Cardiac Impairment Due To Hypocalcemia In A Multitransfused Patient With Thalassemia Major

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Abstract

We report a case of a 16-year-old Iranian girl with transfusion-dependent thalassemia major who presented with chest pain. Laboratory investigations showed marked hypocalcemia, hypomagnesaemia, hyperphosphatemia, and an extremely low vitamin D3 level. She had a low parathyroid hormone (PTH) level. She was refractory to calcium and magnesium supplementation. However, she responded to oral cacitriol. She was diagnosed to have hypoparathyroidism most likely due to iron overload due to multitransfusions and vitamin D3 deficiency. Vitamin D3 deficiency most likely was independent of iron overload. Cardiomyopathy in this patient could have been secondary to iron overload and/or hypocalcemia. Hypocalcemia could have been due to hypoparathyroidism and/or the low vitamin D3 level. Her response to calcitriol but not to calcium and magnesium supplementation suggests that the hypocalcemia was due to hypoparathyroidism and/or vitamin D3 deficiency. The response to calcitriol also indicates that iron overload was not responsible since cardiac impairment due to iron overload would be refractory to calcitriol treatment. Cardiac failure in multitransfused patients is usually ascribed to hemosiderosis. This case demonstrates that hypocalcemia related to vitamin D3 insufficiency also can cause myocardial dysfunction. Patients with thalassemia minor should be periodically screened for calcium and vitamin D3 levels to avoid complications secondary to hypocalcemia.

INTRODUCTION

Chronic transfusion therapy often leads to hemosiderosis in mulltitransfused thalassemic patients. Iron overload can impair cardiac function and other organs and is a well-known cause of heart failure. Deposition of iron in the parathyroid glands can cause symptomatic hypoparathyroidism.1 Hypocalcemia due to hypoparathyroidism is a rare endocrine complications in thalassemic patients and can be underdiagnosed. Long-standing hypocalcemia can cause congestive heart failure.2-8. We report the case of a hyper-transfused thalassemic patient with severe hypocalcemic cardiomyopathy due to hyperparathryroidism and/or low vitamin D3 levels.

CASE REPORT

A 16-year-old female with beta homozygous thalassemia came to our clinic with a 3 day history of acute chest pain radiating to her left arm that was aggravated by breathing and bending forward. She was admitted for medical care. Her medical history revealed that she had been receiving transfusions at 14 day intervals since she was 3 years old. At the age of 10 years she underwent chelation therapy with Desferal (deferoxamine). However, chelation had been inconsistent due to poor compliance during the last six months.

On physical exam, she was pale, her temperature was 370 C, pulse rate was 107 beats per minute, and blood pressure was 95/70 mm Hg. Her O2 saturation on pulse oximetry was 98%. Lung auscultation was normal with no rales. She had hepatomegaly (liver span=9cm) and splenomegaly (3 cm under costal margin).The Chvostek's and Trousseau's signs were present. Laboratory tests at the time of admission revealed severe hypocalcemia and elevated phosphate levels (Table 1). A random urine collection revealed normal urine calcium levels (Ca2+, 2.7 mEq/dl, Phos, 30.5 meq/dl, Creatinine, 17.2mg/dl).

Table 1

The patient's laboratory data at the time of admission

	Patient's Lab Data	Reference levels
Total calcium (mg/dL)	5.5	8.5-10.6
Phosphorus (mg/dl)	7.3	2.4 - 4.1
Magnesium (mg/l)	1.5	1.6-2.6
Hematocrit (%)	27.5	37 - 51
Hemoglobin (g/dl)	9.4	12-16
White blood cell count/L	18.9 x 10^9	4.0-11.0 x 10^9
Platelets/L	321 x 10^9	150-400 x 10^9
Na (mmol/L)	134	135-147
K+ (mmol/L)	3.5	3.5-5.1
Creatinine (mg/dL)	0.3	0.9-1.6
Blood urea nitrogen (mg/dL)	9	7 - 20
Aspartate Aminotransferase (U/L)	33	10-36
Alanine Aminotransferase (U/L)	59	7-35
Alkaline phosphatase (U/L)	717	44 to 147
Albumin (g/dL)	4.7	3.5 - 5.0
Ferritin,(ng/dL)	3100	7 to 140

Table 2

Endocrine laboratory data

	Patient's endocrine Data	Reference levels
T4 (µg/dL)	6.5	4.5 - 12.5
T3 (ng/dL)	133	102 -200
TSH (mIU/L)	1.5	0.5 - 4.70
25(OH) vitamin D (ng/ml)	4	< 10 mg/ml (severe deficiency)
PTH (pg/ml)	14.3	15.0–65.0

The patient was euthyroid, her PTH was low, and her 25-hydroxyvitamin D level was 4ng/ml as shown in Table 2.

