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Iatrogenic Iron Overload in a Sudanese Thalassemic Patient Exacerbates Kidney Dysfunction: A Case Report

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1. Abstract

1.1. Background: Iatrogenic iron excesses or chelators can exacerbate kidney dysfunction in patients with thalassemia. Kidney dysfunction is a significant consequence of thalassemia, mostly attributable to iron overload resulting from recurrent blood transfusions and the disease itself.

1.2. Case Presentation: We present a 42-year-old male with β-thalassemia major who experienced a reduction in glomerular filtration rate (GFR) of 3 ml/min, with a creatinine level of 18.6 mg/dl and a blood urea nitrogen (BUN) level of 152 mg/dl. He is receiving subcutaneous deferoxamine and oral deferiprone as iron chelation therapy, along with packed red blood cell transfusions during each dialysis session. The complete blood count revealed significant hypochromic microcytosis, many erythroblastoses, leukocytosis with a left shift in granulocytes, and thrombocytosis. He had extreme hyperferritinemia. Upon initiating hemodialysis, his metrics improved, except for the refractory anemia.

1.3. Conclusion: This case report clarifies the signs of kidney failure in thalassemic transfusion recipients.

2. Introduction

Thalassemia is a genetic ailment characterized by several genetic sorts, including α-thalassemia, β-thalassemia, and hemoglobin S/β-thalassemia. Molecular abnormalities in the α-globin gene cluster on chromosome 16 or the β-globin gene cluster on chromosome 11 lead to impaired hemoglobin production [1]. Thalassemic illnesses exist along a continuum of severity, characterized by varying clinical presentations, consequences, and therapeutic approaches. An imbalance in the relative quantities of α-globin and β-globin chains induces premature apoptosis of developing nucleated erythroid cells, accompanied by hematopoietic expansion as a compensatory response. This condition, termed ineffective erythropoiesis, results in chronic hemolytic anemia characterized by minimal reticulocytosis and various secondary pathophysiological mechanisms [2]. Non-transferrin-bound iron can be especially detrimental, as it may promote the generation of free radicals, resulting in oxidative stress and tissue injury [2,3].

Kidney impairment may be a significant problem in thalassemia patients, primarily resulting from iron excess due to frequent blood transfusions or iron chelator therapy. The incidence of kidney dysfunction in thalassemic individuals is notably elevated due to the chronicity of the condition and problems associated with iron overload. Research indicates that thalassemia patients possess a markedly elevated chance of acquiring end-stage renal disease (ESRD) in comparison to the general population [4]. The worldwide epidemic of thalassemia is considerable, with the highest prevalence rates found in Southeast Asia, the Mediterranean, and the Middle East [5]. The prevalence of ESRD in these people is affected by factors like the accessibility and quality of medical care, particularly iron chelation therapy and consistent monitoring of renal function. Primary risk factors for the onset of ESRD in individuals with thalassemia encompass the duration and frequency of blood transfusions, the efficacy of iron chelation therapy, and the existence of additional comorbidities such as diabetes and hypertension [4]. Thalassemic patients in Sudan, similar to those in other areas, are susceptible to kidney failure as a consequence of complications related to their illness [6]. Iron overload management often necessitates iron chelation therapy to diminish iron accumulation and prevent organ harm. Consistent assessment of iron levels and organ function is essential for thalassemic patients to reduce the hazards linked to iron overload [3].

3. Case presentation

A 42-year-old male of Sudanese descent arrived at the thalassemia ward with a progressive exacerbation of widespread edema, little frothy urine, and dyspnea on exertion over the preceding two months. He is diagnosed with β-thalassemia major and has required monthly transfusions since the age of 12. At the age of 38, he underwent hemodialysis due to an escalating need for transfusions linked to elevated ferritin levels. He is undergoing subcutaneous deferoxamine and oral deferiprone iron chelation treatment. He possesses a familial predisposition to β-thalassemia, with no other notable medical history. There is no record of parental consanguinity. He is a nonsmoker and a teetotaler, employed in a governmental job.

A physical evaluation indicated a male exhibiting small stature, hyperpigmentation, pronounced frontal bossing, a depressed nasal bridge, and maxillary protrusion. Generalized anasarca was observed. His lungs exhibited bibasilar crackles. He exhibited hepatomegaly measuring 4 cm. Shifting idiocy was seen, and he was indicative of ascites. Other systems were inconspicuous. The patient was non-diabetic and normotensive. The patients presented the following vital signs: Tachycardia (HR > 110), Blood Pressure 110/65, Tachypnea (RR > 28), SPO2 < 88% on room air, and a Glasgow coma score (GCS) of 15/15. The total blood count showed pronounced hypochromic microcytic anemia, numerous erythroblastoses, leukocytosis [with left shift granulocytes], and thrombocytosis. He exhibited significant hyperferritinemia with a level of 6380 ng/mL. All other laboratory parameters are presented in (Table 1). The peripheral blood film (Figure 1), obtained three weeks before transfusion [due to the patient's transfusion dependence], exhibited hemoglobinopathy correlated with chronic hemolysis. Hemoglobin electrophoresis stated an absence of HbA, a raised HbA2 level of 5.3%, and an excessive HbF concentration of 38%. A DNA test of the β-globin gene showed a change at IVS 1–110 (G to A), a sign of β-thalassemia major.

