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Splenic Sequestration Crisis As An Index Manifestation Of Heterozygous Hemoglobinopathy: A Case Report.

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ABSTRACT

Sickle β+-thalassemia rarely manifests with acute splenic sequestration crisis. We report a case of a 14-year-old female with no previous significant history, who presented with fever, icterus, left and right upper quadrant abdominal pain. Laboratory studies revealed hemolytic anemia. Tests for autoimmune hemolysis were negative, peripheral blood smear was suggestive of normocytic normochromic RBC's with sickled cells, tests for hemolytic diseases such as sickling test was positive and Hemoglobin (Hb) electrophoresis, which revealed sickle cell thalassemia (Hb A1 C). Infectious workup was unremarkable. Computed tomography scan of the abdomen showed marked splenomegaly with multiple splenic infarcts. Patient was diagnosed as a case of sickle cell thalassemia.

Keywords: Sickle β+-thalassemia, acute splenic sequestration crisis, Hemoglobin (Hb) electrophoresis

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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 F) 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 patients 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 14-year-old female of Indian descent with no significant medical history presented with a 5-day history of fever for 5 days, on and off, associated with chills and not associated with rigors, icterus since 3 days, left and right upper quadrant abdominal pain since 3 days. This was associated with chills, generalized weakness and abdominal distension. She reported high coloured urine and yellowish discoloration of her eyes but denied nausea, vomiting or change in bowel habits. She had no previous history of blood transfusions or family history of anaemia, sickle cell disease or any hemoglobinopathy. Vital signs revealed a BP of 90/60 mmhg, PR- 142/min in sinus tachycardia, respiratory rate of 36/min, spo2- 90% at room air and was febrile with a temperature of 103F. Physical examination was remarkable for conjunctival icterus, abdominal distension, left upper quadrant tenderness, hepatomegaly and splenomegaly, which was palpable about 13cm below the right costal margin and 14cm below the left costal margin respectively.

Laboratory studies revealed Hb of 2.6 (11.5–15.5) g/dl, hematocrit of 7.7 (34.5–46.5)%, mean corpuscular volume 81.9 (79.0–95.0) fl, mean corpuscular Hb 27.7 (26.0–32.0) pg and elevated leukocyte count of 15.17 (4.0–11.0) K/uL with a left shift. Iron and total iron binding capacity were within normal limits of 90 (37–170) ug/dl and 208 (265–497) ug/dl, respectively, and ferritin elevated: 1000 (6.2–137) ng/ml and serum vitamin b12 of 159 pg/ml. Lactate dehydrogenase (LDH) was elevated 5000 (313–618) u/l and elevated reticulocyte percentage 3.4% (0.5–2.5)%. Liver function test revealed indirect hyperbilirubinemia of 7.2 mg/dl and slightly raised liver enzymes. Peripheral blood smear showed markedly normocytic normochromic red blood cells admixed with macrocytic RBC's and severe anisopoikilocytosis and tear drop cells, sickled cells and few schistocytes seen with the impression of severe hemolytic anemia with thrombocytopenia. Her direct and indirect coombs test was negative, sickling test was positive. Patient was provisionally diagnosed as case of hemolytic anemia. Urine culture, tests for human immunodeficiency virus, Malaria, dengue, Leptospirosis, Hepatitis and acid fast bacilli were negative. Blood culture was suggestive of staphylococcus aureus sensitive to clindamycin, chloramphenicol and linezolid. Computed tomography (CT) scan of the abdomen with contrast revealed splenomegaly (14 cm) with diffuse hypodense areas noted predominantly involving the entire spleen, not showing enhancement on all phases suggestive of splenic infarcts. Also, mild hepatomegaly and multiple non-obstructing gallstones were noted.

HB Electrophoresis

Hemoglobin electrophoresis was sent out to a reference lab and results are shown in Table below.

	PATIENT RESULTS	REFERENCE RANGE
HEMOGLOBIN A1 (Hb A)	9.5%	70-96
HEMOGLOBIN A2 (Hb A2)	4.4%	1.5-3.5
HEMOGLOBIN F (Hb F)	35.8%	0.2-2.0
HEMOGLOBIN S (Hb S)	48.8%	-

