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CASE SERIES

Case Series of Sickle Cell Disease with Spectrum of Clinical Presentation

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ABSTRACT
Sickle cell disease (SCD) is a genetic disorder autosomal-recessive in nature effecting millions worldwide. Replacement of hydrophilic Glutamic acid (Glu) with hydrophobic Valine (Val) at the sixth position in the β-globin chainforming a mutated hemoglobin (Hb) tetramer HbS,causing distortion of the erythrocyte membrane. This leads to erythrocyte sickling. Deoxygenated HbS tetramersbind to each otherinitiating the nucleation of HbS polymer.These polymers grow & form long fibers. HbS causes cellular energetic failure, premature hemolysis, dehydration & stress. Authors, here presented Three (03) Cases of Sickle cell disease with spectrum of clinical presentation. First case was case of Sickle Cell Trait with severe anemia showing Sickle Window of 15.7 %, HbF<0.8%, HbA2- 2.6%, HbA0- 71.6%.Second case was case Co-Inheritance of Sickle cell trait and Beta Thalassemia Trait with severe anemia in obstructed labour showing S-window 16.3%, HbA2- 5.8%, HbF<0.8%, Hb A0- 67.3%. Third case was case of a Sickle cell anemiashowing S-window 73.2%, HbA2- 2.5 %, , Hb A0- 4.1 %.

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder effecting millions worldwide. It is autosomal-recessive in nature. Sickle cell anemia is caused due to homozygosity of the beta-S (β^S) allele on chromosome 11p15.5 & wild-type β-allele due to a single nucleotide polymorphism dbSNP Rs334(T;T) substituting GTG for GAG at 6th (Sixth) codon of β-globin gene leading a replacement of hydrophilic Glutamic acid (Glu) with hydrophobic Valine (Val) at the sixth position in the β-globin chain. This results in forming a mutated hemoglobin (Hb) tetramer HbS ($\alpha_2\beta^s{}_2$) in erythrocytes. There is a spectrum of clinical conditions due to Homozygous inheritance of β^S mutation (HbSS) or even co-inheritance of β^S with other forms of mutations like β^C (HbSC), β^O (HbSO/Arab), β^D (HbSD), β^E (HbSE), or β-thalassemia allele (HbS/β-thal^0 or HbS/β-thal$^+$). SCD affects millions worldwide, 3.2 million people live with SCD, 43 million people have sickle cell trait & it was found 176,000 people die every year due to SCD-related complications. Deoxygenation in tissues promotes the exposure of hydrophobic motifs on deoxygenated HbS tetramers (T-state). Due to which, β^S-globin chains in deoxygenated HbS tetramers bind to each other to hide the hydrophobic motifs, this initiates the nucleation of HbS polymer. These polymers grow & form long fibers, increasing the cellular rigidity and causing distortion of the erythrocyte membrane. This leads to erythrocyte sickling. Sickling ultimately causes cellular energetic failure, premature hemolysis, dehydration and stress. The rate of polymerization of erythrocytes is proportional to concentration of HbS (to the 34th power) and it is inversely proportional to the concentration of fetal Hb (HbF). Vaso-occlusion leading to ischemia is the predominant pathophysiology responsible for vaso-occlusive crisis (VOC) which is an acute systemic painful condition which require emergency medical care. Co-inheritance of other genetic mutations such as α-thalassemia or hereditary persistence of HbF or β^C-allele alongside β^S may modulate disease severity.[1]SCD is the most common Monogenetic disease, effecting millions worldwide. The majority of SCD births documented in sub-Saharan Africa. 50 to 90% of these children die undiagnosed in the first five years of life due to lack of newborn screening.

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Whereas, in well-resourced countries, due to proper newborn screening programmes & comprehensive treatment programs we can see increased life expectancy of patients with sickle cell disease, with almost all infants reaching adulthood.[2]In India first description of sickle haemoglobin was by Lehman and Cutbush in the tribal populations in the Nilgiri hills in 1952. Dunlop and Mazumder also reported the same in Upper Assam among tea garden workers, who were migrant labourers from Bihar & Odisha,in same year. The prevalence of sickle cell carriers among the different tribal groups varies from 1 to 40 per cent. Among them Madhya Pradesh has the highest load, with other members namely Kerala, Gujarat, Tamil Nadu and Odisha. There are evidences of presence of associated α-thalassaemia, heterozygosity (β^s/β^{thal}) for the sickle gene and a β-thalassaemia gene & also co-inheritance of HbS with HbD Punjab, HbE and HbC. [3]Authors, here presented Three (03) Cases of Sickle cell disease with spectrum of clinical presentation from their work.

