RESEARCH PAPER

Sickle-β Thalassemia Presenting with Sepsis and Multi-organ Dysfunction in a 12-Year-Old Boy: A Case Report

Dr. Deepali Jain[1], Dr. Anita Deshmukh[2*], Dr. Pradnya J Phalak[3]

[1]Post Graduate Resident, Dept. of Biochemistry, Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune – 411018

[2*]Professor & Guide, Dept. of Biochemistry, Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune – 411018. Corresponding Author.

[3]HOD, Dept. of Biochemistry, Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune – 411018

ABSTRACT

Sickle Beta Thalassemia is a compound heterozygous condition resulting from the inheritance of one sickle cell gene (HbS) and one beta-thalassemia gene. It presents with a variable clinical spectrum, often mimicking both sickle cell disease and beta-thalassemia, making diagnosis and management complex. We present the case of a 12-year-old male who reported fatigue, progressive weight loss, intermittent joint and bone pain (especially in long bones), and a history of low-grade fever during vaso-occlusive episodes. Additional symptoms included pallor, jaundice, joint tenderness (knees and elbows), delayed signs of puberty, and multiple infections, leading to sepsis and multi organ failure. The patient had a history of repeated blood transfusions, contributing to increased susceptibility to infections and iron overload. Clinical examination revealed hepato splenomegaly and growth retardation. Laboratory findings demonstrated anemia with microcytic hypochromic indices, elevated reticulocyte count, and characteristic features on hemoglobin electrophoresis (HPLC), consistent with Sickle Beta Thalassemia. This case highlights the overlapping features of sickle cell disease (pain crises, vaso-occlusion) and beta-thalassemia (chronic anemia, growth failure), emphasizing how dual pathology can complicate diagnosis and long-term management. It reinforces the importance of a multidisciplinary approach, including transfusion management, infection prophylaxis, hydroxyl urea therapy, and endocrine follow-up. Furthermore, this case underlines the critical need for early diagnosis, parental carrier screening, and genetic counseling to prevent recurrence in future pregnancies, particularly in high-prevalence regions. Early intervention can significantly improve the patient's quality of life and long-term prognosis.

Keywords: Sickle-β thalassemia, hemoglobin electrophoresis, sepsis, multi-organ dysfunction syndrome, pediatric hemoglobinopathy, genetic counseling.

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INTRODUCTION

Hemoglobinopathies constitute a major global health burden, particularly in developing countries. Among them, sickle cell disease (SCD) and β-thalassemia are common autosomal recessive disorders affecting hemoglobin synthesis and structure.

The compound heterozygous state known as sickle-β thalassemia results from inheritance of a sickle cell gene from one parent and a β-thalassemia gene from the other. The clinical manifestations depend on the severity of β-globin chain deficiency and the proportion of hemoglobin fractions present.

Patients with sickle-β thalassemia frequently present with:

- hemolytic anemia
- vaso-occlusive episodes
- organ dysfunction
- susceptibility to severe infections and sepsis

Sepsis in such patients can precipitate multi-organ dysfunction syndrome (MODS) due to hemolysis, inflammation, endothelial damage, and micro vascular occlusion.

This case report describes a pediatric patient with sickle-β thalassemia presenting with severe sepsis and

laboratory evidence of multi-organ involvement, highlighting the role of biochemical and hematological investigations in diagnosis and management.

CASE PRESENTATION

A 12-year-old male child presented with complaints of:

- persistent fatigue
- progressive weight loss
- intermittent fever
- bone and joint pain, particularly in long bones
- generalized weakness

The symptoms were associated with episodes suggestive of vaso-occlusive crises. On clinical examination, the child appeared pale and febrile. Signs suggestive of systemic infection and anemia were noted.

The patient was evaluated at Dr. D. Y. Patil Medical College and Research Centre, Pune. A comprehensive diagnostic workup including hematological, biochemical, inflammatory, coagulation, and hemoglobin fraction analysis was performed.

Laboratory Investigations

Hematological Profile

Parameter	Value	Reference	Interpretation
Hemoglobin	1.7 g/dL	12–16	Severe anemia
RBC Count	0.90 ×10⁶/µL	4–5.5	Markedly reduced
Hematocrit	7.6 %	36–45	Severe anemia
MCV	84.8 fL	80–96	Normocytic
MCH	18.9 pg	27–32	Low
MCHC	22.3 g/dL	32–36	Hypochromia
RDW	24.3 %	<15	Anisocytosis
Platelet Count	144000/µL	150000–400000	Thrombocytopenia
WBC Count	1552/µL		Leukopenia

Differential Leukocyte Count

- Neutrophils: 62%
- Lymphocytes: 28%
- Monocytes: 9%
- Eosinophils: 1%

These abnormalities indicate bone marrow stress and systemic inflammatory response. The hematological findings indicate severe pancytopenia with life-threatening anemia, along with leukopenia and borderline thrombocytopenia. This suggests significant bone marrow suppression or dysfunction, possibly in the setting of severe systemic illness such as sepsis, with a need to rule out hemolysis and primary marrow pathology.

