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Roadway to A Rare Hemolytic Anemia - A Case Series of Cooley's Anemia

B. S. Chinna Devi, M. Preethi*
Department of Pathology, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

Abstract

Thalassemia is a hemolytic anemia resulting from an inherited autosomal recessive genetic disorder. It is characterized by reduced hemoglobin synthesis due to defective production of either the alpha or beta globin chains. In our case report, we have discussed 3 case reports with exact similarity. All 3 cases were 5-year-old sex presented to the outpatient pediatric department at Sree Balaji Medical College and Hospital with complaints of cough, cold, dyspnea, irritability, and fatigue. On examination, the patient exhibited scleral pallor and a whitish tinge over the fingernails and extremities. There was evidence of a decayed upper tooth, though it was not associated with pain or swelling. Head and neck examination revealed maxillary prominence, a retracted upper lip, and a saddle nose, collectively giving the classical appearance of "chipmunk facies." The patient's hemoglobin level was critically low at 3.5 g/dL. Hematological investigations showed microcytic hypochromic anemia with anisopoikilocytosis and nucleated red blood cells (RBCs). Peripheral smear findings were consistent with hemolytic anemia, strongly suggesting thalassemia with concurrent hemolytic crisis.

Keywords: *Hemolytic Anemia, Hemoglobin Electrophoresis, Thalassemia, Target Cells.*

Introduction

Thalassemia is a group of inherited hemolytic anemias caused by mutations affecting the synthesis of alpha or beta globin chains of hemoglobin [1, 2]. Among them, beta-thalassemia is more prevalent and clinically significant, especially in populations with high rates of consanguineous marriages [3, 4]. It follows an autosomal recessive inheritance pattern, meaning that both parents must be carriers for a child to inherit the disease [5]. Early identification within families is crucial for genetic counseling, carrier screening, and prenatal diagnosis to prevent disease [6]. Recognizing the familial nature of beta-thalassemia is essential for breaking the transmission cycle and reducing the disease burden in future generations [7]. Treatment and regular follow up is required for the bata thalassemia patient. Early, the diagnosis and treatment increases the life expectancy of the people.

Case Report 1

A 5-year-old female child was brought to the Pediatric Outpatient Department at Sree Balaji Medical College and Hospital with complaints of cough, cold, dyspnea, irritability, and fatigue. There was no history of fever. Her family history with beta thalassemia trait for grandmother, explained in pedigree chart (figure 3).

On general examination, the child appeared ill-looking but had stable vital signs. Clinical evaluation revealed signs of anemia, including brittle hair and nails, severe koilonychia, and pallor of the sclera. The skin was ashen-grey, with yellowish discoloration of the fingernails. The patient was underweight (10.11 kg),

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****Corresponding Author: drpreethi1290@gmail.com***

underbuilt, and undernourished and exhibited short stature. Mild icterus and dehydration were noted. Craniofacial features included maxillary expansion, a retracted upper lip, and a saddle nose, giving a classical "chipmunk facies" appearance. Intraoral examination revealed periodontitis and broken lower anterior teeth, along with a decayed upper tooth, not associated with pain or swelling.

Ultrasonography, ophthalmologic, and audiologic examinations were within normal limits. Initial hematological evaluation revealed a critically low hemoglobin level of 3.5 g/dL. Peripheral smear examination demonstrated microcytic hypochromic anemia with marked anisopoikilocytosis and the presence of nucleated red blood cells (Figure 2), suggestive of hemolytic anemia and raising a strong suspicion of thalassemia with an ongoing hemolytic crisis. Subsequent hemoglobin electrophoresis confirmed the diagnosis of beta-thalassemia major, showing HbA at 94.6%, HbA2 at 5.1%, and HbF or variant at 0.3% (Figure 1). Additional investigations revealed a post-transfusion hemoglobin level of 7.5 g/dL and a markedly elevated serum ferritin level of 3452.69 ng/mL, while screening for HIV, Hepatitis B, and Hepatitis C was negative. Liver and renal function tests were within normal limits. The patient was immediately initiated on supportive care with transfusion therapy, receiving 3 units of packed red blood cells at a rate of 220 mL/hr. Her vital signs remained stable during the transfusion, and no adverse reactions were noted. On follow-up, her hemoglobin levels remained persistently low (5.5 g/dL), necessitating transfusions every 18 to 20 days. Given the iron overload, iron chelation therapy was initiated with Deferoxamine 2 g, administered four times weekly, along with oral Deferasirox 400 mg once daily. She is currently under regular follow-up with monitoring of liver and thyroid function tests every 20 days, and her growth and developmental milestones are assessed during each outpatient visit. The patient and her family have been counseled, and she has been advised to undergo bone marrow transplantation, which remains the definitive curative treatment for beta-thalassemia major.

