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A SILENT CASE OF SICKLE CELL DISEASE: A SERENDIPITOUS DISCOVERY

Haematology

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ABSTRACT

We present here a 4-year-old male child who came to hematology out-patient department for follow up for anemia which had required blood transfusion one and half year back. On clinical examination child was found to neither have pallor nor icterus. Blood was sent for complete hemogram. The hemogram showed a total hemoglobin of 8.4 gm%. Other RBC indices and WBC and platelet counts were within normal expectations. The reticulocyte count however was raised to 11%. Based on such a hemogram, on a high index of suspicion of a chronic hemolytic condition, despite clinical absence of any hemolytic features, a hemoglobin HPLC was performed in the Biochemistry laboratory. The HPLC revealed a percentage of HbS compatible with a HBS homozygous state. Based on this finding, the routine hemograms of both the parents were performed. These were found to be within normal limits. However, HPLC analyses for hemoglobin variants revealed HbS percentages compatible with HbS carrier i.e., heterozygous states. We thus provisionally concluded that this child was a case of Sickle cell homozygous, but atypical as because there was no history or clinical evidence of sickle cell disease symptomatology.

KEYWORDS

Sickle cell, homozygous, HPLC.

Case Report

A four-year-old male child presented to the hematology out-patient department with a one-and-a-half-year history of anemia which had necessitated blood transfusion at that time. On clinical examination the child was found to neither have pallor nor icterus. There was also no clinically obvious evidence of organomegaly, with both the liver and spleen being non-palpable.

As a matter of course the child's routine hemogram was asked for. The routine hemogram of the child performed on an automated platform, the ABX Pentra XL (Horiba) revealed as significant finding a total hemoglobin of 8.4 g/dL [Biological reference interval 12-15 g/dL]. The routine hemogram of the child is depicted in **Fig 1a.** The only other significant finding in the routine hemogram was a reticulocyte count of 11.0% [Biological reference interval 0.5-2.0%]. Based on such a hemogram, on a high index of suspicion of a chronic hemolytic condition, despite clinical absence of any hemolytic features, a hemoglobin HPLC (High Performance Liquid Chromatography) analysis, was performed in the Biochemistry laboratory on Bio-Rad D10 analyzer. The chromatogram, revealed a very prominent S-window with an area percentage of 69.8% **[Fig 1b].** The fetal hemoglobin (HbF) percentage was also significantly raised to 21.1%; with the biological reference interval in a four-year-old being 1.3+/-0.5% [1].

Based on these findings an attempt was made to screen the parents of the affected child for presence of disease or carrier status. Routine hemograms of both parents revealed a within normal limits picture for the father **[Fig 2a],** but mild anemia in the mother **[Fig 2b],** with a hemoglobin of 11.9 g/dL [Biological reference interval 12.0-15.0 g/dL], mean corpuscular volume (MCV) of 76 fL [Biological reference interval 83-101 fL], mean corpuscular hemoglobin (MCH) of 24.4 pg [Biological reference interval 27-32 pg] and mean corpuscular hemoglobin concentration (MCHC) of 32.1 g/dL [Biological reference interval 31.5-34.5 g/dL].

Based on the routine hemogram findings and high index of suspicion of an underlying carrier status, hemoglobin HPLC analyses were performed for both parents **[Fig 3a and 3b].** The HPLC analyses revealed an S-window with an area percentage of 38.1% for the father and 33.3% for the mother. Such area percentages are compatible with presence of Sickle cell trait i.e., heterozygous status [2]. Genetic counselling was done for both parents including disease education and preventive measures to be adopted for the child including avoidance of any form of oxygen challenge namely, travel to high altitudes. Currently, the child has been kept under watchful scrutiny and regular follow-up advised.

Sickle cell disease (SCD) was first reported by Herrick in 1910. It may present either as homozygous or compound heterozygote inheritance of a mutation in the β-globin gene [3]. The basic pathogenesis lies in a a single base-pair point mutation (GAG to GTG) resulting in substitution of the amino acid glutamic acid (hydrophilic) to valine (hydrophobic) in the 6th position of the β-chain of haemoglobin. The resultant hemoglobin is designated as referred to as hemoglobin S or HbS [4].

Red blood cells (RBCs) that contain HbS, when exposed to environment with low oxygen, undergo polymerisation and become rigid. The rigid RBCs are more prone to undergo hemolysis and due to increased density may affect blood flow and endothelial vessel wall integrity. The dense rigid RBCs lead to vaso-occlusion, tissue ischaemia, infarction and account for episodes of "sickling crisis". The various acute and chronic complications are more likely to occur once the protective effect of fetal haemoglobin (HbF) drops towards the adult level by five to six months of age [5].

Our case report is based on a four-year-old child who was diagnosed with sickle cell homozygous condition quite by chance, following a tell-tale history and routine hemogram. The child's current asymptomatic state was in contrast to the Hemoglobin HPLC findings of sickle cell homozygous.

In consequence both parents were found to be heterozygotes i.e., carriers for the disease. The parents though amenable to counselling did not reveal any history of consanguinity. The case was found to be an exception since normally the disease does not remain asymptomatic for such a long period [4 years], with only a single episode of blood transfusion that too 1.5 years prior to current contact.

Such cases need to be more thoroughly screened for and investigated minutely for proper management of such individuals.

