

## Rare Case Report of Hemoglobin S $\beta$ Thalassemia.

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### ABSTRACT

Interaction of Hb S with beta thalassemia is being reported here as this type of case is rare. Hb S ( $\beta 6 \text{ glu} \rightarrow \text{val}$ ) is a genetic disorder which occurs due to beta globin gene mutation of hemoglobin. In India, the Hb S is prevalent in the central part, in the eastern, western and southern tribal belt regions. The Hb S carriers (Sickle cell trait) lead a normal life but the Sickle cell disease patients show certain clinical manifestation like joint pain, anemia and jaundice. The HPLC report of the patient showed Compound heterozygous for Hb S-  $\beta$  thalassemia. The complete blood count was measured in automated hematology analyser.

**Keywords:** Haemoglobinopathies, Hb S,  $\beta$  thalassemia.

### INTRODUCTION

Hb S  $\beta$  thalassemia is a double heterozygote state of Hb S and  $\beta$  thalassemia. Clinical features and hematologic findings are determined in part by  $\beta$  thalassemia gene with a more severe disease in  $\beta 0$  gene cases than in  $\beta +$  gene cases. Clinical picture resembles that of thalassemia intermedia. There is mild growth retardation, pallor, splenomegaly, vaso-occlusive crises, leg ulcers and aseptic necrosis of femoral heads. Peripheral smear shows microcytic hypochromic red cells, basophilic stippling and target cells and both MCV and MCH are decreased. There is increase in Hb F and Hb S levels. Prognosis is better than that of thalassemia major or sickle cell anemia.

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### CASE REPORT

A 32 years old male resident of Bihar and now living at Village Mangewal, Dist. Barnala for 10 months presented to Medicine OPD at Rajindra Hospital, Patiala with chief complaints of fever associated

with chills and rigors for 7 days. Fever was continuous, relieved for some time after taking medicine. He also complained of nasal bleeding, pain in legs and hip joint. On clinical examination, hepatosplenomegaly was present per abdomen. Investigations were done. On CBC, MCV was 68.4 fl, MCH was 32.2pg, MCHC was 47.1g/dl, Hb was 6.7g/dl, TLC was 7000/cumm, DLC- Neutrophils 48%, Lymphocytes 42%, Mixed 10%, Platelet count- was 23,000/cumm. On PBF, RBC picture showed microcytes, many target cells, normocytes, and few sickle cells. Polychromasia was mild. 3NRBC/100WBC were seen.

To confirm sickle cells, Sodium metabisulfite sickling test was done which showed immediate sickling. Urine examination showed 2-3 pus cells/hpf, 3-5 RBCs/hpf. LDH-1483 IU/L, S. bilirubin-2 mg/dl (direct-0.8mg/dl and indirect-1.18mg/dl), RBS-168mg%, Na<sup>+</sup>- 137 meq/L, K<sup>+</sup>- 5.7 meq/L, B. urea-78 mg/dl, S. creatinine- 1.1 mg/dl, ESR-27mm 1 hr, WIDAL- negative, RA-negative, Dengue- NS1 Ag- negative, Ig Ab-negative. Hb electrophoresis showed HbA- 61.9%(↓), HbF- 0.7%(normal), HbS/D- 33.9%(↑), HbA2- 3.5% (normal). To differentiate between HbS and HbD, HPLC was advised which showed HbA- 28.6%(low), HbA2-4.4% (high), HbF-23% (high), HbS- 44.7% (high), HbD-0.0%. From the above findings, it was concluded that patient is a case of double heterozygous Hb S $\beta$  thalassemia.

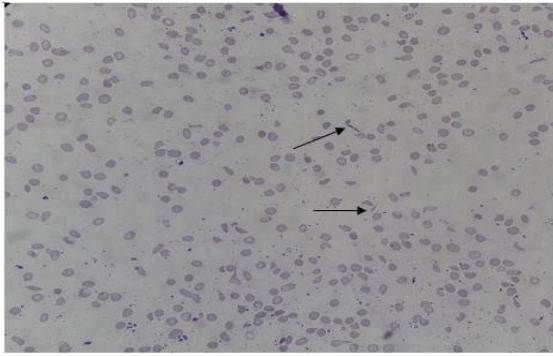


Figure 1: PBF showing sickled cells (arrows).

