

Two Case reports on Sickle Cell Disease: Presented with Pallor and recurrent Attacks of Bones and Joints Pain

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Abstract

Sickle cell disease is a hereditary hemolytic anaemia due to abnormal haemoglobin. Sickling of RBCs occurs due to abnormal hemoglobin which leads to vaso-occlusive crisis. The highest frequency of sickle cell disease is found in tropical regions, particularly in Sub-Saharan Africa, tribal regions of India and in Middle-East. Though sickle cell disease is not common in our country, recently we have two cases of sickle cell disease presented with fatigue and pallor with bones and joints pains. These cases were diagnosed by electrophoresis of hemoglobin, peripheral smear, Sickling test and relevant investigations. The most significant advance in the therapy of sickle cell anaemia is the introduction of Hydroxyurea to prevent acute chest syndrome, number of pain crisis, repeated transfusions and number of trips to hospital. Hydroxyurea is considered in first case (case no. 1) as he has frequent episodes of acute attack and recover well after blood transfusion. Case no.2 also a good candidate for Hydroxyurea but not given as his acute attack is less frequent and in close contact for further observation and evaluation.

Keywords: Hereditary hemolytic anaemia, acute chest syndrome, nephrotic syndrome, sickle cells.

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Introduction

Sickle cell disease results from a single glutamic acid to valine substitution at position 6 of the beta globin polypeptide chain. Sickling was first discovered by Linus Pauling and colleagues in 1949¹. It is inherited as an autosomal recessive trait². The disease mainly occurs in Africans (25% carry the gene). But is also found in India, the Middle East, and Southern Europe^{3,4}. When haemoglobin S is deoxygenated, the molecules of hemoglobin polymerise to form pseudocrystalline structures known as 'tactoids'. These distort the red cell membrane and produce characteristic sickle shaped cells. The polymerization is reversible when re-oxygenation occurs. The distortion of the red cell membrane, however, may become permanent and the red cell 'irreversibly sickled'. This process may be enhanced or retarded by the presence of other hemoglobins. Thus, the abnormal hemoglobin C variant participates in the polymerization more readily than haemoglobin A, whereas haemoglobin F strongly inhibits polymerisation. These abnormalities provoke unpredictable episodes of microvascular vaso-occlusion and premature RBC destruction (hemolytic anaemia)^{5,6}. Hemolysis occurs because the spleen destroys the abnormal RBC. The rigid adherent cells also clog small capillaries and venules, causing tissue ischaemia, acute pain, and gradual end-organ damage⁷.

This veno-occlusive component usually dominates the clinical course. Prominent manifestations include episodes of ischaemic pain, infarction in the spleen, central nervous system, bones, liver, kidneys and lungs⁸. Most patients with sickle cell syndromes suffer from hemolytic anaemia with hematocrit from 15-30% and significant reticulocytosis. Usually nephrotic syndrome and acute chest syndrome are seen as complications. Acute chest syndrome characterized by fever, chest pain, wheezing, cough, hypoxia and lung infiltrates. lung infiltrates is a lethal complication that affects half of all the patients with

sickle cell anaemia⁹. Repeated acute chest syndrome episodes may also predispose to scarring and pulmonary hypertension¹⁰. It is unclear that the patients with sickle cell disease are more prone to nephrotic syndrome, but the histological picture of membranoproliferative glomerulonephritis accounts for over one half of adult cases¹¹. Patients with sickle cell anaemia adapt well to their low hemoglobin levels and regular blood transfusion is not required¹².

Case report 1:

A 18 years old male with acute onset of pain in bones and joints for last 6 days and recurrent attacks of pallor, weakness and fatigue for last 10 years. On physical examination temperature -101° F, pulse rate - 120 beats/min, respiratory rate - 32 cycles/min, blood pressure - 120/82 mm Hg, pallor present and mild oedema present, Cardiovascular system - normal heart sounds, no murmur, Respiratory system - bilateral crepitations, abdomen - hepatosplenomegaly present. Investigations shows Hb - 5.88 gm %, RBS - 110 mg %, blood urea - 25 mg %, Serum creatinine - 1.2 mg %, 24 hours urinary protein - 1.1 gm %. ECG - sinus tachycardia, Chest X-ray PA view - bilateral infiltrates. Complete hemogram shows moderate microcytic hypochromic anaemia with sickle cells, poikilocytes, target cells, fragmented RBC and no haemoparasites.

Sickling test of case no. 1 done in department of Haematology & BMT Dhaka Medical College Hospital (Fig - 1 & 2):

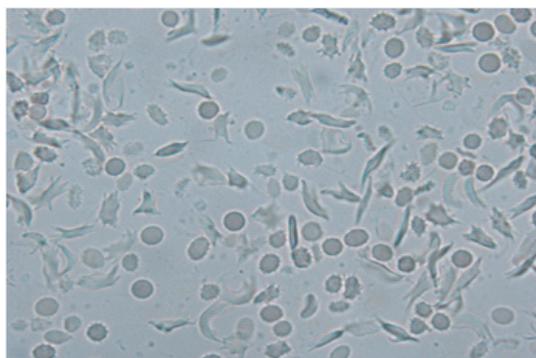


Fig - 1: Sickling test.

