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Case Report

Heart failure secondary to severe anemia in beta-thalassemia major: a case report

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ABSTRACT

The profile of cardiac involvement in beta-thalassemia major patients in the absence of significant cardiac iron overload is quite rare. This case report focuses on a 3-year-old child with a history of beta-thalassemia who presented with acute heart failure following missed blood transfusions, despite consistent chelation therapy. Clinical evaluation revealed severe anaemia, and cardiac ischemia leading to cardiovascular compromise, despite desirable ferritin levels. The patient's condition improved with guideline-directed medical therapy, transfusions, and continued chelation. We hypothesize that tissue hypoxia plays a significant role in the development of cardiac ischemia leading to heart failure, highlighting the critical importance of adherence to treatment schedules to prevent severe complications.

Keywords: Beta-thalassemia, Anaemia, Congestive heart failure, Hypoxia

INTRODUCTION

Beta-thalassemia is an inherited blood disorder, reported more frequently in the Mediterranean, Middle East, and Southeast Asia.[1] Symptomatic cases are estimated to occur in approximately 1 in 100,000 individuals within the general population.[2] Beta-thalassemia is classified into β-thalassemia carrier state, β-thalassemia intermedia, and β-thalassemia major based on the disease severity. Beta-thalassemia cardiomyopathy manifests in two distinct phenotypes; dilated cardiomyopathy characterized by left ventricular dilatation and impaired contractility, and restrictive phenotype, presenting with restrictive left ventricular filling, pulmonary hypertension, and eventual right heart failure.[3] While clinical progression can be variable and occasionally fulminant, currently there are less severe cases reported compared prior to chelation and bone marrow transplantation. In paediatric patients, myocarditis and pulmonary hypertension represent significant complications demanding a multidisciplinary approach in management. Estimation of the patient's cardiac risk is based on the severity of clinical presentation and other factors such as age, gender, and family history. The disease is anticipated to see a long-awaited cure due to recent advancements in gene therapy.[4] Our case report signifies that tissue hypoxia, resulting from an oxygen supply-demand mismatch in the myocardium, can induce heart failure due to severe anaemia. This anaemia was caused by missed blood transfusions, emphasizing the critical importance of adherence to treatment for optimal patient outcomes.

CASE REPORT

A 3-year-old female child with a documented history of beta-thalassemia major, on regular blood transfusions presented to a tertiary care hospital with acute onset of breathlessness and pedal edema, noted since the previous day, accompanied by a week-long history of fatigue. The patient had been consistently receiving blood transfusions along with iron chelation therapy as needed since the age of one but had missed her last three scheduled sessions. Upon clinical evaluation, the patient appeared acutely ill, displaying marked conjunctival pallor. Additionally, she had a depressed nasal bridge, frontal bossing, and prominent forehead, suggestive of thalassemia facies. There were no signs of active bleeding. The patient's growth parameters were below the expected levels for her age. Her vital signs include a heart rate of 162 beats per minute, a respiratory rate of 22 breaths per minute and oxygen saturation was 88% on ambient air. Auscultation revealed systolic murmur with bilateral basal crepitus. Abdominal examination identified firm, non-tender splenomegaly extending 2 cm below the left costal margin, along with mild hepatomegaly.

The patient presented with severe anaemia with haemoglobin of 3.0 g%, and hematocrit of 30.8%. Iron profile revealed a picture of iron overload and anemia of chronic disease indicated by ferritin level was under 1000 ng/mL, with low serum iron at 25 µg/dl, reduced total iron binding capacity (TIBC) at 49 µg/dl, and a decreased reticulocyte count. Peripheral smear of the patient revealed target cells and findings consistent with chronic hemolytic anemia (Figure 1).

Figure 1 depicts a peripheral smear showing microcytic, hypochromic red blood cells with notable anisopoikilocytosis. The characteristic target cells (erythrocytes with central staining area surrounded by a clear zone) are prominent, which is associated with thalassemia.

