

Refractory Anemia Associated Iron Overload in a Four-Year-Old Child with Chronic Transfusion-Dependent Microcytic Anemia Related to Abdominal Tuberculosis: A Case Report

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Abstract: Background: Iron overload is a serious complication of chronic blood transfusion therapy in pediatric patients with transfusion-dependent anemia. Early recognition through iron studies is essential to prevent irreversible organ damage. **Case Presentation:** A four-year-old Sudanese boy presented with persistent pallor since six months of age requiring repeated blood transfusions, the last occurring 40 days before evaluation. Previous investigations for β -thalassemia, sickle cell disease, and glucose-6-phosphate dehydrogenase deficiency were reportedly negative. Two months before presentation, he underwent abdominal surgery for intestinal obstruction secondary to abdominal Tuberculosis, no hepatosplenomegaly. Laboratory evaluation demonstrated severe anemia (hemoglobin 5.3 g/dL), microcytosis (MCV 78 fL), Normal Reticulocytes count (1.5%), leukocytosis with absolute lymphocytosis, thrombocytosis ($788 \times 10^3/\mu\text{L}$), serum ferritin >2000 ng/mL, serum iron $266 \mu\text{g/dL}$, transferrin saturation 70.3%, and normal TIBC ($378 \mu\text{g/dL}$), indicating marked transfusional iron overload. No evidence of hemolysis, normal bilirubin (total bilirubin 0.5 mg/dl and direct bilirubin 0.3 mg/dl). **Conclusion:** This case emphasizes the importance of routine monitoring of iron status in children receiving chronic blood transfusions. Early diagnosis and initiation of iron chelation therapy are essential to reduce morbidity associated with iron overload.

Keywords— Iron overload; Ferritin; Blood transfusion; Pediatric anemia; Hemosiderosis; Sudan.

INTRODUCTION

Pediatric refractory anemia refers to persistent, treatment-resistant anemia that often requires chronic red blood cell transfusion support to maintain adequate oxygenation and growth [1]. While blood transfusions are life-saving, humans lack an active physiological mechanism to excrete excess iron [2]. Consequently, chronic transfusions lead to secondary hemosiderosis, characterized by iron accumulation in vital organs including the liver, heart, and endocrine glands [3].

Diagnosing the underlying etiology of pediatric refractory anemia can be intricate, particularly in resource-limited settings where rare congenital bone marrow failure syndromes, congenital dyserythropoietic anemias (CDA), or sideroblastic anemias must be differentiated from common causes [4,5]. Furthermore, coexisting systemic infections and inflammatory diseases—such as abdominal tuberculosis—serve as major risk factors that exacerbate anemia through mechanisms of chronic disease, impaired intestinal absorption, and systemic inflammation [6]. Timely evaluation of iron parameters (ferritin, serum iron, and transferrin saturation) is vital for initiating iron chelation therapy before tissue damage becomes irreversible [7,8].

CASE PRESENTATION

A four-year-old Sudanese boy presented with a history of severe, progressive pallor noted since six months of age. The patient had been dependent on recurrent blood transfusions since infancy, receiving his last transfusion approximately 40 days prior to laboratory assessment. On physical examination, the child appeared chronically ill and markedly underweight, with a body mass index (BMI) of 13.9 kg/m^2 . No hepatosplenomegaly was detected on clinical palpation.

According to the managing pediatrician, previous comprehensive screening for common causes of hereditary hemolytic anemia—including β -thalassemia trait/disease, sickle cell hemoglobinopathy, and glucose-6-phosphate dehydrogenase (G6PD) deficiency—was completely negative. Additionally, celiac disease screening was negative.

Two months prior to this evaluation, the child developed acute abdominal distension and features of intestinal obstruction. He underwent emergency laparotomy with resection of an obstructed segment of the small intestine. Histopathological and clinical examination confirmed abdominal tuberculosis, and anti-tuberculosis therapy (ATT) was commenced.