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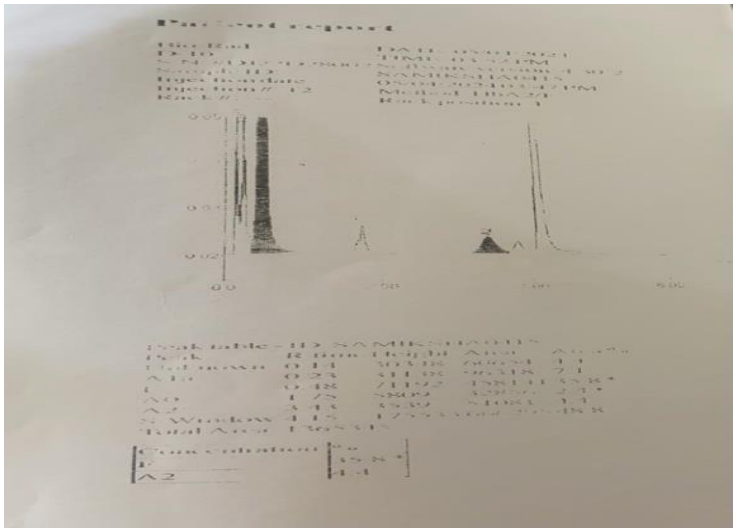
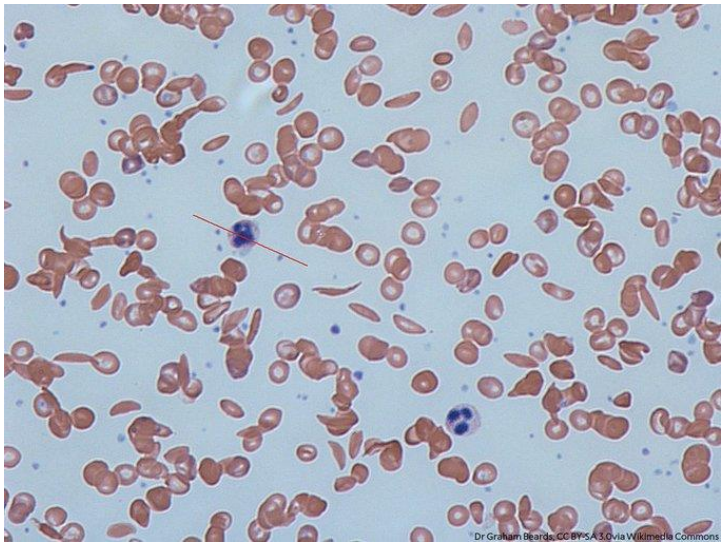
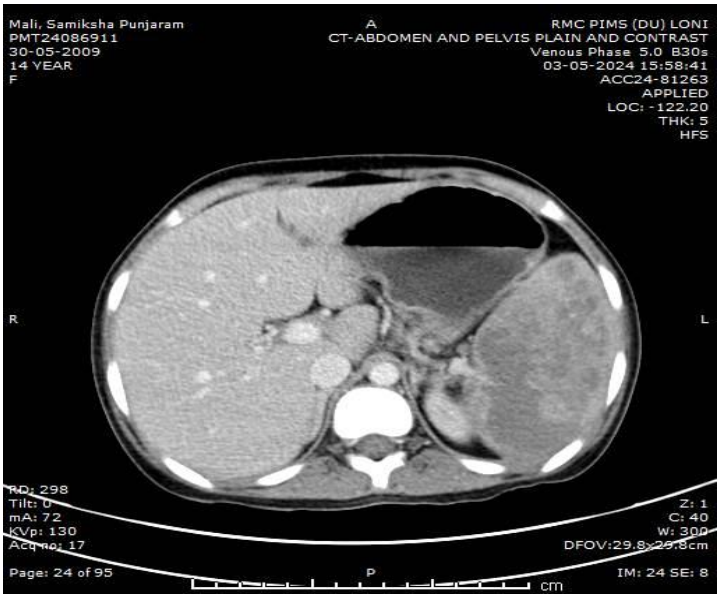


Peripheral blood smear showing sickled RBC's



CECT of Abdomen And Pelvis



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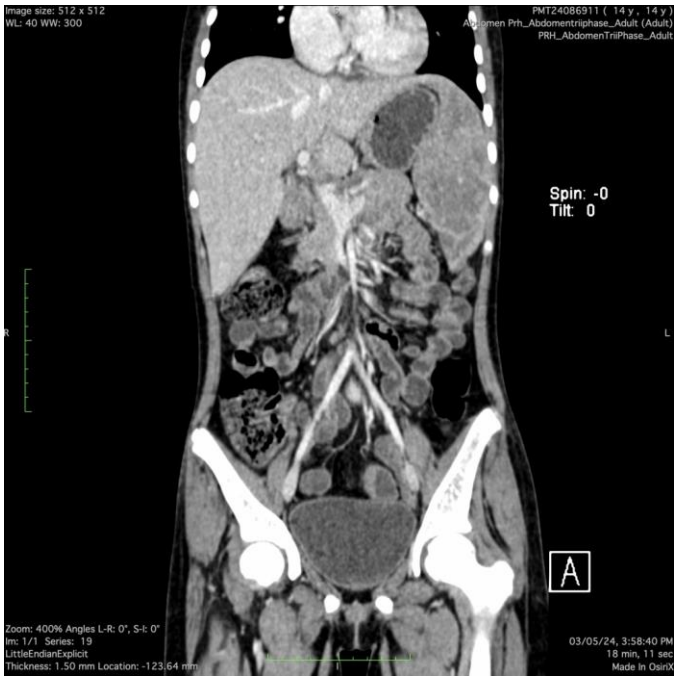
Coronal section of CT abdomen with contrast showing splenomegaly.



Axial section of CT abdomen with contrast showing massive splenomegaly.

DNA test for beta globin gene mutation was pending. She was managed conservatively with blood transfusion and empiric antibiotics, adequate hydration, folic acid and multivitamins followed by antibiotics according to her culture senstivity and was discharged on hydroxyurea.

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) 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-beta0 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-βo 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 9.5%, which is lower than the reported average but the quantity of hbF was 35.4 % that is higher than the average which might explain the late presentation of the disease, with an apparent precipitating factor being the blood borne infection with staphyloccus aureus. Several authors have implied a possible relationship between the acute splenic sequestration syndrome and massive splenic infarction [3]. 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]. 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. 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], In conclusion, this case highlights the wide variety of clinical phenotype encountered with S-β + thalassemia. Severe complications such as ASSC causing massive splenomegaly is rare in HbAS/B+ thalassemia, more so as an initial manifestation of the disease 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.

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