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Case Report

CASE REPORT

Splenic sequestration crisis as an index manifestation of heterozygous hemoglobinopathy in an adult

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Abstract

Sickle β^+-thalassemia rarely manifests with acute splenic sequestration crisis in adults. We report a case of a 20-year-old female who presented with fever and left upper quadrant abdominal pain. Laboratory studies revealed hemolytic anemia. Tests for autoimmune hemolysis and hemolytic diseases were negative except for Hemoglobin (Hb) electrophoresis, which revealed sickle cell trait (Hb AS). Infectious workup was unremarkable. Computed tomography scan of the abdomen showed marked splenomegaly. The patient received blood transfusions and empiric antibiotics with no improvement; thus, splenectomy was performed. Pathology specimen revealed peripheral serpiginous infarcts alternating with surrounding acute inflammation and small capillaries plugged with sickle cell shaped red blood cells consistent with splenic sequestration. DNA test later revealed beta-globin mutations consistent with sickle cell-beta$^+$ thalassemia. Post-splenectomy, there was a gradual improvement in her clinical symptoms with concomitant rise in Hb to 10.6 g/dl at discharge.

INTRODUCTION

Sickle cell disease (SCD) causes significant morbidity and mortality, particularly among African and Mediterranean ancestry. The factors responsible for variations in the clinical manifestation of SCD patients are the presence of alpha-thalassemia mutation, fetal hemoglobin (Hb) and β-globin gene haplotype [1]. Beta-thalassemia results from impaired production of beta globin chains. It has an estimated rate of heterozygosity in the population of ~13% in Africa, 4% in Asia and 2% in the USA [2]. Acute splenic sequestration crisis (ASSC) is a well-recognized complication in children with SCD but is a rare manifestation in adults with sickle β^+-thalassemia, and reports are sporadic. It is also not known to occur as a first presentation of the hemoglobinopathy. We report a case of a young female without any significant medical history who presented with symptoms consistent with ASSC and found to have S-β^+ thalassemia.

CASE REPORT

A 20-year-old Guyanese female of Indian descent with no significant medical history presented with a 5-day history of fever and left upper quadrant abdominal pain. This was associated with chills, generalized weakness and abdominal distension. She reported dark brown urine and yellowish discoloration

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of her eyes but denied nausea, vomiting or change in bowel habits. She had no previous history or family history of anemia, sickle cell disease or any hemoglobinopathy. Vital signs revealed fever with a temperature of 103F and tachycardia. Physical examination was remarkable for conjunctival icterus, abdominal distension, left upper quadrant tenderness and splenomegaly, which was palpable about 12 cm below the left costal margin. Laboratory studies revealed Hb of 6.5 (11.5–15.5) g/dl, hematocrit of 19 (34.5–46.5)%, mean corpuscular volume 64.8 (79.0–95.0) fl, mean corpuscular Hb 22.2 (26.0–32.0) pg and elevated leukocyte count of 14.72 (4.0–11.0) K/uL with a left shift. Iron and total iron binding capacity were low 28 (37–170) ug/dl and 168 (265–497) ug/dl, respectively, and ferritin elevated: 737 (6.2–137) ng/ml. Lactate dehydrogenase (LDH) was elevated 3420 (313–618) u/l with decreased haptoglobin <15 (43–212) mg/dl, and elevated reticulocyte percentage 7.5% (0.5–2.5)%. Liver function test revealed hyperbilirubinemia. Peripheral blood smear showed markedly hypochromic microcytic red blood cells and target cells with increased reticulocytes. Blood culture, urine culture, tests for human immunodeficiency virus, cytomegalovirus, Epstein–Barr virus, Echinococcus, Toxoplasma, Malaria, Babesia, Bordetella, Brucella, Coxiella, Leptospirosis, Hepatitis and acid fast bacilli were negative. Computed tomography (CT) scan of the abdomen with contrast revealed massive splenomegaly (22 cm) with a markedly abnormal appearance, consisting of circumferential peripheral and centrally diffuse infiltrative cystic attenuation within the parenchyma (Fig. 1). Also, mild hepatomegaly and multiple non-obstructing gallstones were noted (Fig. 2). An acute hemolytic anemia was suspected based on the clinical presentation, hyperbilirubinemia, elevated LDH, hemosiderinuria and decreased haptoglobin. Coomb's test for autoimmune hemolysis was negative as was osmotic fragility test and G6PD assay. Sickling test done was positive and Hb electrophoresis revealed sickle cell trait (AS) with Hb percent consisting of HbA-48% (>96%), HbS-26.8% (0.0%), Hb F-24.0% (<2%) and normal HbA2–1.2% (<3.3%). DNA test for beta globin gene mutation was pending. She was initially managed conservatively with blood transfusion and empiric antibiotics. Symptoms persisted despite supportive treatment; therefore, splenectomy was performed on Day 5 of admission. Pathologic examination of the spleen demonstrated a spleen weighing 1183 gm and measuring 25x14.5x7 cm with peripheral serpiginous yellow infarcts (Figs 3 and 4), acute inflammation surrounding the infarcted areas and small capillaries plugged with sickle cell shaped red blood cells consistent with splenic sequestration (Figs 5 and 6). Postoperatively, there was a gradual improvement in her clinical symptoms and improvement of Hb to 10.6 g/dl. She was then discharged home with appropriate follow-up. At presentation to clinic 2 weeks later, she was completely asymptomatic. DNA test for beta globin gene mutation revealed heterozygous positive for HbS and c.380_396de117 beta-globin mutation consistent with a diagnosis of sickle cell-beta^{+} thalassemia.

