

Anemia in Children-Needs Pervasive Work Up

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Received: July 31, 2019; **Published:** September 16, 2019

Abstract

Sickle cell disease is a hereditary hemoglobinopathy caused by point mutation in sixth codon of beta chain of hemoglobin leads to replacement of glutamate residue with valine causes formation of HbS. Sickle cell disease is a group of disorders that affects hemoglobin, the molecule in red blood cells that delivers oxygen to cells throughout the body. People with this disorder have atypical hemoglobin molecules called hemoglobin S, which can distort red blood cells into a sickle, or crescent, shape. The signs and symptoms of sickle cell disease are caused by the sickling of red blood cells.

Keywords: Anemia, Sickle cell, Hemoglobin

Introduction

Sickle cell disease is a hereditary hemoglobinopathy caused by point mutation in sixth codon of beta chain of hemoglobin leads to replacement of glutamate residue with valine causes formation of HbS. Normal red blood cells have biconcave shape which gives them the flexibility to travel through even the smallest blood vessel but in sickle cell disease, the RBCs have an abnormal crescent shape resembling a sickle which makes them sticky and rigid and prone to getting trapped in small vessels, which blocks blood to reach different parts of the body thus cause pain and tissue damage. Here we present a case of child whose elder brother died undiagnosed due to severe anemia and painful crisis and this female child of five years age came at our hospital with chief complaints of weakness, fatigue, giddiness and fluctuating jaundice since past one and half years.

Case Report

A five years old female child referred to our hospital with complaints of weakness, giddiness and fluctuating jaundice since one and half years with family history of having an elder brother of eight years old. Her brother died ten days before. As he also had fluctuating jaundice with total bilirubin- 16 mg/dl, direct bilirubin- 0.8 mg/dl, Indirect bilirubin- 15.2 mg/dl along with anemia, for that he received packed red cells and fresh frozen plasma. During transfusion he suffered from painful crisis and succumbed to death with no identified cause query?? Unknown etiology. This female was having the same clinical sign and symptoms as her brother with this history she was referred to our hospital.

Physical examination showed presence of pallor. Vitals were showing heart rate 86/minute, respiratory rate as 26/minute oxygen saturation 100%, with normal temperature. Systemic examination revealed no focal neurological deficit, S1 S2 were normal with no murmur, bilateral air entries were equal with no added sounds and spleen was just palpable. Biochemical investigation were serum ionic calcium 0.97 mmol/litre, ferritin- 29.3 mg/dl, creatinine- 0.2 mg/dl, SGOT- 52 U/L, SGPT- 25 U/L, Total Bilirubin- 5.1 mg/dl, Direct Bilirubin- 1.0 mg/dl, Indirect bilirubin- 4.1 mg/dl. Sodium- 135 mmol/l, Potassium- 4.1 mmol/l, Total serum protein- 7.9 gm/dl, albumin- 4.4 gm/dl, globulin 3.5 gm/dl, alkaline phosphatase- 199 U/L, serum ferritin- 39.9 ng/ml. Hepatitis B was non reactive and Widal was negative. The complete blood count showed wbc- 15.98 thousand/cmm, hemoglobin- 7.7 gm%, platelets- 3.9 lakh/cmm, Reticulocyte count was 7.4%, G6PD was not deficient with normal curve of Osmotic fragility. On peripheral examination of blood smear white

blood cells and platelets were normal in morphology. Red blood cells were microcytic hypochromic with presence of few cells appeared with tapering ends looked morphologically as sickle cells, on basis of peripheral blood finding we advised sickling test and hemoglobin electrophoresis which is confirmatory test for work up of sickle cell disease. The sickling test performed and presence of sickle cells were seen under microscope (Figure 1). Thus with presence of family history and sickle cell on smear it would reach to the diagnosis of sickle cell disease. Hemoglobin electrophoresis was done as HbF-17.7%, HbA0 1.8%, HbA2-2.5%, HbS 77.3% by high performance liquid chromatography, this pattern was consistent with homozygous state for HbS (Figure 2). Her parents were also investigated for sickling both of them were Heterozygous for HbA/S on electrophoresis thus the case was diagnosed as sickle cell disease.



Figure 1: Peripheral blood smear showing sickle cell (Leishman stain, 1000x).

