Case Report

Hemoglobin SS Nigerian Woman First Diagnosed at the Age of 52 years with Manifestation Mimicking Tuberculosis of the Spine

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Abstract

Sickle cell anemia (SCA) is an inherited disorder of hemoglobin due to the presence of abnormal hemoglobin in a homozygous state. Manifestation is usually in infancy or early childhood due to gradual decrease in hemoglobin F level as age advances. Diagnosis in middle age is unusual. We present a woman who was diagnosed of SCA for the first time at middle age. The aim was to bring to the knowledge of physicians that patients with SCA can also present late so high index of suspicion is required to make diagnosis. A 52-year-old woman presented to orthopedic clinic with complaints of generalized bone pain and low back pain. There was no history of trauma prior to the onset of the pain. There was no associated fever, weight loss, loss of appetite, nor weakness of the lower limbs. X-ray of the spine done showed wedge collapse of the 12th thoracic and first lumbar vertebrae with posterior angulation of the thoracolumbar junction giving dorsal kyphosis. Her mode of presentation raised a suspicion of tuberculosis of the spine to rule out multiple myeloma. However, investigations for tuberculosis and multiple myeloma were all negative. This necessitated the investigation for SCA and the diagnosis was confirmed. The diagnosis of SCA is usually made in infancy or early childhood. High index of suspicion is required to make the diagnosis at middle age.

Keywords: Hemoglobin SS, late diagnosis, sickle cell anemia

Introduction

Sickle cell anemia (SCA) is an inherited disorder of hemoglobin due to the presence of abnormal hemoglobin in a homozygous state. Clinically, SCA is characterized by episodes of acute illness referred to as crisis and progressive end-organ damage and disfunction.[1] The World Health Organization has designated sickle cell disease (SCD) as a global public health problem.[2] Over 300,000 infants with SCD are born annually; and about 70% of the affected births are in sub-Saharan Africa, where access to medical care and public health strategies to decrease the mortality and morbidity are not uniformly available.[2]

Nigeria has the highest population of people affected with SCA in the world with prevalence that ranges from 2% to 3% and contributes substantially to child morbidity and mortality.[3] About 25% of the population has the sickle cell trait, and about 150,000 births are affected annually by sickle cell disorder.[3] SCA is caused by a mutation in the S-globin gene located on the short arm of chromosome 11, in which adenine replaces thymine in the 17th nucleotide resulting in glutamic acid being replaced by valine in the 6th position of β-globin chain. In deoxygenated state, the sickle hemoglobin (HbS) precipitates and forms crystals which grow and form polymers within the erythrocyte, thereby distorting its wall architecture, shape, and malleability.[4] This results to change in shape of the affected erythrocyte from the normal biconcave to sickle shape from where this disorder derived its name. This change in architecture makes the red blood cells less flexible to pass through microvasculature easily and are, therefore, vulnerable to destruction (hemolysis)

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by the reticuloendothelial cells as well as entrapment in the microcirculation (vaso-occlusion) with resultant anemia and infarction in various organs, respectively.[4] The rate and extent of polymerization is dependent on certain factors such as hypoxia, concentration of HbS, and the amount of fetal hemoglobin (HbF) in the erythrocyte.[5]

SCD can present with remarkably different clinical courses, varying from death in childhood, to recurrent painful vasooclusive crises and multiple organ damage in adults, to being relatively well.[5] Usually, HbS is present at birth, but the disease does not manifest until about 6 months of age or less due to high level of HbF at birth which gradually decreases as time progresses.[5] Early diagnosis of the disease in the neonatal period has been shown to improve the quality of life (QOL) and reduce the mortality rate among affected individuals.[6] Studies have shown that the age of diagnosis is usually in infancy or childhood period.[6,7] Diagnosis at middle age is unusual. We, therefore, present an adult female who was first diagnosed at middle age. The aim was to bring to the knowledge of physicians that patients with SCA can also present late and so high index of suspicion is required.