Electrocardiograms revealed prolonged QT intervals (QTc: 0.58 sec). An echocardiogram revealed left ventricular systolic and diastolic dysfunction (LVEF=25-30%), eccentric left ventricular hypertrophy, and mild mitral regurgitation, PAP=25mmHg. There was evidence of heart failure.

Systemic treatment of both heart failure and hypocalcemia was started. Calcium gluconate, 30 ml of 20% stock, was administered intravenously every 6 hours. Intramuscular magnesium sulfate, 3 ml of a 50% stock, was given daily. Digoxin (0.25mg/day), losartan (12.5 mg twice a day), furosemide (40 mg once a day), and spironolactone (50 mg once a day) were administered. To treat iron overload, eight ampules of Desferal (deferoxamine) were infused over 24 hours daily. Ferriprox®, 500 mg daily, was started.

Table 3

The patient's calcium levels during hospitalization

Day of admission	1	3	4	5	6	7
Total calcium (mg/dL)	5.5	6.2	6	6.4	8.1	8.6

After 5 days of parenteral treatment, her serum calcium was 6.4 mg/dL. Table 3 displays that calcium levels remained low during the first 5 days of hospitalization. On day 5, we initiated Cacitriol therapy (0.25 mcg per day orally), and after 24 hours the patient's calcium became normal as shown in Table 3, and her chest pain resolved. An ECG and an echocardiogram were repeated 1 week later. The QT interval in the ECG was normal and her LVEF was increased to 55-60%. The patient was discharged 10 days after admission with a stable cardiac status. The patient was continued on oral calcium and oral Calcitriol, and intensive chelation therapy.

DISCUSSION

Cardiac failure in multitransfused patients is usually ascribed to hemosiderosis. This case demonstrates that hypocalcemia related to vitamin D3 insufficiency also can cause myocardial dysfunction.

Hypocalcemia may be associated with a spectrum of clinical manifestations, ranging from minimal with mild hypocalcemia to life-threatening seizures, refractory heart failure, or laryngospasm with severe hypocalcemia. She had Trousseau's and Chvostek's signs. Trousseau's sign is due to an ischemia related increase in excitability of the nerves and is more specific than Chvostek's sign.9 Hypocalcemia characteristically causes prolongation of the QT interval in the electrocardiogram.10,11 Severe hypocalcemia can depress myocardial function to such an extent that congestive heart failure ensues.

The patient's cardiac impairment responded dramatically to Calcitriol therapy and not to calcium and magnesium supplementation. This indicates hypocalcemia due to low vitamin D levels and/or to hypoparathyroidism was instrumental in cardiac impairment. Both of these conditions would have responded to calcitriol therapy but not to calcium and magnesium supplementation. Marked deficiency in vitamin D3 levels also limits the absorption of calcium.

Iron overload that can occur in multitransfused patients is known to cause cardiac dysfunction. However, the rapid response to calcitriol is not consistent with iron-overload cardiomyopathy since this condition would have been refractory to calcitriol. Iron overload can cause endocrinopathies such as hypoparathyroidism .12 Most patients with thalassemia major have received multitransfusions. It is not surprising that the prevalence of hypoparathyroidism in thalassemia major has been reported from 3.6% to 13.5%.13, 14

The patient's extremely low vitamin VITAMIN 25(OH)D3 level most likely was independent of iron overload and most likely due to her dark complexion and lack of exposure to sunlight.

The lifespan in the thalassemic population has increased in part due to the availability of chelation therapy. As shown in this case report, thalassemic patients may develop hypocalcemia. Therefore, calcium vitamin D3 levels should be periodically monitored in these patients. In addition, hypocalcemic-induced cardiomyopathy should be considered in the differential diagnosis of congestive heart failure in thalassemic patients even in the absence of a history of cardiac disease.15 This indicates the importance of making clinicians aware of the possibility of hypocalcemic cardiomyopathy in the thalassemic population.

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