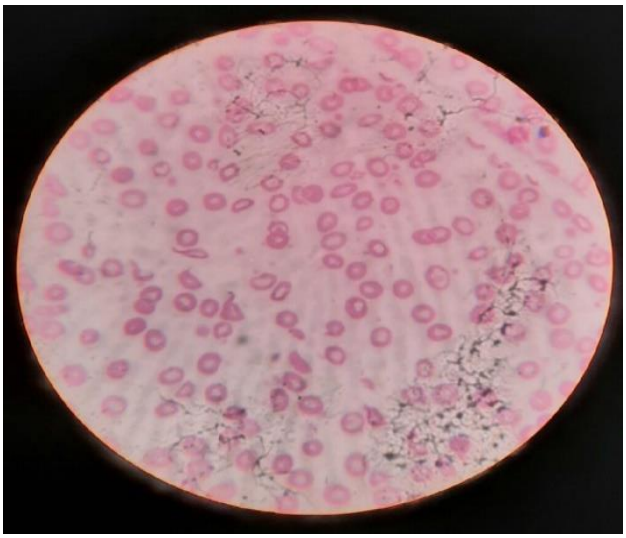

Figure 1: Peripheral blood smear.

A chest radiograph showed mild cardiomegaly (Figure 2), while electrocardiogram (ECG) showed low voltage QRS complexes, right axis deviation, and T wave inversions, findings suggestive of cardiac ischemia that eventually led to heart failure due to mismatch in oxygen demand and supply. Echocardiography revealed a mildly dilated aortic root with normal ventricular wall thickness and unremarkable valvular motion. The ejection fraction was noted to be 55%, with no other significant cardiac abnormalities. High-performance liquid chromatography revealed elevated HbF and HbA2 levels. Coagulation studies, including bleeding and clotting times, were within normal limits, and the stool occult blood test was negative.

Plain radiograph of the chest showing enlarged cardiac silhouette (cardiomegaly), signs of pulmonary edema, consistent with heart failure is given in Figure 2. Elevated left hemidiaphragm suggest splenomegaly due to extramedullary hematopoiesis.

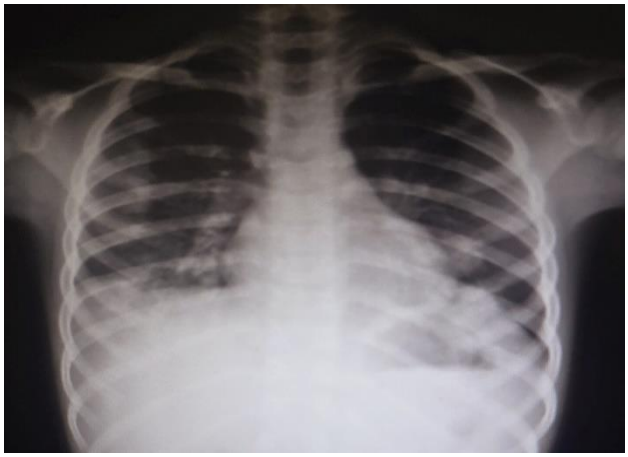

Figure 2: Plain chest X-ray.

The patient was admitted in the paediatric intensive care unit for continuous telemetry monitoring and oxygen supplementation. Guideline directed medical therapy comprising angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, beta blockers plus digoxin were administered to address the volume overload and alleviate heart failure symptoms. Additionally, four units of packed RBC were transfused due to severe anaemia, with the transfusion rate carefully titrated to maintain normal fluid balance.

Haematological investigations later in the week indicated markedly elevated ferritin levels at 2694 ng/ml, secondary to recent blood transfusions. Chelation therapy with deferoxamine was continued to manage the iron levels. Upon achieving clinical stability, the patient was referred for consideration of bone marrow transplantation.

