fig-1]. His Anti-HCV Immunoglobulin M (IgM) was positive and HCV RNA was negative. Lactate Dehydrogenase (LDH) level was 300 U/L. Ultrasound of abdomen revealed hepatomegaly with coarse echotexture. Computed Tomography (CT) Brain was suggestive of multiple, small, bilateral scattered punctate white matter hypodensities.

Parameters	Before exchange transfusion	After exchange transfusion
Haemoglobin	6.2 g/dL	9.7 g/dL
WBC count	13,000/cumm	8,000/cumm
Platelet count	1,56,000/cumm	1,84,000/cumm
S. Ammonia	64 µg/dL	14 µg/dL
PT (INR)	2.28	1.3
S. Creatinine	1.1 mg/dL	0.8 mg/dL
Bilirubin (Total/Direct/Indirect)	7.5/2.7/4.8 mg/dL	1.1/0.6/0.5 mg/dL
SGOT	3234 U/L	42 U/L
SGPT	3286 U/L	48 U/L
Lactate dehydrogenase	300 U/L	180 U/L
HbS (area %)	75.5%	16.5%
HbF (area %)	18%	4.2%

[Table/Fig-1]: Investigation reports before and after the automated exchange transfusion.
SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase
HbF: Foetal haemoglobin

Distinguishing sickle hepatopathy from other causes of acute liver dysfunction is clinically challenging. Differential diagnoses include viral hepatitis flare (exhibits direct hyperbilirubinaemia), sepsis-related cholestasis (exhibits raised alkaline phosphatase), drug-induced liver injury, ischaemic hepatitis (exhibits very high LDH) and acute liver failure (exhibits very high LDH). The presence of markedly elevated indirect bilirubin, transaminases, coagulopathy and hyperammonaemia in conjunction with altered mental status supported the diagnosis of HE secondary to acute sickle hepatopathy rather than isolated viral hepatitis exacerbation.

Based on clinical, biochemical and radiological findings, a diagnosis of HE secondary to acute sickle hepatopathy precipitated by VOC in the background of chronic hepatitis C infection was made. The patient was managed in the intensive care unit with airway

protection and supportive care, syrup lactulose 30 mL twice daily (titrated for 4-5 loose stools daily) and rifaximin (550 mg twice daily) for HE, broad-spectrum antibiotics and correction of coagulopathy. Given the worsening encephalopathy and rising bilirubin levels, the patient underwent single cycle of A-RCE transfusion (one litre volume exchanged with five red cell concentrates, done over three hours on the next day of admission, within two hours of obtaining consent), targeting HbS <30% which eventually led to improvement in oxygen-carrying capacity, reduction of sickling-related hepatic ischaemia and marked neurological improvement within 48 hours, along with gradually progressive normalisation of liver function tests. There were no complications related to automated transfusion (viz., hypotension). Tachycardia settled within 24 hours of this treatment to within normal limits. Blood pressure was 110/70 mmHg post-exchange transfusion and was within normal limits till discharge. His reports after automated transfusion were as described in [Table/Fig-1].

He was discharged in a stable condition with plans for antiviral therapy for hepatitis C, continuation of syrup lactulose 30 mL after dinner and rifaximin 550 mg twice daily after meals to prevent recurrence of HE regular haematology follow-up and counselling regarding transfusion-related delayed complications. On follow-up after five days, patient had normal haemodynamic parameters, with absolutely normal neurological assessment and his repeat Hb was 9.7 g/dL with normal liver function test.