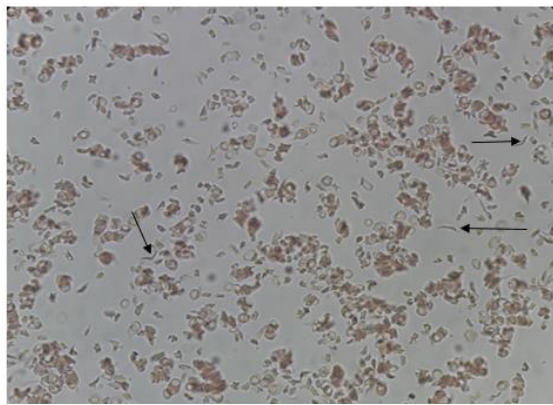


Figure 2: photomicrograph showing sickled cells (arrows) in sickling test by 2% sodium metabisulphite.

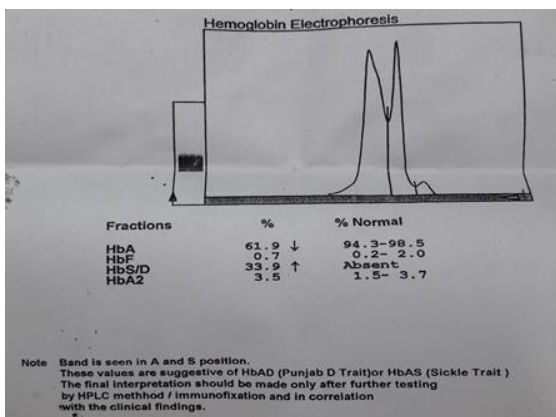


Figure 3: photomicrograph showing Hb electrophoresis.

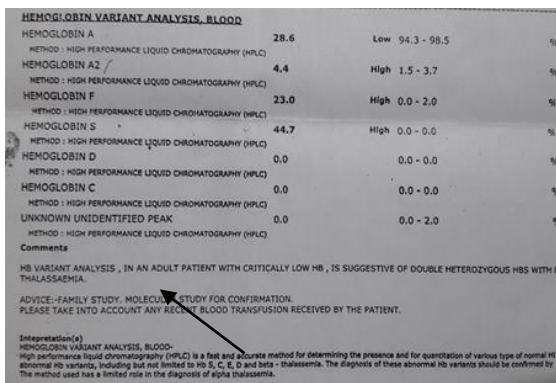


Figure 4: photomicrograph showing HPLC report.

## DISCUSSION & CONCLUSION

Haemoglobinopathies occur due to structural defect in the globin gene, whereas the thalassemias are due to defect in the production of globin chain. The sickle hemoglobin (Hb S) is of clinical importance because of their worldwide prevalence. Sickle cell anemia (Hb SS) is the most common heritable hematological disease affecting humans [1]. It is seen frequently in Africa and amongst black populations in North and South America and the West Indies. It is also found in certain regions in Greece, Turkey, Italy, Middle East and India [2]. In some parts of Africa, around 45% of the population have sickle cell trait and about 8% of blacks in United States, Latin America and Caribbean carry the sickle cell gene.<sup>[1]</sup> Sickle cell hemoglobin occurs due to mutation (Hb S,  $\beta 6$  glu $\rightarrow$ val).<sup>[1]</sup>

