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# Hepatic Sequestration in Sickle Cell Anemia

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**Hepatic Sequestration in Sickle Cell Anemia**

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**INTRODUCTION**

Sickle cell anemia is a chronic debilitating disease affecting a significant portion of patients of African American origin. These patients present to the physicians with myriad of life threatening complications like acute chest syndrome, septic shock, decompensated congestive heart failure secondary to severe pulmonary hypertension, stroke, and multi-organ failure. However, there are multiple other less common clinical presentations which would require a high index of suspicion. One such condition is hepatic sequestration which though infrequent is potentially life threatening.

The clinical diagnoses of a sickle cell patient with hepatic vaso-occlusion vary from a relatively benign sickle cell hepatic crisis, to a more severe hepatic sequestration, to an extremely fatal sickle cell intra-hepatic cholestasis. [1,2] There is quite a bit of variability and overlap of these entities leading to difficulties in effective management. This case report and the accompanying review, tries to elucidate the clinical presentation, diagnosis, and treatment strategies in adult patients with hepatic sequestration.

**CASE REPORT**

A 38-year-old African American male with a history of sickle cell anemia (hemoglobin SS) presented to the emergency room with a two day history of generalized body pain, shortness of breath and fever. Review of systems was otherwise unremarkable. His past history was significant for acute chest syndrome, iron overload, and pulmonary hypertension. He was alert and oriented, pale and had icterus. His abdomen was distended and a tender liver was palpable 5 cm below the right costal margin.

Initially he was managed conservatively with intravenous hydration and narcotics. His clinical condition deteriorated over the course of the next two days. His hemoglobin dropped (6.3 g/dl to 4.7 g/dL), his liver became extremely tender and increased in size to 10 cm below the costal margin. His total bilirubin (5 to 32 mg/dl), BUN (11 to 60 mg/dl) and creatinine (1 to 3.8 mg/dl) increased. The platelet count plummeted (200,000 to 84,000/microliters) while the reticulocyte count remained elevated (218,000/cu.mm). Schistocytes were not observed on peripheral smear and the coagulation profile remained unchanged.

A clinical diagnosis of hepatic sequestration crisis was made. The patient was managed with exchange red cell transfusions (2 sessions of 1 liter each) and simple transfusions (3 instances of 400 ml each). This approach led to a rapid recovery, hemoglobin stabilized and liver size decreased to 4 cm below the costal margin. Serum bilirubin and creatinine reduced to (5 mg/dl and 1.5 mg/dl).

**DISCUSSION**

PubMed was searched with key words such a hepatic sequestration and sickle cell anaemia, hepatic cholestasis and sickle cell anaemia, hepatic vaso occlusion and sickle cell anaemia, and hepatic crisis and sickle cell anaemia. Only publications that was published after the year 1980 and which were in English were included. A total of 64 non-duplicated records were identified. Both STS and SKM reviewed the records independently for suitability to be

included in the analysis. In all, six manuscripts were identified for hepatic sequestration and summarized in Table 1 (Norris *et al* [3]; Lee *et al* [4]; Koduri *et al* [5]; Hernandez *et al* [6]; Gutteridge *et al* [7]; Hatton *et al* [2]).

The mean age of patients was 26.8 (±5.8). The percentage of male patients was 40 percent. All the patients (4 patients) for whom the genetic information was available were homozygous. One of the cases with hepatic sequestration was precipitated by a Parvo B19 virus infection (Koduri *et al*).[5] The diagnosis of hepatic sequestration was predominantly a clinical diagnosis. The lag period varied from 1 to 5 days from the time of presentation to the time of rapid increase in the liver size. The liver size in patients with hepatic sequestration ranged from 6 cm below the costal margin to the liver extending up to the pelvic brim.

A sudden drop of hematocrit, a characteristic feature of hepatic sequestration was noted in all reported cases of hepatic sequestration. The median drop in hematocrit during the rapid enlargement of liver was 2.5 mg/dl. Lee *et al* reported a sudden increase in hematocrit after the resolution of hepatic sequestration, possibly due to the return of the sequestrated blood back into the circulation (reverse sequestration). [4] This phenomenon was not observed in any of the other cases. The ten cases had a median bilirubin level of 6.4 mg/dl. The AST level was not markedly elevated with a median level of 93.5 IU/L. There was no evidence of encephalopathy or coagulopathy in all the patients. None of the patients reported thus far developed non-oliguric acute renal failure except the new case reported by us in this manuscript.