Liver Function Tests

Parameter	Value	Interpretation
Total Bilirubin	2.17 mg/dL	Hyperbilirubinemia
Direct Bilirubin	0.96 mg/dL	Hepatocellular injury
Indirect Bilirubin	1.21 mg/dL	Hemolysis
AST	249 U/L	Hepatic injury
ALT	52 U/L	Hepatocellular involvement
ALP	401 U/L	Cholestasis / liver involvement

The findings suggest a mixed pattern of liver injury with both hepatocellular and cholestatic features. This may be seen in conditions like sepsis-associated liver dysfunction, with a possible contribution from hemolysis.

Inflammatory and Sepsis Markers

Parameter	Value
CRP	214 mg/L
Procalcitonin	2.91 ng/mL
Ferritin	4973.61 ng/mL
LDH	3378 U/L
D-dimer	>10,000

Electrolytes and Coagulation Profile

Parameter	Value
Sodium	130 mmol/L
Potassium	4.46 mmol/L
Chloride	101 mmol/L
PT	13.8 s
INR	1.01
aPTT	41.9 s

These findings indicate severe systemic inflammation consistent with sepsis, accompanied by marked hyperferritinemia, elevated LDH, and significantly increased D-dimer, suggesting widespread tissue injury and activation of the coagulation pathway with evolving coagulopathy. The overall picture is indicative of multi-organ involvement.

Reticulocyte Count

Parameter	Value	
Reticulocyte Count	8.5 %	

The markedly elevated reticulocyte count indicated bone marrow response to severe hemolysis.

Renal Function Parameters

Parameter	Value
Blood Urea	72 mg/dL
Serum Creatinine	1.9 mg/dL
eGFR	52 mL/min/

The reduced eGFR suggested early renal impairment secondary to systemic inflammation and hemolytic stress.

Serum Lactate

Parameter	Value
Serum Lactate	5.6 mmol/L

Elevated lactate indicated tissue hypoxia and metabolic stress, commonly observed in Sepsis and severe hemolytic crises.

Imaging and Special Tests

Investigation	Result
Abdominal Ultrasound	Hepatosplenomegaly
Echocardiography	Pulmonary hypertension
Chest X-ray	Acute chest syndrome
HPLC Report	Iron overload in liver/heart

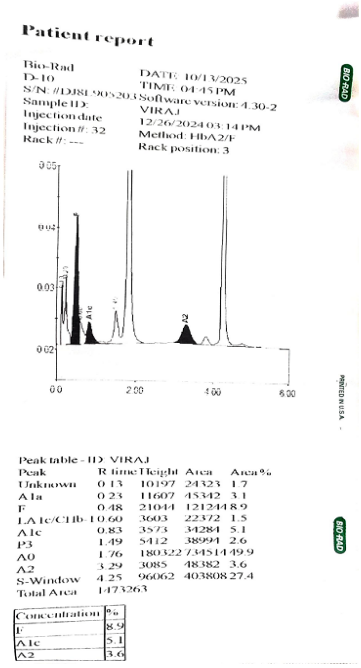

Figure 1: Patient Report

Critical Arterial Blood Gas Findings

Parameter	Value	Interpretation
pH	7.12	Severe acidemia
$PaCO_2$	28 mmHg	Respiratory compensation
HCO_3^-	9 mmol/L	Severe metabolic acidosis
PaO_2	58 mmHg	Severe hypoxemia
O_2 Saturation	82 %	Impaired oxygen delivery
Lactate	7.8 mmol/L	Severe tissue hypoxia
Base Excess	−17 mmol/L	Profound metabolic acidosis

INTERPRETATION

The ABG findings demonstrate:

- Severe metabolic acidosis
- Respiratory compensation
- Hypoxemia
- Marked lactic acidosis

This pattern is highly suggestive of systemic hypo perfusion and tissue hypoxia, which can occur during hemolytic crisis and septic shock in patients with Sickle Cell Disease.

Severe anemia combined with vascular occlusion in sickle disorders can impair oxygen delivery to tissues,

resulting in lactic acidosis and multi-organ dysfunction, a hallmark of Multiple Organ Dysfunction Syndrome.