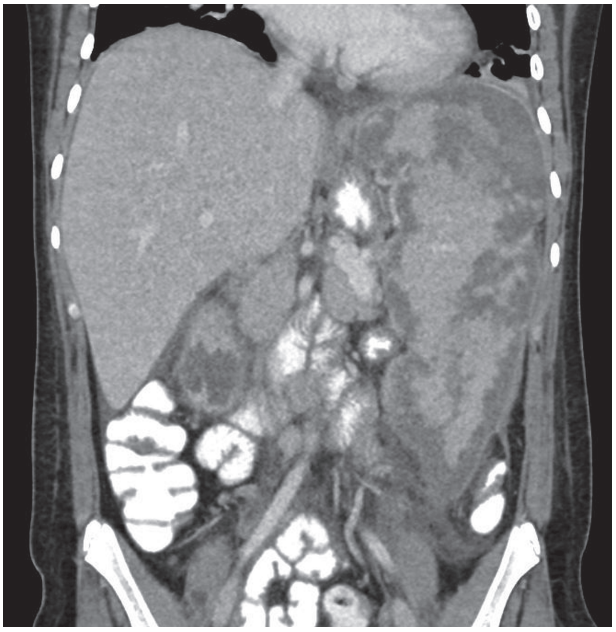

Figure 1: Coronal section of CT abdomen with contrast showing massive splenomegaly.

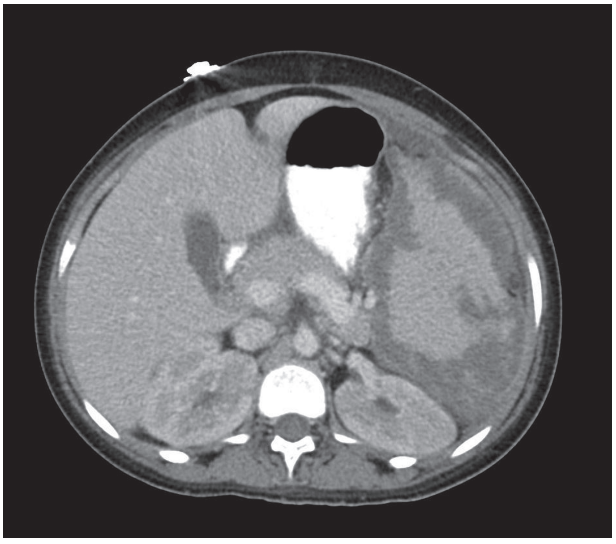

Figure 2: Axial section of CT abdomen with contrast showing massive splenomegaly.

DISCUSSION

ASSC and acute splenic infarction are sequelae of sickle Hb disorders. It presents with splenomegaly followed by a sudden drop in Hb. This phenomenon is known to occur in children with sickle cell disease (Hb SS) and adults with Hb SC but occurs rarely with sickle cell-beta thalassemia (Hb S-β thalassemia) [3] despite the common finding of splenomegaly in these patients [7]. According to various case reports the association of S-β thalassemia with splenic sequestration crisis is uncommon [4]. Based on the complete absence or reduced amounts of beta globin chains, S-β thalassemia is categorized to sickle cell-beta^{0} thalassemia and sickle cell beta^{+} thalassemia, determined by the level of HbA. The clinical and hematologic severity of S-β thalassemia is an inverse function of HbA quantity [5]. HbA is absent in Hb S-β^{0} thalassemia and has more severe clinical course, similar to SS disease. Hb S-β^{+} thalassemia usually has 20–30% of HbA and a milder clinical course [6]. This may possibly explain the late onset sickling phenomenon and few sickling crises afterward. The quantity of HbA in our patient was 48%, which is higher than the reported average and might explain the lack of clinical symptoms until adulthood. There are no apparent precipitating factors for S-β thalassemia associated ASSC in adults [7], even though some hypothesize that high altitude and infections

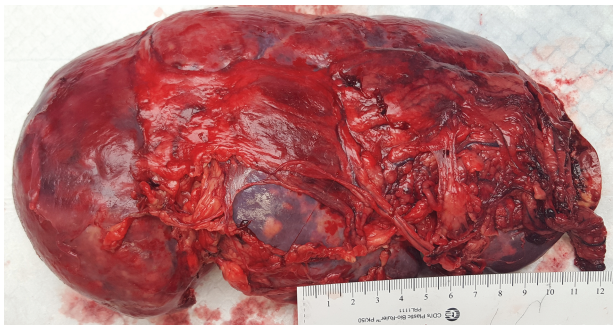

Figure 3: Spleen showing subcapsular paler areas corresponding to underlying infarcts.