LABORATORY INVESTIGATIONS

Complete blood count (CBC) was performed using the Zybio 3PD automated hematology analyzer. Comprehensive biochemical, hemolysis, and iron profile panels were systematically evaluated as presented in Tables 1, 2, 3, and 4.

Table 1: Complete Blood Count (CBC) Parameters (Zybio 3PD Analyzer)

parameter	Patient Value	Normal Reference Range	Interpretation
Hemoglobin (HGB)	5.3 g/dL	11.5 – 15.5 g/dL	Severe Anemia
RBC Count	2.04 × 10 ⁶ /μL	4.00 – 5.30 × 10 ⁶ /μL	Decreased
Hematocrit (HCT)	15.9 %	35.0 – 45.0 %	Markedly Decreased
Mean Corpuscular Volume (MCV)	78.0 fL	80.0 – 97.0 fL	Microcytosis
Mean Corpuscular Hemoglobin (MCH)	25.8 pg	27.0 – 32.0 pg	Hypochromia
MCHC	33.1 g/dL	32.0 – 36.0 g/dL	Normal
Red Cell Distribution Width (RDW-CV)	17.1 %	11.5 – 14.8 %	Increased (Anisocytosis)
White Blood Cells (WBC)	18.26 × 10 ³ /μL	4.50 – 11.00 × 10 ³ /μL	Leukocytosis

Lymphocytes (%)	74 %	20 – 45 %	Absolute Lymphocytosis
Platelet Count (PLT)	788 × 10 ³ /μL	150 – 450 × 10 ³ /μL	Marked Thrombocytosis

Table 2: Clinical Chemistry & Hemolysis Evaluation

Test Name	Patient Result	Normal Reference Range	Clinical Interpretation
Total Bilirubin	0.5 mg/dL	0.2 – 1.2 mg/dL	Normal (No evidence of hemolysis)
Direct Bilirubin	0.3 mg/dL	0.0 – 0.3 mg/dL	Normal
Reticulocyte Count	1.5 %	0.5 – 2.0 %	Inappropriately Normal (Hypoproliferative)
Celiac Disease Screening	Negative	Negative	Excludes Celiac Malabsorption

Table 3: Biochemical Iron Profile Parameters

Parameter	Patient Value	Normal Reference Range	Clinical Interpretation
Serum Ferritin	> 2000 ng/mL	30 – 400 ng/mL	Severe Iron Overload
Serum Iron	266 μg/dL	50 – 120 μg/dL	Elevated
Total Iron Binding Capacity (TIBC)	378 μg/dL	250 – 425 μg/dL	Normal
Transferrin Saturation	70.3 %	20 – 50 %	Markedly Elevated

Table 4: Peripheral Blood Picture (PBP) Findings

CELL LINE	MICROSCOPIC MORPHOLOGY	FINDINGS &
RED BLOOD CELLS (RBCs)	DIMORPHIC PICTURE COMPRISING SEVERE MICROCYTIC HYPOCHROMIC RED CELLS ALONGSIDE NORMOCYTIC NORMOCHROMIC CELLS (TRANSFUSED POPULATION). FREQUENT PENCIL CELLS PRESENT. NO NUCLEATED RBCs (NRBCs) SEEN.	
WHITE BLOOD CELLS (WBCs)	MARKEDLY INCREASED IN NUMBER WITH ABSOLUTE LYMPHOCYTOSIS AND MILD REACTIVE LYMPHOCYTES.	
PLATELETS (PLTs)	MODERATELY TO MARKEDLY INCREASED IN NUMBER (THROMBOCYTOSIS) WITH FOCAL MILD PLATELET AGGREGATION.	
DIAGNOSTIC IMPRESSION	FASTING IRON PROFILE DOES NOT CORRELATE WITH CLASSICAL IRON DEFICIENCY ANEMIA (IDA) OR ANEMIA OF CHRONIC DISEASE (ACD); FINDINGS PRIMARILY INDICATE TRANSFUSIONAL IRON ACCUMULATION.	