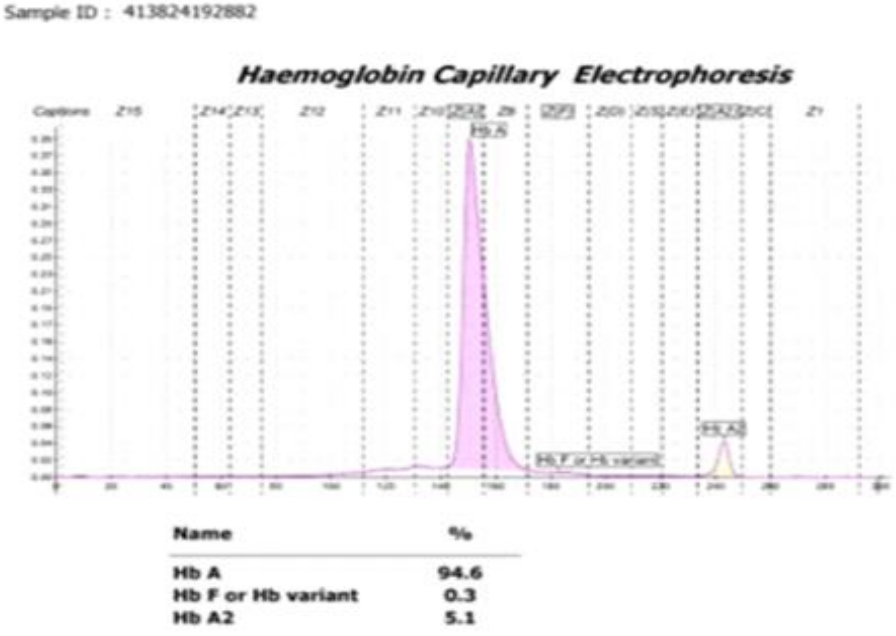

Figure 1. Hemoglobin Electrophoresis Graph with Values HbA 94.6%, HbF -0.3% and HbA2-5.1%

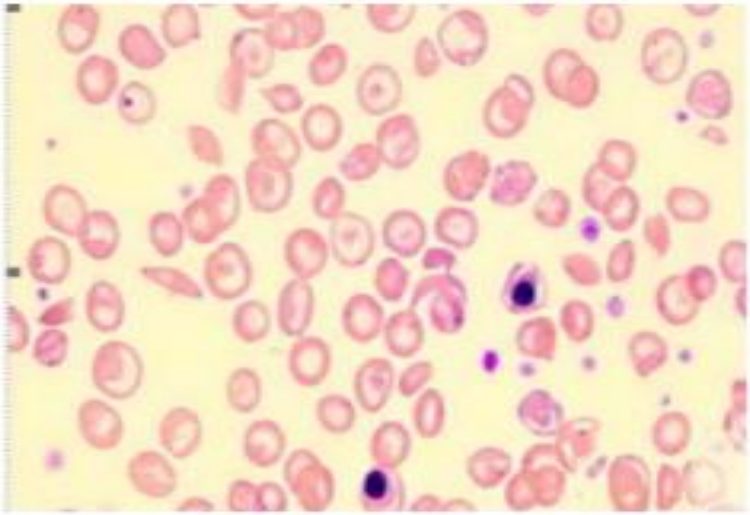

Figure 2. Smear (Case Report 1) Shows Microcytic Hypochromic Anemia with Severe Anisopoikilocytosis, Nucleated Red Blood Cells (RBC), Tear drop Cells, Target Cells (Codocytes), Acanthocytes and Macroovulocytic RBC)