DISCUSSION

Hemoglobinopathies are among the most prevalent inherited genetic disorders globally and represent a major public health concern, particularly in low- and middle-income countries. In India, the burden of hemoglobin disorders is substantial due to the high prevalence of carrier states within certain populations. One such condition is Sickle Beta Thalassemia, which occurs when an individual inherits one sickle hemoglobin gene and one β-thalassemia gene. The clinical manifestations of this compound hemoglobinopathy can vary widely depending on the specific β-globin mutation and the relative proportions of hemoglobin fractions present in the circulation. Patients may present with mild anemia and intermittent symptoms, while others experience severe hemolytic crises and life-threatening complications.[1]

In the present case, the patient exhibited severe anemia accompanied by markedly elevated markers of hemolysis and inflammation. Such findings are consistent with the pathophysiological processes underlying Sickle Cell Disease, where de-oxygenation of hemoglobin S leads to polymerization within red blood cells. This process results in the distortion of erythrocytes into the characteristic sickled shape, causing reduced deformability and obstruction of small blood vessels. The resulting vaso-occlusion contributes to tissue ischemia, endothelial damage, and activation of inflammatory pathways, ultimately leading to systemic complications.[2]

Another striking feature of the present case was the presence of markedly elevated inflammatory biomarkers suggestive of systemic inflammatory response. Individuals with sickle hemoglobinopathies are particularly vulnerable to infections due to functional hyposplenism, which arises from repeated splenic infarctions during vaso-occlusive episodes. Loss of effective splenic function significantly increases susceptibility to bacterial infections, especially those caused by encapsulated organisms. Consequently, patients may develop clinical features that resemble Sepsis, including fever, elevated inflammatory markers, and hemodynamic instability.[3]

The patient in this report also demonstrated severe metabolic acidosis with elevated serum lactate levels on Arterial Blood Gas analysis. Lactic acidosis in hemoglobinopathies is generally a consequence of impaired oxygen delivery resulting from severe anemia and micro vascular occlusion. Reduced oxygen availability at the tissue level forces cells to rely on anaerobic metabolism, leading to the accumulation of lactate. Such metabolic disturbances may indicate significant tissue hypoxia and are often associated with poor clinical outcomes in critically ill patients.[4]

Furthermore, laboratory investigations revealed evidence of hepatic and renal dysfunction, suggesting early development of Multiple Organ Dysfunction Syndrome. Renal involvement is a recognized complication of sickle hemoglobinopathies and may occur due to chronic hemolysis, oxidative stress, and recurrent ischemic injury to renal microvasculature. Similarly, hepatic abnormalities may arise from intrahepatic sickling, cholestasis, or hemolysis-related hyperbilirubinemia. The combination of severe anemia, hypoxia, and inflammatory activation can therefore contribute to progressive organ dysfunction in susceptible patients.[5]

An important aspect of this case was the significant family history, with three siblings reported to have died during childhood from similar clinical manifestations. Familial clustering of hemoglobinopathies is frequently observed in regions with high carrier frequencies. In India, the prevalence of hemoglobinopathies varies considerably across different geographic regions and ethnic groups, but overall contributes substantially to childhood morbidity and mortality. Population-based screening programs and genetic counseling have therefore been recommended to enable early identification of carriers and prevent severe disease in future generations.[6]

Early and accurate diagnosis of compound hemoglobin disorders is crucial for effective patient management. Laboratory techniques such as hemoglobin electrophoresis and high-performance liquid chromatography remain the gold standard for detecting abnormal hemoglobin variants and determining hemoglobin fractions. These diagnostic methods allow differentiation between various hemoglobinopathies and guide appropriate clinical management strategies.[7]

Taken together, this case highlights the diverse clinical spectrum of sickle β-thalassemia and underscores the importance of integrating clinical findings with hematological and biochemical investigations. Prompt recognition of severe complications, including hemolytic crisis, systemic inflammation, and organ dysfunction, is essential to improve outcomes in affected patients.

CONCLUSION

The present case describes a severe manifestation of Sickle Beta Thalassemia characterized by profound hemolytic anemia, systemic inflammatory response, metabolic acidosis, and early evidence of multi-organ dysfunction. Comprehensive laboratory evaluation including hemolysis markers, inflammatory biomarkers, arterial blood gas analysis, and hemoglobin electrophoresis was instrumental in establishing the diagnosis and assessing disease severity.

The presence of a strong family history with multiple sibling deaths further highlights the importance of early detection, carrier screening, and genetic counseling in regions where hemoglobinopathies are prevalent. Early diagnosis and timely clinical intervention are critical to preventing severe complications and reducing disease-related morbidity and mortality in patients with compound hemoglobin disorders.

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