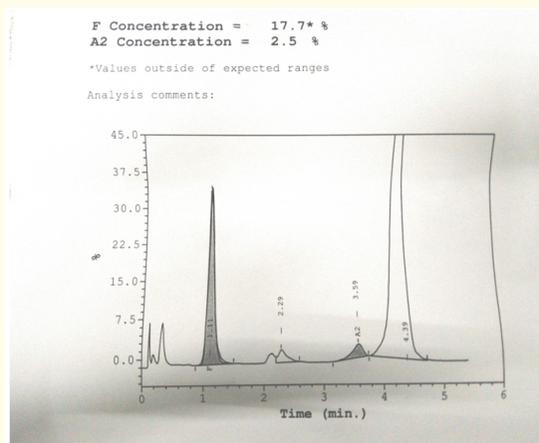


Figure 2: Hemoglobin electrophoresis showing 'S' window.

Discussion

Hemoglobin is a tetrameric protein composed of two pairs of globin chain each with its own haeme group. Normal adult red cells contain mainly Hb A along with small amount of HbA2 and fetal hemoglobin HbF. Sickle cell disease is caused by point mutation in sixth

codon of beta chain that leads to replacement of glutamate residue with valine, this abnormal physiochemical property results formation of sickle hemoglobin HbS. Sickling was first discovered by Linus Pauling in 1949 [1].

Pathogenesis of sickle cell shows HbS molecules to undergo polymerization when deoxygenated. Initially the red cell cytosol converts from a freely flowing liquid to a viscous gel as HbS aggregate form. With continued deoxygenation aggregated HbS molecules assemble into long needle like fibres within red cells, producing a distorted sickle shape.

The pathologic manifestation is due to chronic haemolytic anaemia, vasoocclusive process and multiple organ infarction resulting from wide spread vascular occlusion [2]. Although all sickle cell patients share the same genetic mutation, the clinical course is highly variable between patients. Several variables affect the rate and degree of sickling for example interaction of HbS with other type of hemoglobin in the cell as HbF which inhibits the polymerization of HbS even more than HbA, hence infants do not become symptomatic until they reach six months of age when level of HbF falls. In hereditary persistence of HbF sickle cell disease is much less severe. Another variant of hemoglobin is HbC in which Lysine is substituted for glutamate in sixth amino acid residue of beta chain of globin. In HbSC cells tend to lose salt and water thus become dehydrated, which increases the concentration of HbS thus lead to polymerization of Hb S, therefore individuals with presence of HbS and Hb C have symptomatic disorder.

Mean cell hemoglobin concentration is high when intracellular dehydration is present which facilitates sickling and vice versa.

Intracellular PH when decreases the oxygen affinity of hemoglobin reduces thereby increases the fraction of deoxygenated HbS at any given oxygen tension and augmenting the tendency of sickling.

Transit time of red cells through microvascular bed normally is too short to get significant aggregation of deoxygenated Hb S to occur; thus sickling is confined to microvascular beds with slow transit times. Transit time is slow in spleen and bone marrow; both of these are prominently affected in sickle cell disease.

Sickling causes cumulative damage to red cell membrane as HbS polymers grow they project out through the membrane skeleton this derangement in membrane causes influx of calcium ions, which induces the cross linking of proteins and activate ion channels which causes potassium and water efflux. With repeated episodes of sickling red cells become increasingly dehydrated, dense and rigid.

When Hb S is deoxygenated the hemoglobin molecules get polymerized to form tactoids which are pseudocrystalline structures. These long strands deform the erythrocyte, giving the characteristic sickle cell.

The distortion of red cell membrane may become permanent the cell get irreversibly sick led. These abnormalities leads to episodes of microvascular vasoocclusion and hemolysis [3,4]. The cells becomes so rigid that they block small capillaries and venules which leads to tissue ischemia, acute pain, and gradual organ damage. These distorted red cells are sequestered by mononuclear phagocytes causes extravascular hemolysis.

The vaso occlusive crises dominates the clinical course with manifestation of ischaemic pain, spleen infarct, bone, liver, lungs and kidneys [5]. These vaso-occlusive crises causes ischaemic tissue injury and painful episodes [6]. Vaso occlusion may be due to stress, dehydration, cold exposure, high altitude, smoking and infections [7]. Parvo virus B19 is the common and may lead to aplastic crisis [8].

Conclusion

This case highlights the agony of sickle cell disease as this patient suffered from sickle cell disease was diagnosed too late and her sibling was un-diagnosed and succumb to death might be due to veno occlusive crises. There is no social and financial support in developing country in course of disease as it is very difficult that care of these patients is only done by parents or care givers, the government must needs to assist these patients with mandatory pre marital counseling to prevent social, economic, mental sheave.

Acknowledgement

We are thankful for Miss Shailja Ahuja for processing Hemoglobin electrophoresis.

Conflict of Interest

Nil.

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Volume 2 Issue 7 October 2019

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