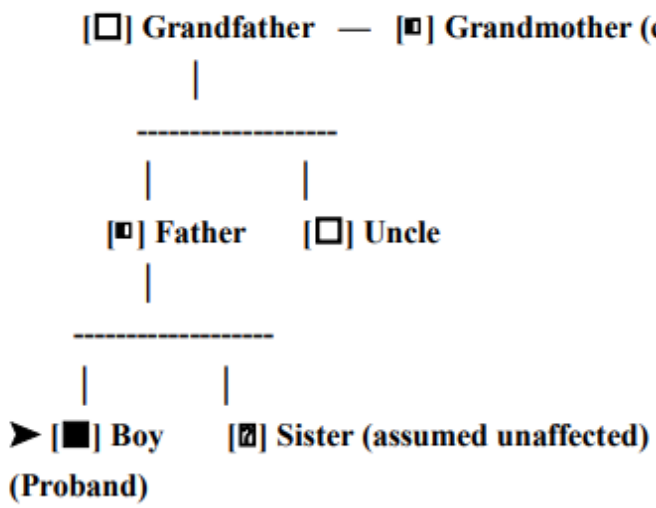

Figure 3. Pedigree Chart of the Case Report 1 with Explanation

■ = Affected male (thalassemia major), ◧ = Female carrier (thalassemia trait) ⍰ / □ = Unaffected male/female and ➤ = Proband (person of interest)

Case Report 2

A 4-year-old child was brought to the Pediatric Outpatient Department of Sree Balaji Medical College and Hospital with complaints of cough, cold, dyspnea, irritability, and fatigue. There was no associated fever. The family history was not significant for any hematological or genetic disorders (Figure 5), as explained in the pedigree chart.

On general physical examination, the child appeared ill-looking but was hemodynamically stable. She exhibited signs of anemia, including brittle hair, brittle nails, severe koilonychia, and pallor of the sclera. The fingernails and distal extremities showed a whitish tinge, and the skin was ashen grey. She was dehydrated and weighed 10.11 kg, indicating that she was underbuilt, undernourished, and had short stature. Mild icterus was noted, along with yellow-tinged fingernails. Dental evaluation

revealed a decayed upper tooth without pain or swelling. Craniofacial examination showed classical “chipmunk facies,” with maxillary expansion, a retracted upper lip, and a saddle nose. Intraoral examination revealed periodontitis and broken teeth in the lower anterior region. Ultrasound imaging and ophthalmologic and audiologic evaluations were within normal limits.

Initial hematological investigations revealed a hemoglobin (Hb) level of 3.5 g/dL. Peripheral blood smear (Figure 4) showed microcytic hypochromic anemia with anisopoikilocytosis and nucleated red blood cells (RBCs), suggestive of hemolytic anemia, raising suspicion for thalassemia in hemolytic crisis. Further evaluation with hemoglobin electrophoresis confirmed the diagnosis of beta-thalassemia major, with the following findings: HbA – 94.6%, HbA2 – 5.1%, and HbF/variant – 0.3% (Figure 2). Post-transfusion Hb was measured at 7.5 g/dL. Viral screening for HIV, Hepatitis B, and Hepatitis C was negative. Liver function test (LFT) and renal function test (RFT) were within normal limits. The child was managed with supportive transfusion therapy and was transfused with three units of packed red blood cells at a rate of 220 mL/hr. No transfusion-related complications were observed, and her vitals remained stable throughout the procedure. She was discharged and advised to follow up after 13 days. On follow-up, her serum ferritin level was found to be significantly elevated at 3452.69 ng/mL, prompting the initiation of iron chelation therapy with Deferoxamine (DFO) 2 grams per dose, administered four times a week, and oral Deferasirox 400 mg once daily. At that time, her Hb was 5.5 g/dL, and she received another unit of packed red blood cells before discharge.

Since then, she has required hospitalization every 20 days for packed RBC transfusions. Her liver and thyroid function tests are monitored every 20 days, and her growth and developmental milestones are evaluated during each outpatient follow-up. The patient has been counseled for bone marrow transplantation, which remains the only curative option.