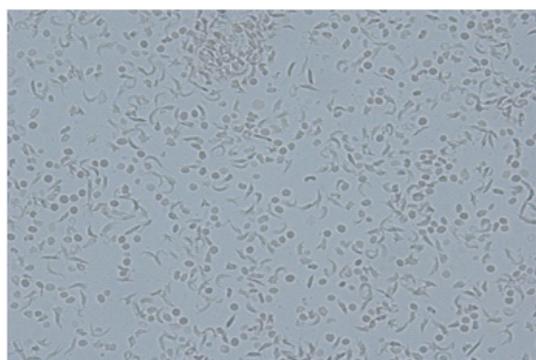


Fig - 2: Sickling test.

Haemoglobin electrophoresis case no. 1 done in department of Haematology & BMT Dhaka Medical College Hospital (Fig - 3): Hb A -28.7%, Hb A2-4.0%, Hb F-19%, Hb S-48.3% on automated Capillarys 2 flex piercing system and Hb A-1.2%, Hb A2-3.4%, Hb F-28.1% HbS/D/ Unknown-67.3% on Hydragel system.

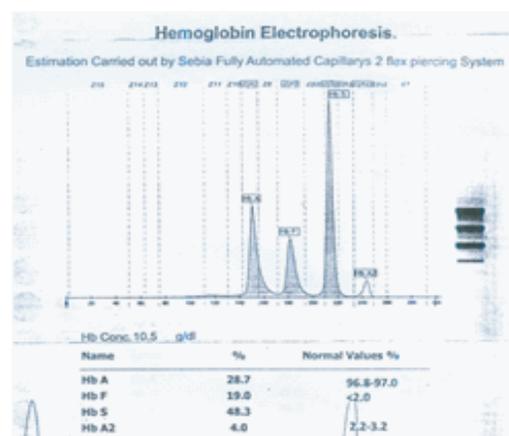


Fig - 3: Haemoglobin electrophoresis.

With the above hemoglobin electrophoresis and haemogram reports, this case is diagnosed as sickle cell disease with hemolytic anaemia and Hand-foot syndrome. This patient treated with diuretics, antibiotics, blood transfusion, analgesics and oxygen inhalation. Patient recovered very quickly and discharged with advice.

Case report 2

A 6 years old boy with recurrent attacks of Pain in bones and joints for last 5 months and Pallor & fatigue for last one year. On examination Temperature 100°F, Heart rate 120/min, Respiratory rate 30/min, BP 110/70 mm Hg, Pallor and mild edema present. Lungs clear, Cardiovascular system -heart sound normal with no murmur, Abdomen-Hepatosplenomegaly present. Investigations shows Hb-6.5%, RBS 105 mg %, Urea 20 mg %, S creatinine 1.1 mg %, Chest X-ray - normal, ECG- sinus tachycardia, USG abdomen- Hepatosplenomegaly, Complete haemogram shows microcytic hypochromic anaemia, anisopoikilocytosis, target cells, with features of haemolysis.

Sickling test of case no. 2 done in department of Haematology & BMT Dhaka Medical College Hospital (Fig - 4 & 5):

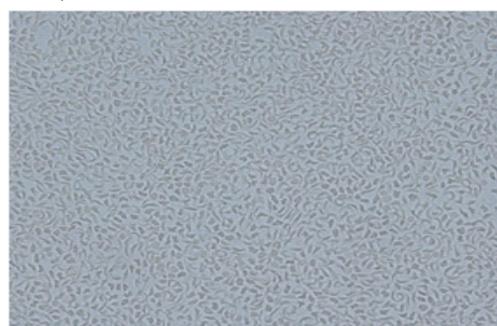


Fig - 4: Sickling test.

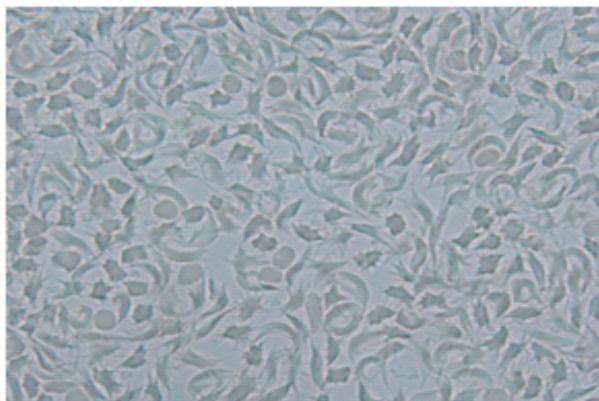


Fig - 5: Sickling test.