There was renal failure, with a blood creatinine level of 18.6 mg/dl and a blood urea nitrogen level of 152 mg/dl. There was also metabolic acidosis (pH 7.19, lactic acid 2.5 mg/dl) and hyperkalemia (5.9 mmol/l). He commenced hemodialysis with two sessions per week along with a packed red cell transfusion, iron sucrose 100 mg biweekly, recombinant erythropoietin [Eprex] 4000 IU biweekly, subcutaneous Deferoxamine 40 mg/kg/day, oral Deferiprone 25 mg/kg/day administered twice daily, and Deferasirox 20 mg/kg/day once daily which improved his parameters except for the refractory anemia. The estimated glomerular filtration rate [eGFR] indicates 3 ml/min [>15 ml/min]. The patient has stage 5 kidney disease, or end-stage renal disease, based on the standards set by the American Society of Nephrology and the National Kidney Foundation. Magnetic resonance imaging [MRI] technology was inaccessible at our facility, making it impossible to investigate liver and heart iron concentrations more precisely. A percutaneous liver biopsy was skipped due to the potential bleeding risk associated with possible simultaneous extramedullary hematopoiesis in the liver, which may already exist. It was thought that iron chelation treatment and iron overload caused the acute kidney damage. A diagnosis was established based on these data. This case report seeks to provide insights into renal impairment in patients with β-thalassemia major.

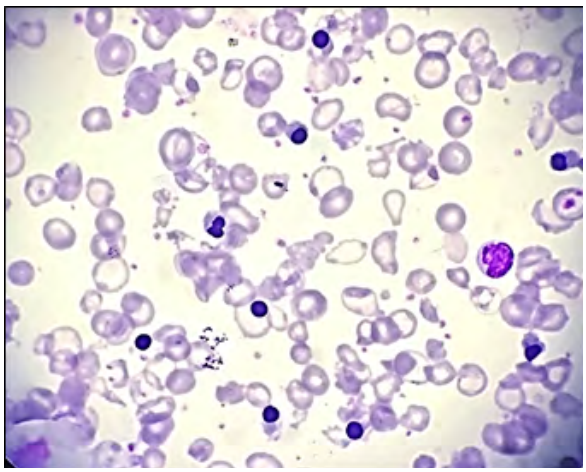

Figure 1: Peripheral blood smear of β-thalassemia major shows anisopoikilocytosis, extreme hypochromic microcytic red cells, numerous erythroblastoses, and few polychromatic cells with features consistent with chronic hemolysis [100X, MGG].

Table 1: Patient's laboratory results

Laboratory parameters	Value (Unit & Control level)
Leukocyte count (Uncorrected)	60.6 [4-10×109/L]
Erythrocytes count	2.57 [4-5.5×1012/L]
Hemoglobin	5.7 [12-16 g/dl]
Hematocrit	18.3 [35-47%]
Mean corpuscular volume	71.4 [78-101 fL]
Mean corpuscular hemoglobin	22.3 [25-35 pg]
Mean corpuscular hemoglobin concentration	31.3 [31-36 g/dl]
Red cell distribution width-CV	26.9 [11-15 %]
Red cell distribution width-SD	67.0 [35-56 fL]
Lymphocytes count	5.3 [1.2-4.3×109/L]
Neutrophils count	14.9 [1.2-7.0×109/L]
Monocytes count	3.0 [0.1-1.3×109/L]
Myelocytes	2.2 [Nil]
Metamyelocytes	2.5 [Nil]
Nucleated erythroblasts	32.7 [Nil]
Leukocyte count (Corrected)	27.9 [4-10×109/L]
Platelets count	667 [150-450×109/L]
Mean platelet volume	9.4 [9-13 fL]
Platelet distribution width	15.4 [9-17 fL]
Plateletcrit	0.627 [0.108-0.282 %]
Platelet large cell count	162 [30-90×109/L]
Platelet large cell ratio	24.3 [11-45%]
Blood Urea	325 [10-50 mg/dl]
Blood Urea Nitrogen	152 [7-21 mg/dl]
Creatinine	18.6 [0.4-1.6 mg/dl]
eGFR	3 [>15 ml/min]
Uric acid	8.7 [3.5-7.2 mg/dl]
Sodium	138 [135-145 mmol/l]
Potassium	5.9 [3.5-5.5 mmol/l]
Calcium	10.7 [8.1-10.5 mg/dl]
Phosphorous	6.4 [2.5-5.0 mg/dl]
Ionized calcium	4.3 [4.65-5.25]
Magnesium	3.5 [1.5-2.6 mg/dl]
Lactic acid	2.5 [< 2.0 mmol/l]
Glucose	104 [80-180 mg/dl]
Albumin	1.86 [3.5-5.0 g/dl]
Alanine transaminase (ALT)	39 [Up to 40 U/l]
Aspartate transaminase (AST)	45 [Up to 40 U/l]
Antinuclear factor antibody (ANA) profile	Negative
Hepatitis C virus screening (HCV)	Negative
Hepatitis B virus screening (HBV)	Negative
Human Immunodeficiency Virus Screening (HIV)	Negative
Glycosylated Hemoglobin	5.1 [4.5-6.5 %]
Iron	73 [10.6-32.8 µmol/l]
Ferritin	6380 [30-400 ng/ml]
Total iron binding capacity (TIBC)	261 [60-80 µmol/l]
Transferrin saturation (TSAT)	28 [15-45%]
Hemoglobin F level	38 [< 0.6%]
Hemoglobin A2 level	5.3 [2.1 – 3.4%]