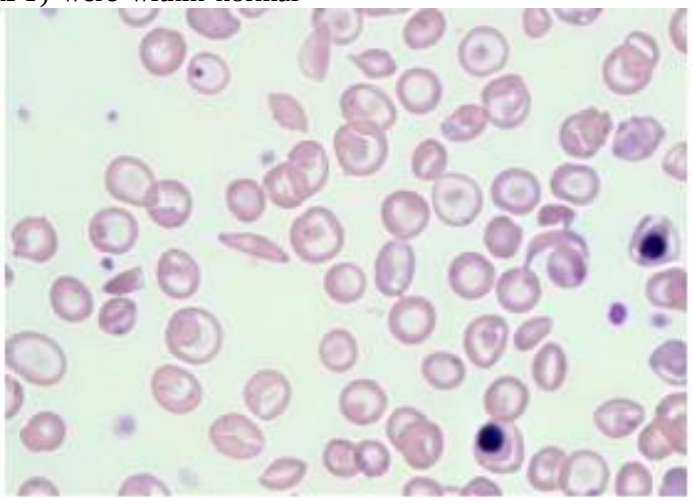

Figure 4. Smear (Case Report 2) Shows Microcytic Hypochromic Anemia with Severe Anisopoikilocytosis, Nucleated Red Blood Cells (RBC), Target Cells (Codocytes), Acanthocytes, Macroovulocytic RBC and Giant Platelet

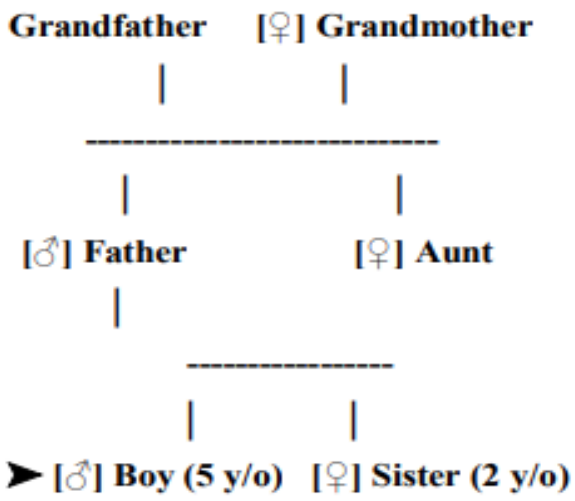

Figure 5. Pedigree Chart of the Case Report 1 with Explanation for Case Report 2

■ = Affected male (thalassemia major), ◧ = Female carrier (thalassemia trait), ⍰ / ☐ = Unaffected male/female, ➤ = Proband (person of interest)

Case Report 3

A 5-year-old boy presented to the outpatient pediatric department at Sree Balaji Medical College and Hospital with a history of cough, cold, Dyspnea, Irritability, and fatigue. She had no fever. Family history reveals beta thalassemia trait for her younger sister, and her mother is also a beta thalassemia trait positive, so it signifies that the blood-related disorder or genetic disease already exists in the family (Figure 7: Pedigree Chart). On physical examination patient was ill looking. Her vitals were stable. She was clinically anemic with brittle hair and nail, severe koilonychia. Patient's finger nails and skin extremities exhibited a whitish tinge, and the sclera showed pallor. Her skin was ashen grey in color, dehydration was present and her body weight of 10.11 kg. She was underbuilt, under-nourished, with a short stature, with mild icterus, and yellow-tinged finger nails. Decayed upper tooth, not associated with pain or swelling. Head and Neck examination showed maxillary expansion, retracted upper lip and saddle nose and resembling classical "Chipmunk facies". Intraoral examination showed periodontitis and broken teeth in the lower anterior aspect. Ultrasound findings were within normal limits, and ophthalmologic and audiologic examinations were within normal limits.

Haematological examination was performed. Her haemoglobin was 3.5 gm/dl. Hematologic investigation revealed microcytic hypochromic anaemia with anisopoikilocytosis and nucleated Red Blood Cells (RBCs) on the peripheral smear (Figure 6). The impression drawn from the peripheral smear study was that of haemolytic anaemia favouring Thalassemia with haemolytic crisis. Later Haemoglobin (Hb) electrophoresis was done which too was in favor of Beta Thalassemia major. Her Human immunodeficiency Virus (HIV), Hepatitis B, and Hepatitis C was negative. Liver function test and Renal function test were within standard limit. She was planned for blood transfusion and 3 points of packed cell transfused at the rate of 220 ml /hr. Her vitals were within normal limits during the transfusion, and no transfusion-related complications were encountered. Then she was investigated for Haemoglobin electrophoresis, which showed elevated HbA 94.6%, HbF or Hb variant 0.3%, HbA2 5.1% fig no. 2), and hemoglobin (Hb) was found to be 7.5 gm/dl. Then she was discharged and advised to follow up in 13 days. On follow-up, her ferritin was measured and found to be 3452.69 ng/mL. Then