Case Report

A 52-year-old woman weighing 50 kg, 168 cm height with body mass index of 29, presented to orthopedic clinic with complaints of generalized bone pain and low back pain. She developed low back pain 7 years before presentation which she had been managing with over-the-counter drugs. Pain does not radiate to any part of the body. There was no history of trauma before the onset of the pain. There was no associated fever, weight loss, loss of appetite, nor weakness of the lower limbs. Low back pain progressively got worse before she decided to present at the orthopedic clinic. There was mild cough productive of whitish sputum. She was treated with analgesic, antibiotics, and other drugs and she got better. Prior to development of the back pain, she occasionally had generalized bone/body pain, for which she took over-the-counter drugs each time. Due to the repeated presentation to orthopedic clinic with bone pain for which no other cause was found in addition to the incidental finding of anemia, hemoglobin genotype was requested for which reported hemoglobin SS by electrophoretic method. The patient was subsequently referred to hematology clinic for follow-up/expert management. Further investigation was subsequently done with high-performance liquid chromatography (HPLC) which confirmed SCA.

The patient had cholecystectomy in 2011 due to calculous cholecystitis. She is 6 years postmenopausal. Her first confinement was in 1990, pregnancy was uneventful, and she was delivered of a female baby. The second pregnancy was in 1995, and she had miscarriage at 8-week gestational age. Third and fourth (last) confinement was in 1996 and 1999, respectively. Pregnancy was uneventful although the 3rd baby (male baby) died at the age of 2 years from diarrhea disease according to her. The deliveries were all through spontaneous vortex delivery, no cesarean section was done. The patient had never received blood transfusion. All the pregnancies were managed in a maternity home. Her level of education is primary school. She is a civil servant working as a cleaner. She is married with two surviving children. She is the last child of her parents with ten children. Seven died in childhood of febrile illness. She is a known peptic ulcer disease patient. She does not smoke nor take alcohol, not a known hypertensive, diabetic nor asthmatic. Husband is a farmer/petty trader.

Physical examination showed a middle-aged woman in no obvious distress, afebrile to touch, mildly icteric, moderately pale, with no pedal edema and no peripheral lymphadenopathy, had dorsal protrusion of the vertebrae at the thoracolumbar region [Figure 1]. Examination of the chest showed no significant findings. The abdomen was full and moves with respiration, supraumbilical vertical surgical scar (had cholecystectomy due to cholecystitis in 2011), mild epigastric tenderness, and no organomegaly. There was no other significant finding.

Some laboratory investigations done showed the following: Mantoux test was 0 mm, Ziehl–Nelson stain for acid-fast Bacilli was negative, GeneXpert for MTB was negative. Bence–Jones protein in urine was negative, and erythrocyte sedimentation rate (ESR) was 27 mm in 1st hour. Total serum protein, albumin, and globulin were within normal as well as serum calcium. Full blood count reported hemglobin level of 8.6 g/dl, packed cell volume 24%, red cell count of 3.6×10^{12}/L, platelet count of 284×10^{9}/L, and total white blood cell count was 7.3×10^{9}/L with a differential of 53.6% neutrophil, 38.5% lymphocyte, 5.4% monoctye, 2.2% eosinophil, and 0.3% basophil, mean cell volume (MCV) 75 fl (80–100 fl), mean cell hemoglobin (MCH) 24 pg (27–34 pg), and mean corpuscular hemoglobin concentration 32 g/dl (32–37 g/dl). HPLC showed the following results: HbF 8.3% (<1%), HbA2 4.4% (<3.5%), and HbS 82.7%. Biochemical parameters include total bilirubin of 46 (3–21 mmol/l), conjugated bilirubin 28.9 (<8 mmol/L), aspartate transaminase 36 (5–18 IU/L), and alanine transaminase 25 (3–15 IU/L). Urea, creatinine, sodium, potassium, chloride, and bicarbonate were all within reference range. C-reactive protein (CRP): 20.7 mg/L (<8 mg/L), lactate dehydrogenase (LDH): 388 U/L (105–333 U/L), ferritin: 171 ng/ml (12–160 ng/ml), copper: 1.72 umol/L (11–24 umol/L), and zinc: 102.2 ug/dl (11.5–15.5 ug/dl).

X-ray of the lumbosacral spine showed wedge collapse of the 12th thoracic and first lumbar vertebrae with posterior angulation of the thoracolumbar junction giving dorsal Kyphosis around the region [Figure 1]. The bones of the lumbar vertebrae were osteopenic. There was no obvious degenerative changes or paravertebral soft-tissue mass. There was normal alignment for the rest of the lumbar vertebrae. The intervening disc spaces were also normal.