Sickle beta thalassemia prevalence was found to be relatively low in contrast to the prevalence of beta-thalassemia trait in various studies.<sup>[3-9]</sup> The average frequency of Sickle cell disorders in India is 4.3%. The highest prevalence has been recorded in the state of Orissa (1-44.4%), followed by Madhya Pradesh (1-40.0%; including Chhattisgarh), Tamil Nadu (1-40.0%), Andhra Pradesh (1-35.7%), Assam (1-35.5%), Maharashtra (0.8-35.0%), Gujarat (1-31.4%), Kerala (1-30.0%), Uttar Pradesh (1.5-18.5%), Karnataka (1-8.0%).<sup>[10]</sup> The eastern Indian states of Bihar, Chhattisgarh and Jharkhand and eastern region of Uttar Pradesh, which comprise ~25 % population of the country, are poorly studied with respect to hemoglobinopathies. A demographic study in eastern Indian states conducted on 1,642 individuals from this region, shows a frequency of 3.4 % for  $\beta$ -thalassemia trait, 3.4 % for sickle cell hemoglobin trait (HbS)/hemoglobin E trait (HbE) and 18 % for  $\alpha$ -globin defects. While  $\beta$  thalassemia trait mutations are distributed rather uniformly across the region, HbS occurs only in Chhattisgarh and Jharkhand, the regions rich in tribal populations.<sup>[11]</sup>

Several of the doubly heterozygous states for HbS and a second disorder of Hb synthesis are characterized by clinical and hematologic aberrations that to some extent mimic the features of sickle cell anemia. The clinically significant disorders resulting from double heterozygosity for Hb S and a second Hb variant are considered to be forms of sickle cell disease. Various other sickle cell disease combinations are- HbSC disease, HbS/HPFH, HbSE disease, Hb SD disease, Hb SO-Arab disease.<sup>[1]</sup> A case of Compound heterozygous for Hb S-  $\beta$  thalassemia was previously reported with severe anemia, massive hepatomegaly, splenomegaly and acute Chest syndrome.<sup>[12]</sup> Another

case from Assam was also reported as a compound heterozygous for HbS  $\beta$  thalassemia.<sup>[13]</sup>

In our case also the patient had severe anemia, epistaxis and complained of joint pain. On physical examination hepatosplenomegaly was observed in the patient. Only after our diagnosis report, patient became aware about his Hb variant carrier state.

The patient is double heterozygote for S gene from one parent and  $\beta$  thalassemia gene from the other parent. This doubly heterozygous condition of HbS and  $\beta$  thalassemia is designated as S $\beta$ 0 thalassemia if there is no  $\beta$ -globin synthesis from the affected allele and S $\beta$ + thalassemia if  $\beta$ -globin synthesis is present but reduced. The clinical manifestations are quite variable and patients may be nearly asymptomatic or have problems similar to those occurring in the worst cases of sickle cell anemia. In general, Hb S $\beta$ 0 thalassemia resembles Hb SS in severity and HbS  $\beta$ + thalassemia is somewhat milder than Hb SC disease. Patients with Hb S $\beta$ 0 thalassemia have a slightly higher Hb level, a greater HbA2 level (4% to 6%), and a smaller MCV (65 to 75 fl) than those with HbSS. HbS  $\beta$ + thalassemia patients have a higher Hb level and lower reticulocyte count than those with Hb S $\beta$ 0 thalassemia.<sup>[1]</sup> Hb electrophoresis shows HbS and HbF in Hb S $\beta$ 0 thalassemia and Hb S, Hb F and Hb A in HbS  $\beta$ + thalassemia.

Signs and symptoms of sickle beta thalassemia may include:<sup>[14,15]</sup>

- Anemia
- Repeated infections
- Frequent episodes of pain
- Pulmonary hypertension
- Acute chest syndrome (pneumonia-like condition due to entrapment of infection or sickle cells in the lungs)
- Stroke
- Enlarged spleen and/or liver
- Heart murmurs
- Delayed puberty
- Slowed growth
- Jaundice

The treatment for sickle beta thalassemia is supportive. The long-term outlook (prognosis) for people with sickle beta thalassemia varies depending on the severity of the condition. Sickle beta zero thalassemia (no normal hemoglobin) is usually associated with a worse prognosis and more severe disease course than sickle beta plus thalassemia (a reduced amount of normal hemoglobin). Although sickle cell diseases, including sickle beta thalassemia, can be fatal and are often associated with a shortened life span, early detection and the introduction of new treatment options have led to significant increases in life expectancy and survival of people with these conditions.<sup>[16]</sup>

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