

Sickle cell disease: Case study with Clinico-pathological aspect

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ABSTRACT

Sickle cell disease is an autosomal recessive inherited disorder of red blood cells. It has also been called a 'molecular' disease because it results from the mutation of one amino acid in haemoglobin molecule. This article reports a case of homozygous sickle cell disease in an adolescent patient with complications. It also advocates for further study on various clinicopathological aspects of the disease and urge for alertness on the part of health care professionals regarding a holistic approach to the management.

Key words: Sickle cell disease(SCD); Autosomal; Haemoglobin.

INTRODUCTION

Sickle cell disease (SCD) is an hereditary hemolytic anemia. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin. Hemoglobin – is the main substance of the red blood cell. It helps red blood cells carry oxygen from the air in our lungs to all parts of the body. Normal red blood cells contain hemoglobin A. Hemoglobin S and hemoglobin C are abnormal types of hemoglobin. Normal red blood cells are soft, round and biconcave and can squeeze through tiny blood vessels. The basic molecular lesion in Hb S is the single point mutation in one amino acid out of 146 in haemoglobin molecule. There is substitution of valine for glutamic acid at six residue position of beta globin.

Sickle-cell anaemia is the name of a specific form of sickle-cell disease in which there is homozygosity for the mutation that causes HbS. Sickle-cell anaemia is also referred to as "HbSS",

"SS disease", "haemoglobin S" or permutations thereof. In heterozygous people, who have only one sickle gene and one normal adult hemoglobin gene, it is referred to as "HbAS" or "sickle cell trait". Other, rarer forms of sickle-cell disease include sickle-haemoglobin C disease (HbSC), sickle beta-plus-thalassaemia (HbS/ β^+) and sickle beta-zero-thalassaemia (HbS/ β^0). These other forms of sickle-cell disease are compound heterozygous states in which the person has only one copy of the mutation that causes HbS and one copy of another abnormal haemoglobin allele.

Life expectancy is short in SCD, with studies reporting an average life expectancy of 42 and 48 years for males and females, respectively¹.

Case report

An 11 years girl patient referred to Centre for Scientific Research and Development (CSRD) of people's group for advance haematology investigations.

Patient has significant skeletomuscular pain off and on, abdominal discomfort with pain and fever off and on. She was recently operated for cholecystectomy for gallstones. There was history of hip surgery nine years ago. No history of jaundice, or any other chronic illness was present. On examination pallor++, and mild splenomagaly was found.

Patient's investigation profile revealed Haemoglobin 7 gms%, Total WBC count within normal limits, differential WBC count ;neutrophilia, haematocrit 20.7%, RBCs indices within normal limits except RDW 15%. Normal platelets count and coagulation profile. Serum Iron studies and Vitamin B12 & Red cell folate were within normal range. Coomb's test, G6PD, and Malaria antigen tests were negative. Liver function tests show mild increase in total and indirect bilirubin. Blood glucose, urea, serum creatinin, electrolytes were normal.

Patient's abdominal ultrasonography report shows cholelithiasis and mild splenomagaly

In CSRD patient's blood samples were investigated for haemoglobin electrophoresis (HPLC). Haemoglobin chromatography revealed high value of fetal haemoglobin (Hb F)-30.7% (normal <1.5%), low value of haemoglobin adult (Hb A) 3.4% (normal range 83.24-90.79%), and very high concentration of haemoglobin sickle (Hb S) 62.9% which is normally absent. With these findings diagnosis of Haemoglobin 'S' homozygous state was considered and haemoglobin electrophoresis (HPLC) of parents and siblings were advised.

Following the patients tests, her parents and brother's investigations performed. Both the parents and brother's reports showed haemoglobin S heterozygous state. Patient was advised to consult haematologist in tertiary care hospital for advance treatment and management .

DISCUSSION

It is estimated that over 2 million Americans are genetic carriers of SCD and that 70-80,000 Americans have sickle cell disease. A common misperception is that SCD affects only people of African ancestry, however, SCD can affect persons of any race or ethnicity. Genes for SCD

are common in persons of African, Mediterranean, Middle Eastern, and Indian ancestry and persons from the Caribbean and parts of Central and South America. SCD occurs in approximately 1 in 350 African-Americans¹⁻².

If one parent has sickle-cell anaemia (SS) and the other has sickle-cell trait (AS), there is a 50% chance of a child's having sickle-cell disease (SS) and a 50% chance of a child's having sickle-cell trait (AS). When both parents have sickle-cell trait (AS), a child has a 25% chance (1 of 4) of sickle-cell disease (SS). In our case both the parents are haemoglobin S heterozygous (AS), hence the patient is (SS) and her brother is (AS).

Clinical expression of the patients with sickle cell disease (SCD) is variable. Some patients need a lot of care while others need only routine check-ups.

Polymerisation of sickle haemoglobin is the catalyst in the development of vaso-occlusion. Additional factors are critical to pathophysiology of sickling including abnormalities incoagulation, white cell, vascular endothelium and damage to red cell membrane resulting in haemolytic anaemia and vasculopathy³⁻⁴.

Ischemic stroke is the most devastating problem in children⁵. Common complications in children include febrile events, acute chest syndrome, sequestration crisis, and aplastic episodes due to infection with parvovirus and bacteria. Prophylactic penicillin has been shown to reduce mortality from pneumococcal infection⁶.

Adolescent SCD patients present with unique needs, including avascular necrosis of hip, gallstones, priapism, delayed sexual development, pulmonary hypertension. In our case study patient has previous history of hip surgery which may be for avascular necrosis, and recent operation of cholecystectomy for gallstones. These are the most common complications for this age group².

The common complications of adult sicklers include painful crisis, gallstones, osteonecrosis of hip and shoulder joints, leg ulcers, renal diseases, priapism, and retinal

problems. Blood transfusion therapy is a key component of the management of SCD patients. It is an effective treatment for many of the serious complications of SCD⁷.

The new therapies for treating SCD, hydroxyurea, a ribonuclease reductase inhibitor, is most promising. Hydroxyurea was initially developed because of its ability to increase fetal haemoglobin production, but it has other beneficial effects too. Other new therapies being evaluated include butyrates and decitabine⁸. Bone marrow transplantation of children has shown cure in some patients⁹. Both bone marrow transplantation and hydroxyurea therapy are expensive modalities.

CONCLUSION

Finding financial resources for such expensive therapies for SCD have been difficult, especially in developing countries like India. For the optimal management of SCD patients, a comprehensive care centre with multidisciplinary team is required. Early diagnosis of patients by screening programme is very important. Diagnosed patients should be referred to centre for periodic evaluation. Parents should be given genetic counseling and support. Presently patient is maintaining normal routine life with proper clinical management.

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