Discussion

SCA usually manifest at infancy or early childhood as the concentration of hemoglobin F begins to fall as it is being replaced with hemoglobin A with advancing age.[7]

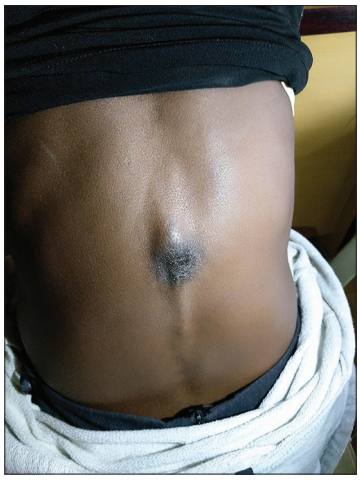

Figure 1: Kyphosis of the vertebrae

Late diagnosis of the disease has resulted in increased mortality in the early lives of individuals with SCA.[7] This case is unusual in that the patient was diagnosed to have SCA for the first time at middle age. She had been relatively stable even without any special care or follow-up; she had never received blood transfusion in the past with no previous hospital admission due to sickle cell crises. It has been reported that the diverse paths and severity of SCA are the result of intrinsic and extrinsic factors ranging from genetic markers, environment, ethnicity, socioeconomic status, religion, and cultural beliefs.[8] These factors affect the QOL of persons who live with SCA.

The patient was found to have high HbF level as well as high HbA2 level. These may have contributed to her clinical stability as high HbF level, and beta thalassemia trait have been reported to ameliorate the effect of SCA.[9] The patient also had high zinc level and low copper level. The high zinc level may be a result of hemolysis which releases zinc within the red blood cell into the plasma. High zinc level has been associated with low copper level since both of them compete for the same binding site. The previous studies have reported low zinc level in SCA which is due to increased demand and increased excretion of zinc in urine due to decreased renal function and decreased tubular reabsorption of zinc due to repeated occlusion of renal blood vessels.[10] However, this patient had normal renal function as evidenced by the normal renal function test. Zinc has also been reported as an antioxidant, and high zinc level may have also contributed to her being stable.

Presentation with low back pain with associated vertebrae collapse and dorsal protrusion of the thoracolumbar vertebrae mimic tuberculosis of the spine. However, the tests done to investigate tuberculosis were all negative. Low back pain also raised a suspicion of multiple myeloma, the investigations of which were also negative. Repeated generalized bone/body pain in the presence of negative investigations for tuberculosis and multiple myeloma also raised a suspicion of possible SCA the investigation of which showed a positive result. Ordinarily, a high index of suspicion will be required to make a diagnosis of SCA at middle age.[7]

The family history of loss of seven of her siblings out of ten in infancy and early childhood was a pointer. This buttresses the high mortality rate in childhood associated SCA in the absence of comprehensive care. This is in keeping with the cultural notion among the Igbo tribe of Nigeria, of the "ogbanje" phenomenon, with repeated cycles of birth, death, and reincarnation.[11]

History of cholecystectomy as a result of cholecystitis secondary to cholelithiasis was a sign of an underline chronic hemolysis. The MCV, MCH, and MCH concentration were all low. This indicates the possibility of iron deficiency considering the fact she has never received blood transfusion, was menstruating, and had three deliveries. Each pregnancy consumes a lot of iron, and in some cases, pregnant women with SCA are not given routine iron tablet during antenatal care as done for pregnant women without SCA to prevent the iron overload. Despite the low red cell indices, serum ferritin was high. This may be because serum ferritin is a positive acute phase protein and levels are usually high in chronic inflammatory conditions like SCA as evidenced by high CRP level and not necessarily due to iron overload.[12]

There was high level of CRP and ESR suggesting inflammation although ESR was not too high. Discordance in CRP and ESR may be explained by the fact that sickle erythrocytes do not form rouleaux to be followed by sedimentation under normal circumstances and that may have resulted in the ESR not being correspondingly as high as expected with the level of CRP.[13]

Conclusion

SCA is highly variable in clinical manifestation. Although commonly diagnosed in infancy or early childhood, a high index of suspicion is required for first diagnosis in middle-aged adult.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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