DISCUSSION

The HE is an uncommon but life-threatening complication in patients with SCD, particularly in the presence of chronic viral hepatitis [1,2]. SCD is a hereditary haemoglobinopathy characterised by chronic haemolysis, vaso-occlusion and end-organ damage. Hepatic involvement in SCD, collectively termed sickle hepatopathy, ranges from asymptomatic transaminitis to acute liver failure and HE [1,3]. The incidence of HCV in SCD patient ranges from 0.5-1.5% in India. There are four types of sickle cell crisis: 1) veno-occlusive (thrombotic); 2) aplastic; 3) hyperhaemolytic; and 4) sequestration crisis [4]. The veno-occlusive event is the most common type of sickling crisis [4]. Hepatic dysfunction in SCD may arise from intrahepatic sickling, ischaemia, haemolysis, iron overload and coexisting liver diseases such as viral hepatitis [5]. Chronic HCV infection predisposes patients to accelerated liver injury and worsens outcomes during acute sickle crisis. The HE is a potentially reversible neuropsychiatric syndrome arising from impaired hepatic detoxification and altered cerebral neurotransmission [6]. The development of HE in this patient was likely multifactorial. Acute sickle cell crisis results in increased haemolysis and catabolic stress, leading to elevated ammonia production. Concurrent hepatic ischaemia from sinusoidal sickling impairs hepatocellular detoxification capacity. Chronic HCV-related fibrosis further compromises hepatic reserve, limiting the liver's ability to compensate for acute metabolic stress [7]. Additionally, systemic inflammation and oxidative stress during VOC may disrupt the blood-brain barrier and potentiate astrocyte dysfunction, amplifying neuropsychiatric manifestations [8]. A-RCE transfusion represents a cornerstone therapy in severe and life-threatening sickle cell complications. Unlike simple transfusion, exchange transfusion rapidly reduces circulating HbS levels without significantly increasing blood viscosity or iron burden. In cases of acute sickle hepatopathy, exchange transfusion improves hepatic perfusion by decreasing microvascular obstruction, thereby halting ongoing ischaemic damage.

The authors planned for immediate automated exchange transfusion to prevent worsening of acute liver failure further helping overcome HE and sickle crisis. Several case series have reported reversal of acute liver failure and prevention of liver transplantation following timely exchange transfusion [3,9]. Gupta A et al., detailed emergency RCE as a life-saving modality in managing a case of SCA with acute chest syndrome and sepsis in their manuscript [10]. An original article by Daniel MJ et al., showcased automated RCEs as a safe and efficient therapeutic procedure for acute management of SCA before surgery to avoid complications. Here 18 patients with SCD posted for surgery (hemiarthroplasty) were managed well with the single sitting of RCE and also reported RCEs as an underutilised therapy in developing countries [11]. Chowdhry M et al., have reported RCEs as a simple and safe treatment modality for managing acute complications of SCA. They have mentioned that the target Fraction of Cells Remaining (FCR) was achieved in one or two sittings of RCE for all five patients and also commented on this as an underutilised therapeutic procedure [12].

In the present patient, early initiation of automated exchange transfusion resulted in rapid neurological recovery and biochemical improvement, underscoring its therapeutic value. The observed clinical response supports the hypothesis that intrahepatic sickling and ischaemia were the predominant drivers of hepatic dysfunction rather than irreversible viral or cirrhotic damage. Sahoo D et al., reported on four cases of SCA with VOC managed well with simple RCE. They also concluded manual RCEs as an affordable and effective measure to reduce the pain of severe VOC [13].

Here the five important learning points are: a) HE can occur as a manifestation of severe sickle hepatopathy; b) Chronic hepatitis C significantly worsens hepatic outcomes in SCD; c) Automated exchange transfusion is an effective therapeutic strategy in severe cases (rarely reported); and d) Early intervention can prevent progression to acute liver failure; e) Early treatment with sofosbuvir 400 mg+daclatasvir 60 mg for 8-12 weeks (for almost 100% cure of HCV infection) along with hydroxyurea 500 mg once daily with careful monitoring of complete blood count and serum creatinine levels can be ideal treatment regime for stable patients of concurrent HCV with SCD (not in sickle cell crisis or HE).

CONCLUSION(S)

The HE in SCD is an uncommon but potentially fatal complication, particularly when compounded by chronic hepatitis C infection. This case illustrates the complex interplay between acute sickle cell crisis and chronic liver disease, emphasising the pivotal role of automated exchange transfusion in reversing hepatic dysfunction. Early diagnosis and aggressive intervention can be life-saving and may prevent progression to irreversible liver failure. Multidisciplinary management involving hepatology, haematology and critical care teams is essential for optimal outcomes.

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