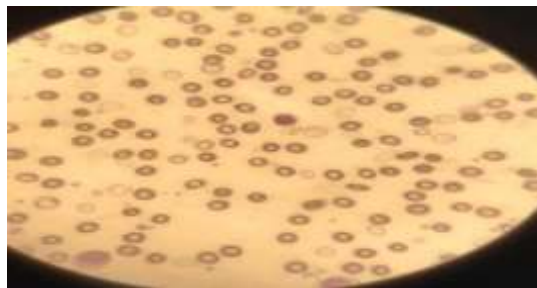


Fig.1. severe microcytic hypochromic red cells alongside normocytic normochromic. Frequent pencil cells, Markedly increased lymphocytosis and mild reactive lymphocytes, Moderately to markedly (thrombocytosis) with focal mild platelet aggregation

DISCUSSION

This four-year-old child presents with a complex clinical dilemma: severe refractory microcytic anemia requiring chronic transfusion support, accompanied by marked secondary iron overload and coexisting abdominal tuberculosis.

The patient's iron profile—highlighted by a serum ferritin level exceeding 2000 ng/mL and a transferrin saturation of

70.3%—provides definitive evidence of severe transfusional iron accumulation (hemosiderosis) [3]. Although the peripheral blood smear demonstrated microcytic hypochromic erythrocytes and frequent pencil cells (morphological features classically associated with iron deficiency), the biochemical iron indices conclusively exclude true iron deficiency [7]. The dimorphic red blood cell picture reflects the dual presence of the patient's intrinsically abnormal microcytic erythropoiesis and the transfused normocytic donor red cells.

Crucially, the normal total bilirubin (0.5 mg/dL), normal direct bilirubin (0.3 mg/dL), and a reticulocyte count of 1.5% confirm the absence of active hemolysis, pointing instead toward a hypoproliferative bone marrow disorder or defective erythroid maturation as the driver of refractory anemia [4]. Negative screening for β -thalassemia, sickle cell anemia, G6PD deficiency, and celiac disease further narrows the differential diagnosis.

The history of abdominal tuberculosis and subsequent bowel resection introduces a significant confounding factor. Abdominal TB serves as a chronic inflammatory risk factor that can aggravate anemia via cytokine-mediated suppression of erythropoiesis and nutrient malabsorption, contributing to the patient's low BMI (13.9 kg/m²) [6,8]. Furthermore, reactive thrombocytosis (platelets $788 \times 10^3/\mu\text{L}$) and lymphocytosis are characteristic systemic inflammatory responses to active mycobacterial infection and recent surgical intervention.

Given the persistence of refractory transfusion-dependent anemia without a definitive primary diagnosis, advanced diagnostic investigations are required to evaluate rare inherited erythroid disorders [9,10].

Conclusion & Recommendations

This case demonstrates severe secondary transfusional iron overload in a young boy with refractory microcytic anemia of undetermined primary origin, complicated by abdominal tuberculosis. Systematic iron monitoring is vital in all pediatric patients undergoing long-term transfusion therapy to guide timely chelation and prevent organ damage.

Recommendations for Management & Diagnostic Workup:

1. Iron Chelation Therapy: Immediate initiation of pediatric iron chelation therapy (e.g., Deferasirox) under hematological supervision to prevent irreversible end-organ damage.
2. Bone Marrow Examination: Bone marrow aspiration and biopsy with Perl's Prussian blue stain to evaluate marrow cellularity, ringed sideroblasts, and dyserythropoiesis.
3. Advanced Genetic & Molecular Testing: Screening for congenital dyserythropoietic anemia (CDA), congenital sideroblastic anemia, and inherited bone

marrow failure syndromes (e.g., Diamond-Blackfan anemia).

4. Tissue Iron Assessment: Hepatic and cardiac MRI (T2*) to quantify non-invasive organ iron deposition if accessible.

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