Haemoglobin electrophoresis case no. 2 done in department of Haematology & BMT Dhaka Medical College Hospital (Fig - 6): HbA2-4.7%, HbF-23.9%, HbS-71.4% on fully automated CapillaryS 2flex piercing system.

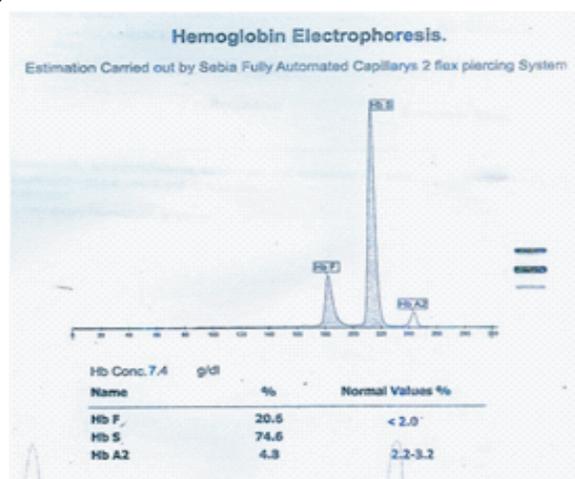


Fig - 6: Haemoglobin electrophoresis.

With above Haemoglobin electrophoresis and haemogram report this case was diagnosed as a case of Sickle cell disease with vaso-conclusive crisis. This patient was treated with oxygen inhalation, IV fluid, blood transfusion, antibiotics, analgesics. With this treatment patient recovered well and discharged.

Discussion

Sickle cell disease is characterized by the pathophysiological feature of chronic haemolytic anaemia, vaso-occlusion resulting in ischemic tissue injury and painful episodes¹³. Vaso-occlusion may result from exercise, stress, dehydration, cold exposure, high altitude, smoking and infections^{14,15}. Among the infections Parvovirus B19 infection is common and may lead to aplastic crisis^{16,17}. The organs of great risk are the spleen, kidney and bone marrow where oxygen tension is low and blood flow is diminished. Sickle cell disease usually presents as vaso-occlusive crisis, acute chest syndrome, hemolytic anaemia, chronic leg ulcer, stroke and nephrotic syndrome¹⁸.

These two patients presented with anaemia and vaso-occlusive crisis. The definitive diagnosis requires hemoglobin electrophoresis to demonstrate the absence of HbA, 2-20% of HbF and the presence of HbS¹⁹. In these cases hemoglobin electrophoresis shows the presence of HbF (19% and 23.9%) and HbS (48.3% and 71.4%). The peripheral blood smear is characteristically abnormal with irreversibly sickled cells comprising 5-50% of red cells²⁰. Peripheral blood smear from this patient shows sickle cells. Sickle cell patients have a known predisposition to bacterial infection, particularly pneumococcal infection²¹⁻²³. Parvovirus B19 infection in these cases are not evaluated as investigations facilities such as antibody of parvovirus identification or PCR are not available in our hospital and local setup. These patients treated with blood transfusion, antibiotics, analgesics, folic acid, diuretics and oxygen inhalation. Both patients were treated conservatively and response was well. The most significant advance in the therapy of sickle cell anaemia has been the introduction of Hydroxyurea. And Hydroxyurea is given to case no.1 as he is suffering for long time with recurrent attack of Pallor requiring blood transfusion and hospitalization. But hydroxyurea is not given in Case no 2 as his response to treatment was well and have less frequent attacks and are in close observation for follow up²⁴. Hydroxyurea was not given to case 2 as detailed clinical data of previous attacks are lacking from first episode and growth and development of parameter are well. With the above treatment patient recovered well, discharged and review after ten days in the OPD revealed that the patient was healthy. Hence even in vaso-occlusive disorder of sickle cell disease patient's recovery is good with early diagnosis and effective treatment²⁵. Recent advancement in sickle cell disease treatment include anti adhesion therapy, monoclonal antibody and autologous stem cell base therapy, which can be use for treatment of disease or its complications^{26,27}.

Conclusion

SCD is a chronic debilitating disease characterized by recurrent episodes of ischemia - reperfusion injury and is the most common cause of overt stroke in children. Sickle cell infarcts (SCI) occur in approximately one-quarter of children with SCD prior to their 6th birthday and approximately one-third prior to their 14th birthday. The lifetime risk of stroke in a patient with SCD lies between 25% and 30%, with 75% being arterial ischemic strokes while 24% of patients with SCD have suffered at least one episode of stroke by the age of 45. Silent or subtle strokes are common and may occur in up to 50% of patients with SCD. Here case no-1 celebrate his 18th birthday and case no-2 celebrate his 6th birthday without any cerebrovascular events. This make us hopeful for better outcome of these cases.

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