A liver biopsy was obtained in two of the cases: (1) Hernandez *et al* (Case 3) observed a liver with markedly dilated sinusoids packed with sickled RBCs [6] and (2) Gutteridge *et al* noted a normal liver architecture with non-caseating granulomas and hepatic sinusoids containing sickled red blood cells. [7] Two of the patients with hepatic sequestration succumbed to their illness.[4,6] Similar to our patient, both of them developed severe hemodynamic instability after hospitalization, but unlike our patient, they were not managed with exchange transfusions. One of them was given only supportive care. [6] The other patient received multiple simple blood transfusions and later developed reverse sequestration and died. [4]

The present review is a retrospective literature review with cases reported from different clinical institutions. We by ourselves did not set any diagnostic criteria and instead relied on the diagnoses as reported by the original authors of the case reports. Due to the potential overlap with relatively benign sickle cell hepatopathy and sickle cell intra-hepatic cholestasis, there is a potential for erroneous classification of the cases due to variance in the diagnostic criteria set by differing reporting clinicians. Our review was limited to patients with adult cases, the manifestation and management of these conditions in pediatric patients could be variable. We are of the opinion that hepatic sequestration is more prevalent than reported making reporting bias a potential confounding factor. A prospective review from institutions with experience in management of a high volume of cases with sickle cell disease would further help in delineation and management.

**Conclusion**

In summary, hepatic sequestration is a relatively rare, but potentially life threatening complication of sickle cell disease in adults. There needs to be a high index of clinical suspicion among physicians to identify this condition. Early expert hematology consultation and aggressive and appropriate therapy with exchange transfusion may be essential for survival.

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**Table 1:** Literature Review of Acute Hepatic Sequestration

| Author (Year) | Genetics | Sex | Age | L.Size | T.Lag | Bili. | AST | ΔHb | Mgmt | Out come |
|---|---|---|---|---|---|---|---|---|---|---|
| Present case | HbSS | M | 38 | 10 | 2 | 29.5 | 183 | 1.5 | E.T | Non-Fatal |
| Norris *et al* (2004) [3] | NA | M | 29 | 16* | 0 | 49.8 | 58 | NA | E.T | Not Fatal |
| Lee *et al* (1996) [4] | HbSS | F | 33 | 12 | 6 | NA | NA | 3.4 | S.T. | Fatal |
| Koduri *et al* (1994) [5] | NA | F | 22 | 16 | 5 | NA | 30 | 1.4 | S.T | Non-Fatal |
| Hernandez *et al* (1989) [6] | NA | M | 25 | PB | 0 | NA | NA | NA | S.T. | Fatal |
| Hernandez *et al* (1989) [6] | NA | M | 27 | 6 | 4 | 8 | NA | 1.3 | N.T. | Non-Fatal |
| Hernandez *et al* (1989) [6] | NA | F | 28 | 10 | 2 | 6.1 | NA | 3.5 | S.T | Non-Fatal |
| Gutteridge *et al* (1985) [7] | NA | F | 26 | PB | 3 | 1.9 | 97 | NA | E.T | Non-fatal |
| Hatton *et al* (1985) [2] | HbSS | F | 22 | 12 | 3 | 6.4 | 90 | 2.5 | S.T. | Non-Fatal |
| Hatton *et al* (1985) [2] | HbSS | F | 18 | 14 | 3 | 1.8 | 120 | 3.5 | S.T. | Non-Fatal |

T.Lag: Time lag of enlargement of liver; L.Size: Liver Size by palpation below costal margin in centi meters; * Liver Span by percussion in centi meters; Bili: Highest Total Bilirubin in mg/dl; ΔHb: Change in hemoglobin in g/dl; M: Male; F: Female; E.T. : Exchange Transfusion; S.T.: Simple packed red blood cell Transfusion; N.T.: No Transfusion; NA: Not available; AST: Aspartate Transaminase;