METHODOLOGY

Blood samples were collected by Venepuncture for testing of Hemoglobin Electrophoresis & Biochemical parameters. Hemoglobin Electrophoresis was done by HPLC Method by BIORAD D-10, Biochemical tests were done by Full Automated Biochemistry Analyzer XL 640 by Erba. Other tests like Complete Blood Count, Bone Marrow Biopsy were done. For Hemoglobin Electrophoresis, Blood samples were collected in EDTA tubes. 10 µL blood is mixed in 1500 µL of Double distilled water in aliquot & analysis is done in BIORAD D-10.

CASE 1

A middle aged Male patient in his early forties, belonging from migrant tribal population, who is a daily labourer by profession came to the Medicine OPD of Agartala Govt. Medical College & GBP Hospital, Tripura with complaints of severe lethargy & generalised weakness. On examination he severely pale. He was admitted in ward & investigated for the cause of anemia. Blood samples were sent to Dept. of Biochemistry, AGMC & GBPH. The patient had history of multiple blood transfusions starting from late teenage till now. Patient also complained of pain in his calves & found to have Pedal edema on examination. Authors examined & investigated the case. Biochemical tests &Hemoglobin electrophoresis was done. HPLC Chromatogram of the Hemoglobin Electrophoresis showed Sickle Window of 15.7 %, HbF<0.8%, HbA2- 2.6%, HbA0- 71.6%. Complete Blood Count (CBC) showed Marked anisopoikilocytosis without any Sickle cell in the peripheral blood smear. Hemoglobin was noted as 1.6 gm%, 1.7gm% & 3.1 gm% on Day0, Day 1 & Day 5 respectively. Bone Marrow Biopsy showed Megaloblastoid changes with Erythroid Hyperplasia with predominance of early & intermediate normoblast. Authors evaluated all the reports & diagnosed this case as Sickle Cell Trait. Patient had Hypolipidemia & Hypoalbuminemia.

CASE 2

A 3rd Gravida Female patient in her late twenties from Tribal Population was referred to AGMC & GBPH from the periphery with complaint of non-progression of labour with Severe Anemia. After the admission, the patient went into Obstructed labour & resulted with Intra Uterine Death. Caesarean section (CS) was done for that patient on emergency basis. Foul smelling meconium-stained liquor was found in CS. In the post operative phase patient developed sepsis & fever, she had history of Jaundice in her childhood for several occasions. Patient had Obstetric history- the 1st Baby with Low IQ & 2nd Baby was Still Born. Anemia was unresolved even after blood transfusion, then cause of anemia was investigated. In CBC Hemoglobin was 4.6 gm%, PCV 19.4%, Total Leukocyte Count (TLC) 24000/cu. mm. Peripheral smear was Predominantly Normocytic Normochromic with Anisocytosis. Hemoglobin Electrophoresis was done by the Authors. HPLC Chromatogram of the Hemoglobin Electrophoresis showed S-window 16.3%, HbA2- 5.8%, HbF<0.8%, Hb A0- 67.3%. After evaluating all the reports Authors diagnosed this case as Co-Inheritance of Sickle cell trait and Beta Thalassemia Trait. Patient had Total Bilirubin 2.0 mg/dL, Conjugated Bilirubin 0.3 mg/dL, unconjugated Bilirubin 1.7 mg/dL, AST 60, ALT 45, ALP 230 IU/L.

CASE 3

A Male patient in his late teens, from indigenous tribal population of Tripura, came to the medicine OPD of AGMC & GBPH with complaints of vertigo & weakness. On Examination the patient was pale. Patient was investigated for the cause of his Anemia. On investigation CBC showed Hemoglobin 6.6 gm%, PCV 28.4%, TLC 8000/cu. mm. Peripheral smear having Predominantly Normocytic Normochromic with marked Anisocytosis with ocassional sickle cells. Authors carried out Hemoglobin electrophoresis. HPLC Chromatogram of the Hemoglobin Electrophoresis showed S-window 73.2%, HbA2- 2.5 %, , Hb A0- 4.1 %. Authors diagnosed this case as Sickle cell Anemia.

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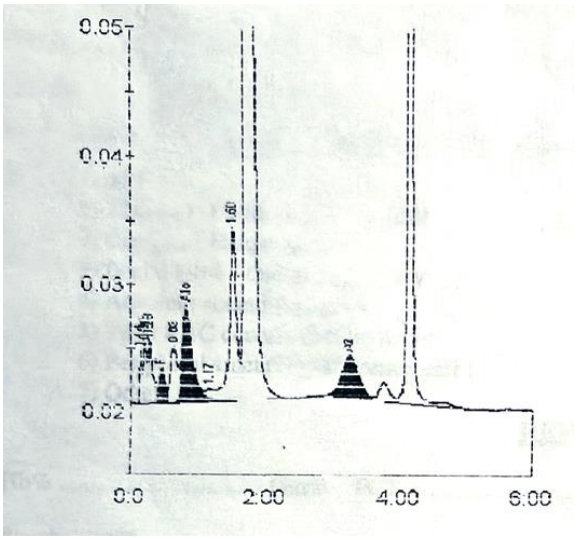