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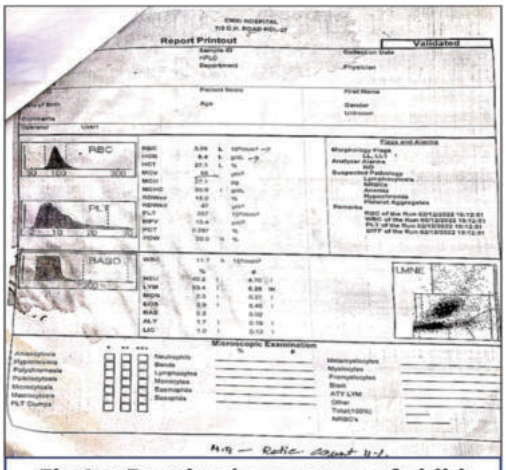

Fig 1a: Routine hemogram of child

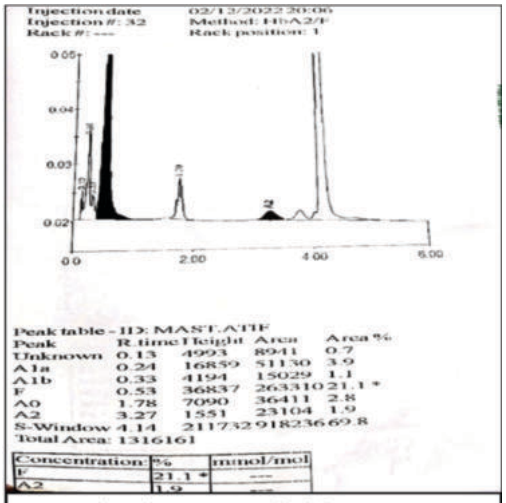

Fig 1b: Hemoglobin HPLC Analysis of child

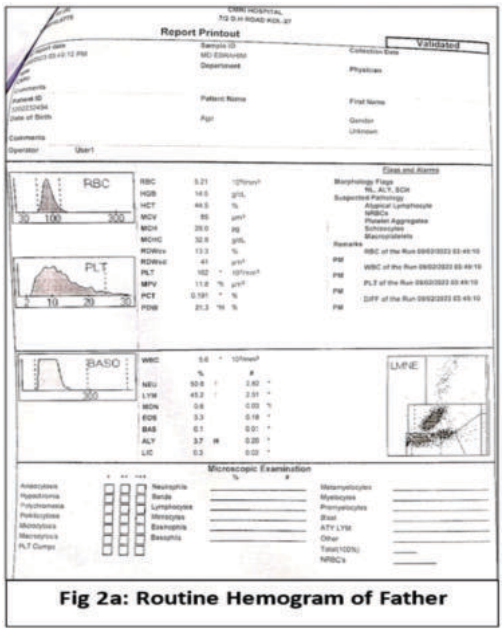

Fig 2a: Routine Hemogram of Father

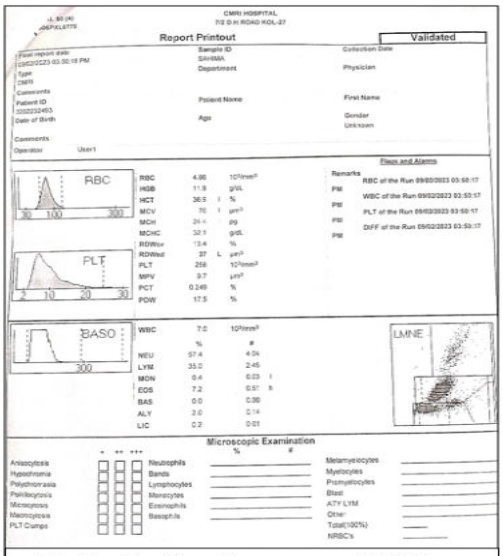

Fig 2b: Routine Hemogram of Mother

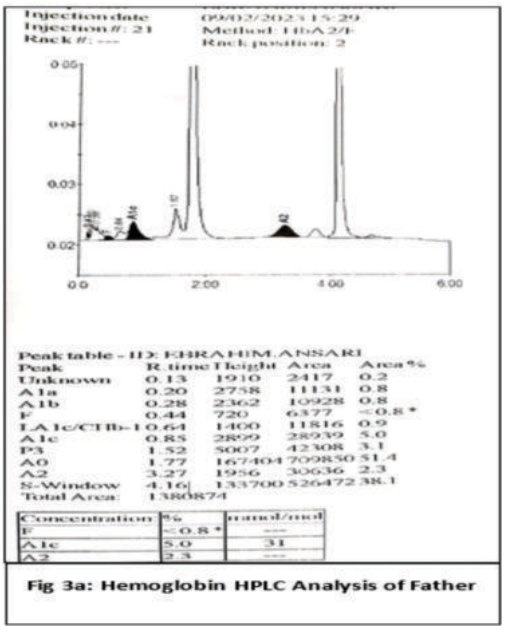

Fig 3a: Hemoglobin HPLC Analysis of Father

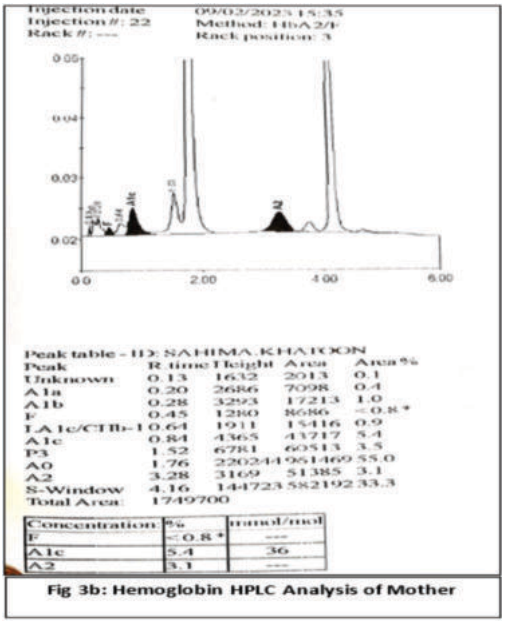

Fig 3b: Hemoglobin HPLC Analysis of Mother

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