DISCUSSION

Beta-thalassemia (β-thalassemia) are a group of congenital hemoglobinopathies inherited in an autosomal recessive

pattern that occurs due to absent or defective synthesis of beta globin chain, which presents with two major clinical forms, β-thalassemia major and β-thalassemia intermedia. Cardiovascular disease is the leading cause of death in patients with thalassemia. Diastolic dysfunction with highest prevalence, followed by tricuspid regurgitation, dilated cardiomyopathy and arrhythmias.[5]

Iron overload is the primary reason behind the development of heart failure. Thalassemia patients have an increase in iron overload which saturated the iron storage and ferroportin. The excess free iron forms free radicals which cause lipid peroxidation, mitochondrial injury, membrane disruption and contractile dysfunction with myocyte death.[6] Chronic iron deposition causes left ventricular myocardial restriction, with elevated ferritin which leads to ventricular dilation predominantly affecting the right side first. According to treatment, there are (TDT) and non-transfusion dependent patients (NTDT). Iron accumulation starts from the early stage of childhood in TDT patients leading to progressive damage to the heart leading to heart failure.

Chronic anaemia leading to tissue hypoxia is another major mechanism behind the leading cause of cardiac dysfunctions leading to high output heart failure.[7] Due to this there is excess alpha chain production which forms an unstable haemoglobin that precipitates (Heinz bodies) in the bone marrow and extramedullary organs causing marrow expansion and hepatosplenomegaly, respectively. Most of them are destroyed by macrophages in the marrow, however, some which escape, precipitate in the vasculature and rest undergo extravascular haemolysis by the reticuloendothelial system in the spleen.[8,9]

Diminished partial pressure of the oxygen in the blood leads to cardiomyocyte injury and direct blood vessel injury. Meanwhile, a vicious cycle develops between ineffective erythropoiesis and cardiomyocyte injury, leading to congestive heart failure secondary to cardiac ischemia.[9]

Ventricular dysfunction leading to heart failure occurs due to high output heart failure, iron overload or myocardial ischemia. High output heart failure can occur due to a combination of factors such as chronic anaemia, compensatory bone marrow. Compensatory mechanisms that occur due to anaemia are kept under check by regular blood transfusion.[10]

In our case, EF, although within the normal range with low haemoglobin levels and the presence of myocardial ischemia, indicates that the heart is under significant stress. Despite this stress, the EF remained normal due to compensatory mechanisms working to maintain normal cardiac function in the context of anaemia, supported by echocardiographic findings revealing insignificant structural changes in the heart. Thus, we hypothesize that the acute onset of symptomatic heart failure was precipitated by the severe anaemia, which resulted from missed transfusions leading to a sudden drop in the haemoglobin levels.

Within one year of the disease, half of the patients died due to cardiovascular compromise. A consistent reduction in iron, monitored by the serum ferritin levels, that does not exceed 2500 ng/ml, is considered the most crucial factor in regards to the prognosis of the patient. Currently, the 5-year survival prognosis is 50% in paediatric thalassaemic patients with cardiac pathologies.[11] In TDT patients, there is increased risk of hepatitis C transmission which further elevates the ferritin concentration, making the interpretation difficult.[12]

Prenatal and postnatal screening in suspected cases with high-risk family history helps to reduce incidence of beta thalassemia. Screening can be done by hematologic tests like Hb analysis by either automatic high-performance liquid chromatography (HPLC) or capillary zone electrophoresis (CE), α- and β-thalassemia genes by next-generation sequencing (NGS) and thalassemia genotyping by real-time polymerase chain reaction (PCR) with melting curve analysis. Despite the accuracy of these tests, the financial burden limits their utilization, leading to an increase in undiagnosed cases until patients with advanced conditions.[13]

Generally**,** despite regular transfusion and chelation therapy chronic iron overload is unavoidable thus, cardiac magnetic resonance imaging (MRI) should be done to keep an eye on the myocardial siderosis (T2 >20 ms) to pre-determine the cardiovascular complications. Generally, pre-transfusion levels of haemoglobin are maintained at 10 g%, with a desirable ferritin level of 1000 ng/ml and cardiac MRI T2 value to >20 ms. MRI T2* is the time measurement that reflects iron content in tissue.[12] More than treatment with single drug dual therapy with deferoxamine, deferasirox or deferiprone is more effective. Disease-specific therapy including blood transfusions, iron chelation and other multidisciplinary measures helps in the prevention and treatment of the cardiovascular complications such as heart failures, left ventricular dysfunctions, and pericarditis.[11]

Current literature reports several cases of heart failure in patients with beta-thalassemia due to iron overload. Additionally, heart block and myocardial infarction have been observed even in the absence of prior cardiac symptoms.[14,15] Notably, congestive heart failure has been reversed, and echocardiographic findings have been restored upon the resumption of chelation therapy.[16] In our case, the patient, who had been consistently receiving chelation therapy, missed blood transfusions, leading to exacerbated anaemia and subsequent acute cardiovascular compromise.