4. Discussion

Thalassemia syndromes are common in the Mediterranean, Africa, and Southeast Asia [7]. The impact of population transfers from countries with a high prevalence of thalassemia is evident in the growing number of affected patients in industrialized nations. However, it's important to note that this is a preventable public health issue, particularly for poorer countries [8]. Approximately 20.7% of the global population possesses a β-thalassemia variation, with around 40,000 infants born yearly [9]. In recent years, particularly in developed countries, the outlook of β-thalassemia has enhanced owing to blood transfusions, iron chelation therapy, and advancements in understanding the condition. The incidence of babies with β-thalassemia has been restricted in Western nations due to the implementation of effective screening programs, offering hope for a future with fewer cases [10]. Despite the enhanced survival rates observed in β-thalassemia, it's important to acknowledge that numerous individuals face significant health challenges. These consequences span across multiple systems, including cardiovascular illnesses, endocrine organ diseases, hepatic dysfunction, renal failure, and thromboses. Understanding these challenges is crucial in our ongoing efforts to improve patient care [10]. The impact of thalassemia on renal function has not been thoroughly assessed. This case report aims to present information contributing to renal injury in patients with β-thalassemia major.

Our current understanding of the epidemiology of renal complications in β-thalassemia is limited. However, recent research across multiple thalassemia cohorts from five North American locations has revealed some significant findings. These include a reduction in creatinine clearance in 7.8% of patients and the presence of albuminuria in up to 59% of participants [11]. Notably, recent investigations identified renal dysfunction in 1.8% of transfusion-dependent thalassemia patients [12], with renal issues ranked as the fourth most prevalent cause of morbidity (4%), following endocrine (44.7%), cardiovascular (41.3%), and hepatic (40.5%) diseases in the same cohort [13]. These outcomes underscore the potential impact of further research in this field on improving patient outcomes. No information is available in our region on the prevalence of renal illness among β-thalassemia patients according to modern standards. Furthermore, multiple variables may lead to renal dysfunction in a patient with thalassemia. These include iron overload, chronic anemia, hypoxia, acquired Fanconi syndrome, improper iron chelation, nephrotoxic medications, infectious agents, post-splenectomy, and nephrolithiasis [2]. Glomerulonephritis is usually overlooked as a significant cause of renal failure in thalassemia patients. However, the importance of conducting renal biopsies cannot be overstated, as it can lead to identifying this critical diagnosis and subsequent appropriate management [14]. The hemosiderosis in this patient may be ascribed to multiple sources. Among these are intramedullary destruction of erythrocyte progenitors, decreased erythrocyte lifespan, increased iron turnover, and routine packed red blood cell transfusions. Numerous analogous studies have demonstrated that excessive iron accumulation generates reactive oxygen species, exacerbating renal cellular damage [14,15]. The introduction of iron chelators has significantly improved patient survival in transfusion-dependent β-thalassemia. However, this milestone has also highlighted a range of previously unacknowledged complications, underscoring the complexity of managing this condition [16]. Currently, three iron chelators are available: the oral medications deferasirox (DFX) and deferiprone (DFP), along with the parenteral deferoxamine mesylate (DFO). It's important to note that renal symptoms associated with chelating drugs are rare, providing a measure of reassurance about their safety. Serum ferritin levels have been inversely linked with GFR; however, it's also been observed that iron chelation treatment can lead to a decline in renal function [17]. Dependence on blood transfusions, administration of iron chelator drugs, and end-stage renal failure constitute the primary elements of a significant catastrophe.

5. Conclusion

This case report underscores the clinical indications of renal impairment in patients with β-thalassemia major. Close monitoring and follow-up of renal function in transfusion-dependent thalassemic patients is essential since their enhanced life expectancy likely elevates the risk of extreme renal ailments.

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