she was started on iron chelating agent (Deferoxamine B(DFO) 2 gm per dose at the rate of 4 times in a week and oral Deferasirox 400 mg once in a day dose). Her Hb was 5.5 mg/dl, she was transfused with a point of packed cells and discharged home with a follow-up in 18 days for transfusion. She was hospitalized every 20 days for transfusion of packed RBC. She is investigated for Liver function test and thyroid function test every 20 days. Her growth and development are assessed in every OPD visit for follow-up, and the patient was advised of bone marrow transplantation.

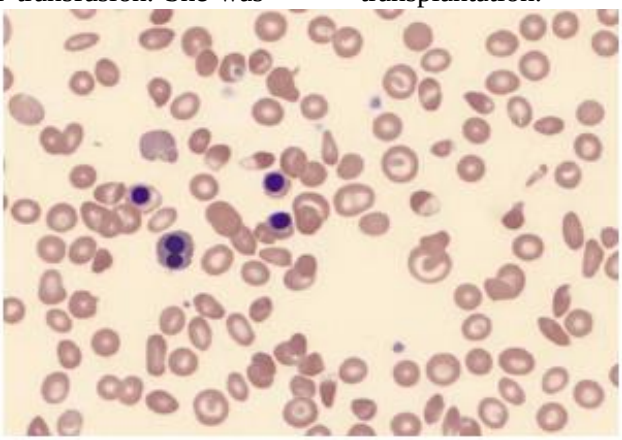

Figure 6. Smear Shows (Case Report 3) Microcytic Hypochromic Anemia with Severe Anisopoikilocytosis, Nucleated Red Blood Cells (RBC), Tear Drop Cells, Elongated Cells, Target cells (Codocytes), Acanthocytes, Macroovulocytic RBC and Neutrophils with Toxic Granules

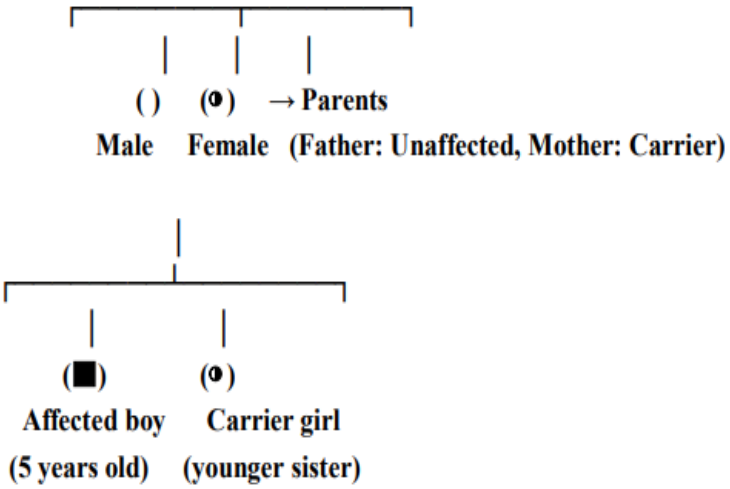

Figure 7. Pedigree Chart for Case Report 3

( ) = Father – unaffected, (◑) = Mother – beta thalassemia trait (carrier), (■) = Son – affected with beta thalassemia, (◑) = Daughter – beta thalassemia trait (carrier)

Discussion

In this case, the development has been hampered due to a loss of blood [8]. Beta-thalassemia major typically presents in infancy or early childhood with symptoms of profound anemia, growth retardation, hepatosplenomegaly, and skeletal deformities. This case highlights the classic clinical stigmata, including "chipmunk facies" and severe anemia, which prompted prompt diagnosis [9, 10].

The cornerstone of treatment remains regular blood transfusions, which help maintain hemoglobin levels and suppress ineffective erythropoiesis. However, chronic transfusions

lead to iron overload, necessitating early initiation of iron chelation therapy. Serum ferritin levels are helpful in monitoring iron burden. Bone marrow transplantation remains the only curative option and offers the best outcomes when performed early with an HLA-matched sibling donor [11, 12]. Genetic counseling for the family is critical for future reproductive planning.