CONCLUSION

This case highlights the importance of maintaining adherence to both blood transfusion schedules and

chelation therapy in beta-thalassemia patients to prevent heart failure. This patient's acute development of heart failure underscores the complex relationship between anaemia and cardiac function. Regular surveillance and a comprehensive approach are essential to mitigate complications and improve positive patient outcomes.

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REFERENCES

1. Sharma DC, Arya A, Kishore P, Woike P, Bindal J. Overview on thalassemias: A review article. Medico Res Chronicles. 2017;4:325-37.
2. Galanello R, Origa R. Beta-thalassemia. Orphanet J Rare Dis. 2010;5:11.
3. Kremastinos DT, Farmakis D, Aessopos A, Hahalis G, Hamodraka E, Tsiapras D, et al. Beta-thalassemia cardiomyopathy: history, present considerations, and future perspectives. Circ Heart Fail. 2010;3(3):451-8.
4. Hahalis G, Alexopoulos D, Kremastinos DT, Zoumbos NC. Heart failure in beta-thalassemia syndromes: a decade of progress. Am J Med. 2005;118(9):957-67.
5. Farmakis D, Triposkiadis F, Lekakis J, Parissis J. Heart failure in haemoglobinopathies: pathophysiology, clinical phenotypes, and management. Eur J Heart Fail. 2017;19(4):479-89.
6. Shahramian I, Razzaghian M, Ramazani AA, Ahmadi GA, Noori NM, Rezaee AR. The Correlation between Troponin and Ferritin Serum Levels in the Patients with Major Beta-Thalassemia. Int Cardiovasc Res J. 2013;7(2):51-5.
7. Akiki N, Hodroj MH, Bou-Fakhredin R, Matli K, Taher AT. Cardiovascular complications in β-thalassemia: Getting to the heart of it. Thalass Rep. 2023;13(1):38-50.
8. Saliba AN, Taher AT. Morbidities in non-transfusion-dependent thalassemia. Ann N Y Acad Sci. 2016;1368(1):82-94.
9. Isa Tafreshi R, Radgoodarzi M, Arjmandi Rafsanjani K, Soheilipour F. Subclinical Left Ventricular Dysfunction in Children and Adolescence With Thalassemia Intermedia. Front Pediatr. 2022;10:774528.
10. Mozos I. Mechanisms linking red blood cell disorders and cardiovascular diseases. Biomed Res Int. 2015;2015:682054.
11. Farmakis D, Porter J, Taher A, Domenica Cappellini M, Angastiniotis M, Eleftheriou A. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. Hemasphere. 2022;6(8):e732.
12. Olivieri NF, Nathan DG, MacMillan JH, Wayne AS, Liu PP, McGee A, et al. Survival in medically treated patients with homozygous beta-thalassemia. N Engl J Med. 1994;331(9):574-8.
13. Munkongdee T, Chen P, Winichagoon P, Fucharoen S, Paiboonsukwong K. Update in Laboratory Diagnosis of Thalassemia. Front Mol Biosci. 2020;7:74.
14. Fridlender ZG, Rund D. Myocardial infarction in a patient with beta-thalassemia major: first report. Am J Hematol. 2004;75(1):52-5.
15. Maleki AR, Nikyar B, Hosseini SM. Third-Degree Heart Block in Thalassemia major: A Case Report. Iran J Pediatr. 2012;22(2):260-4.
16. Politi A, Sticca M, Galli M. Reversal of haemochromatotic cardiomyopathy in beta thalassaemia by chelation therapy. Br Heart J. 1995;73(5):486-7.

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