Fig: Case 1

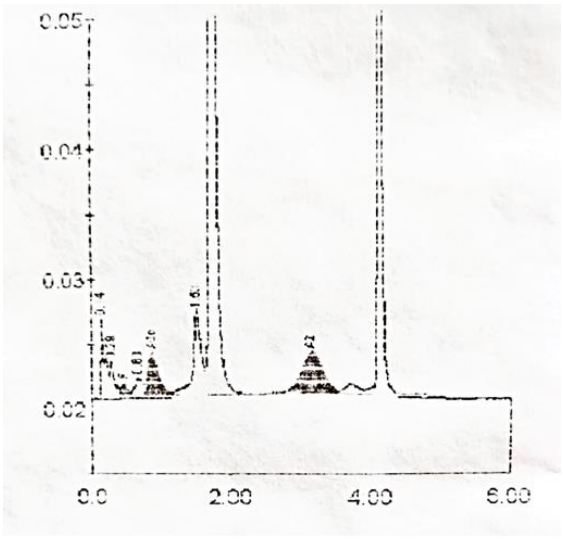

Fig: Case 2

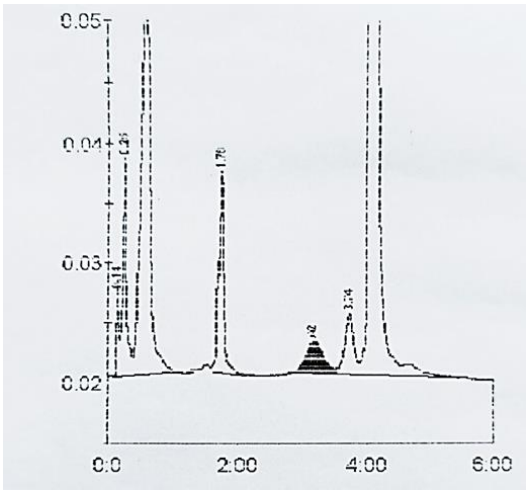

Fig: Case 3

DISCUSSION

SCD is a clinical syndrome with variety of inheritance, presentation & complications. Here Authors showed Three Cases of SCD from their work. In the First Case, patient was diagnosed to have Sickle cell trait. But this much severe Anemia is unusual in Sickle cell Trait. [4]Hypoalbuminemia supports the finding Pedal Edema in that patient. Patient alsobelonged to Tribal community among whom these hemoglobinopathies are common. In the Second case increased Total Leukocyte count supports the diagnosis of Sepsis & explains the unresolving fever. Patient's history of several episodes of Jaundice supported with the diagnosis of Sickle cell trait. Here too, this much Anemia is uncommon among sickle trait, but co inheritance of Beta Thalassemia Trait might have attributed to it. Co-inheritance of such cases have been documented from different ethnic groups. [3] Pregnancy in SCD is associated with increased risk of pre-eclampsia, eclampsia, gestational diabetes, spontaneous abortions and stillbirths (due to Microvascular damage & decreased uteroplacental circulation). [5]

CONCLUSION

SCD is a condition which can get complicated and cause morbidity & mortality of the patients. So early detection & comprehensive management of this condition is beneficial for the patients suffering with this condition.

AST- Aspartate Transaminase
ALT-Alanine Transaminase
ALP- Alkaline Phosphatase

REFERENCES

1. Sundd P, Gladwin MT, Novelli EM. Pathophysiology of sickle cell disease. Annual review of pathology: mechanisms of disease. 2019 Jan 24;14:263-92.
2. Houwing ME, De Pagter PJ, Van Beers EJ, Biemond BJ, Rettenbacher E, Rijneveld AW, Schols EM, Philipsen JN, Tamminga RY, van Draat KF, Nur E. Sickle cell disease: clinical presentation and management of a global health challenge. Blood reviews. 2019 Sep 1;37:100580.
3. Colah RB, Mukherjee MB, Martin S, Ghosh K. Sickle cell disease in tribal populations in India. Indian

DOI: 10.69605/ijlbpr_13.6.6

Journal of Medical Research. 2015 May 1;141(5):509-15.

4. Ashorobi D, Ramsey A, Killeen RB, Bhatt R. Sickle Cell Trait. 2024 Feb 25. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 30725815.
5. Jain D, Atmapoojya P, Colah R, Lodha P. Sickle cell disease and pregnancy. Mediterranean journal of hematology and infectious diseases. 2019;11(1).