This case reports highlights the typical presentation of beta-thalassemia major in early childhood, including progressive anemia, growth retardation, and characteristic craniofacial abnormalities [13]. Early detection based on clinical and hematologic features followed by confirmatory hemoglobin electrophoresis is critical for initiating prompt therapy. Chronic transfusion therapy improves survival and quality of life but leads to secondary iron overload, necessitating chelation therapy [14, 15]. Serum ferritin levels are a valuable marker of iron burden. Bone marrow transplantation, if performed early, offers the potential for a cure, especially in patients with an HLA-matched donor [16].

This case illustrates the typical presentation of beta-thalassemia major, with severe anemia, classical craniofacial deformities, and failure to thrive. Peripheral smear and hemoglobin electrophoresis remain key diagnostic tools [17, 18]. The mainstay of treatment is lifelong blood transfusion combined with iron chelation therapy to prevent secondary hemosiderosis. Regular monitoring is crucial to detect complications such as endocrine dysfunction, growth failure, and organ damage. Bone marrow transplantation offers the potential for a cure and is best performed at an early age with an HLA-matched sibling donor. Genetic counseling plays a vital role in preventing disease transmission and informing future family planning [19, 20].

Early diagnosis of beta-thalassemia major is essential for optimal disease management and improved patient outcomes. Delayed diagnosis often results in severe anemia, growth failure, skeletal deformities, and end-organ complications due to chronic hypoxia and iron overload [21, 22]. Neonatal screening and early clinical suspicion—based on signs such as pallor, poor weight gain, hepatosplenomegaly, and characteristic facial changes—allow for the timely initiation of transfusion therapy and iron chelation before complications develop. Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) is a definitive diagnostic tool that helps distinguish thalassemia from other causes of microcytic anemia [23, 24]. Once diagnosed, early genetic counseling and family screening are pivotal for identifying carriers and preventing recurrence through informed reproductive choices. Additionally, early initiation of therapy improves growth and developmental outcomes and enhances long-term quality of life. For patients with a matched sibling donor, early evaluation for bone marrow transplantation offers a curative opportunity, especially before transfusion-associated complications occur [25, 26].

The cornerstone of treatment in beta-thalassemia major is regular red blood cell transfusions to maintain adequate hemoglobin levels, suppress ineffective erythropoiesis, and promote normal growth and development [27, 28]. Transfusion therapy typically begins during infancy or early childhood and continues throughout life unless curative therapy is achieved. While transfusions improve quality of life and survival, they are associated with the risk of iron overload. Thus, iron chelation therapy is initiated once serum ferritin levels rise above 1000 ng/mL or after approximately 10–20 transfusions. Common chelating agents include Deferoxamine, which is administered subcutaneously or intravenously, and oral agents such as Deferasirox and Deferiprone, which offer improved compliance. Regular monitoring of serum ferritin, liver, and cardiac iron load (via MRI), and organ function is critical in patients receiving long-term chelation. Supportive care also includes folic

acid supplementation, vaccination against hepatitis viruses, endocrine evaluation, and management of complications such as growth retardation, hypothyroidism, and delayed puberty. In eligible patients, hematopoietic stem cell transplantation (HSCT) from an HLA-matched sibling donor is considered the only curative therapy and has shown the best outcomes when performed at a younger age before the onset of iron-related organ damage.

Although a common disease among the South Asian Population, case reports are very few and have been reported under different circumstances. We have tried to report cases that have failed to follow up despite the diagnosis. Complications can occur in any patient who refuses to follow up, so proper counselling should be provided to ensure the patient attends regular follow-ups and is saved, which can be prevented with timely intervention. Along with this, the community should take an active role in helping the patients with regular follow-up and proper supply of blood needed for the patient.

Conclusion

The Cooley's anemia or Beta-thalassemia major is a chronic hematologic condition that presents with severe clinical manifestations in early childhood. Timely diagnosis, comprehensive transfusion care, iron chelation, and growth monitoring are essential for optimal patient outcomes. Bone marrow transplantation remains the definitive cure and should be considered early in eligible patients. This case underscores the importance of a multidisciplinary approach and regular follow-up in the management of children with thalassemia.

Conflict of Interest

The Consent Form was signed by the patient for publishing the details.

Acknowledgements

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