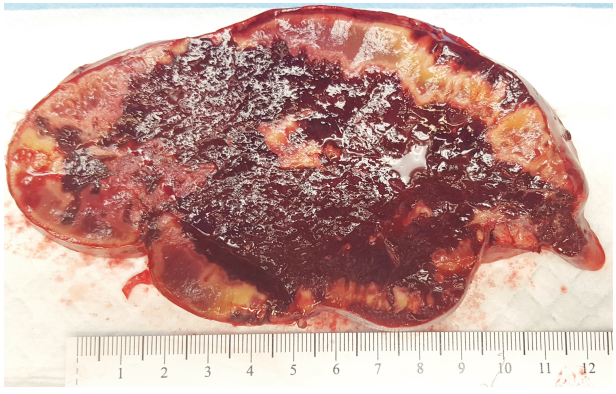

Figure 4: Cross section of the spleen showing peripheral serpiginous yellow infarcts.

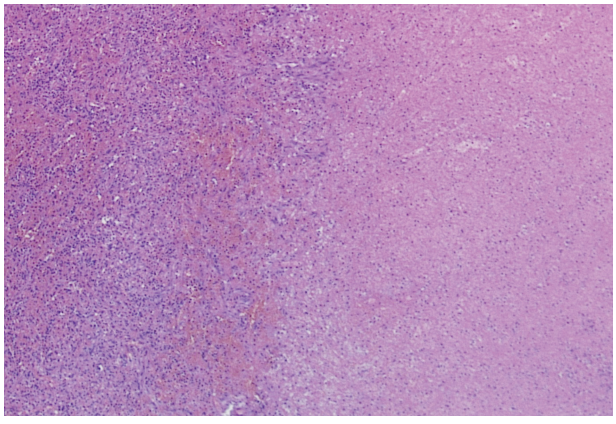

Figure 5: H&E, 40x. Viable splenic tissue (left) with adjacent infarct (right).

can precipitate the crisis. In our patient, there was no obvious precipitating factor. Several authors have implied a possible relationship between the acute splenic sequestration syndrome and massive splenic infarction [3, 8]. Sickling of erythrocytes in efferent channels of the spleen sets off a chain reaction that progressively involves more afferent channels until the entire spleen is infarcted [3]. The findings of substantial infarction at the time of splenectomy, which occurred in this patient as shown in Fig. 3, is unusual as it has rarely been reported in the literature. Diagnostic modalities include 99mTc/sulfur colloid scan, which shows complete lack of splenic uptake, or CT scan, which may reveal multiple, peripheral, non-enhancing low-density areas or large diffuse areas of low density in the majority of the

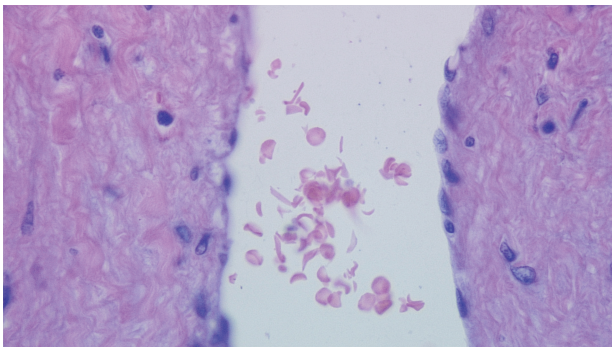

Figure 6: H&E, 600x. Splenic vessel with red blood cells, some of which are sickle-shaped.

splenic tissue [8] as demonstrated in Fig. 1. Pathologic examination of the spleen during ASSC reveals marked splenomegaly, with weights, reported up to 1870 grams [8]. The spleen in our patient weighed 1183 grams. Microscopic examination shows extensive pooling of red blood cells within the splenic cords with extensive sickling and numerous areas of necrosis and infarction as also seen in our patient. Supportive care with blood transfusion, intravenous fluids, oxygen and pain control can reduce the severity of the crisis. In cases with recurrent splenic sequestration crisis, splenectomy can be an option for those who achieve remission following the recurrence [9, 10]. Splenectomy can also be considered in cases of double heterozygous sickle hemoglobinopathies with ASSC and suspicion for massive splenic infarction which fail to show clinical improvement following blood transfusions [3], as was the case in our patient.

In conclusion, this case highlights the wide variety of clinical phenotype encountered with S-$\beta+$thalassemia. Severe complications such as ASSC causing massive splenomegaly is rare in HbAS/B^{+} thalassemia, more so as an initial manifestation of the disease in an adult without any prior history or symptoms of anemia. A high index of suspicion should therefore be maintained in such clinical scenario to minimize unnecessary testing and ensure prompt and appropriate management.

CONFLICT OF INTEREST

No conflict of interest reported by each author.

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ETHICAL APPROVAL

No institutional review board (IRB) approval was needed. Exempt from IRB approval.

CONSENT

Patient given written consent for writing and publication for this case report.

GUARANTOR

Eseosa Edo-Osagie is the guarantor of the article.

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