

Right Ventricular Dysfunction in Thiamine-Responsive Megaloblastic Anemia Syndrome: A Case Report

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Abstract

Thiamine or Vitamin B₁ is an essential cofactor for many metabolic processes in numerous tissues. Thiamine-Responsive Megaloblastic Anemia Syndrome is a genetic disorder affecting thiamine transportation with consequent bone marrow, pancreatic, neurological, and cardiac functional and developmental anomalies. There are limited reports of the cardiac manifestations of this syndrome. Here, we present a case of this syndrome in a male patient with right ventricular dysfunction and atrial dysrhythmias (*Iranian Heart Journal* 2011; 12 (2):6-9).

Keywords: Thiamine ■ Responsive Megaloblastic Anemia Syndrome ■ Right Ventricular Dysfunction

The Thiamine-Responsive Megaloblastic Anemia (TRMA) Syndrome or Rogers syndrome is a rare autosomal recessive inherited progressive disorder, consisting of megaloblastic anemia (responsive to thiamine), diabetes mellitus, and sensorineural deafness.¹ Mutations in SLC19A2, the gene encoding high-affinity thiamine transporter protein (THTR), has been described in individuals suffering from this syndrome.² Responsible gene is located on chromosome 1q23. Associated ocular, cerebrovascular, and cardiac anomalies have been reported.^{1,8}

We present a 20-year-old male who was referred to our hospital with a diagnosis of the Ebstein anomaly. He was the first child of consanguineous parents from Arab descent and was deaf and mute since he was 12 months old. At 18 months old, he was evaluated because of pallor and increasing weakness, through which megaloblastic anemia was noted. Considering bilateral sensorineural deafness, megaloblastic anemia, and mild hyperglycemia, he was diagnosed as having the TRMA Syndrome.

The patient had received thiamine and folic acid since he was 18 months of age. There had been no overt diabetes mellitus requiring insulin, and hyperglycemia was controlled by dietary changes. Recent genetic studies by his hematologist confirmed the diagnosis.

He mentioned the onset of diabetes in his father at age 30 but no other family history of similar problems. He had a history of blood transfusions for hemoglobin concentrations as low as 4.5 g/dl. There was also an unclear history of syncope four years previously.

General physical examination showed no failure to thrive. There was pale conjunctiva and a horizontal nystagmus. He had severe ascites but no significant peripheral edemas. Cardiac auscultation revealed III/VI diastolic murmur in the second left intercostal space and II /VI systolic murmur at the left parasternal region. There were also bilateral inguinal hernias.

He was receiving Vit B₁ (300 mg daily), Vit B₆, folic acid, furosemide, spironolacton, and propranolol at the time of admission.

He had normal liver function tests and serum electrolytes, except for FBS, which was 133mg/dl. The patient also had hemoglobin concentration of 11.2g/dl, MCV of 95fl, retic count of 0.5%, WBC of 6100 cells/ml, and

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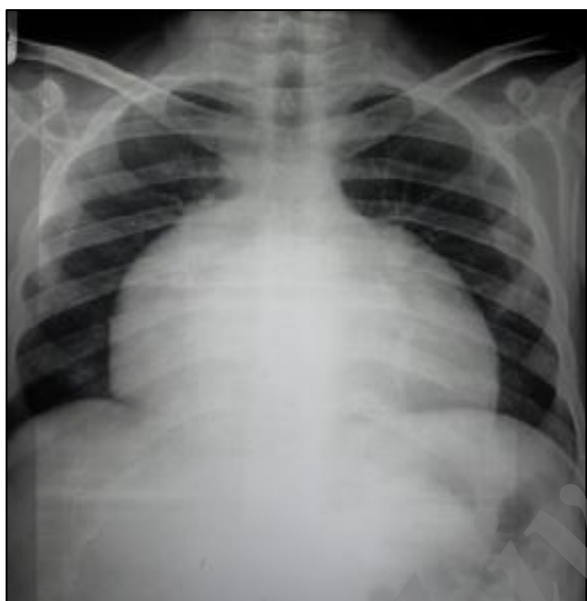
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platelet count of 224000/ml. Additionally, serum iron ($12.1 \mu\text{mol/L}$), TIBC ($50 \mu\text{mol/L}$), and ferritin (149) were within normal laboratory range. Chest X-ray showed cardiomegaly with right atrial (RA) and right ventricular (RV) enlargements. (Fig.1).

Fig 1. Chest X-Ray depicting massive cardiomegaly



In twelve-lead ECG, there was baseline atrial fibrillation (AF), right-axis deviation, and right bundle branch block (RBBB) (Fig. 2). Transthoracic and transesophageal echocardiographic examinations showed a normal left ventricular (LV) size with mild to moderate dysfunction (LVEF:40-45%), severe RV enlargement and dysfunction, huge RA with severe smoky pattern, malcoapted tricuspid valve with severe low pressure regurgitation, moderate to severe pulmonary insufficiency (PI), and tricuspid septal leaflet displacement less than 8mm/m2 (Fig.3).

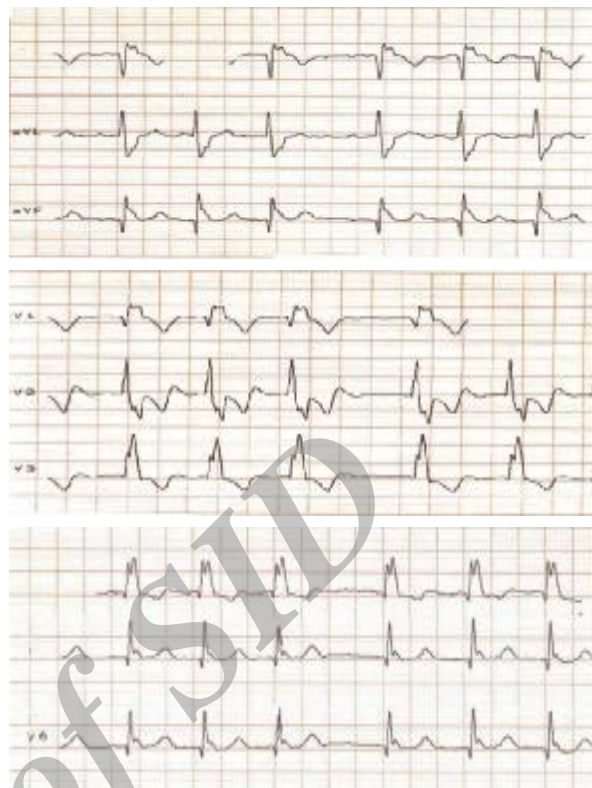


Fig. 3. Twelve-lead ECG showing irregular rhythm and RBBB



Fig. 4. Transthoracic echocardiography four-chamber view with evident RA and RV enlargement

Catheterization and saturation study showed no significant intracardiac shunt, pulmonary artery pressure (PAP) of 28/16 mmHg, RV pressure of 28/0-18, systemic arterial saturation of 90%, and pulmonary artery saturation of 62%.

After discussing the high surgical risks of tricuspid valve replacement due to severe right-sided heart failure with his parents, it was decided to continue medical heart failure management plus Vit B supplementation for anemia. Also, he has been prepared for cardiac transplantation in the near future.

Discussion

Thiamine (Vitamin B₁) is an essential micronutrient and cofactor for humans and its deficiency causes Beriberi (neurological and cardiovascular involvement) and the Wernicke-Korsakoff syndrome (with encephalopathy or psychotic features).^{3, 4} It is required for many anabolic and catabolic intermediary metabolisms like intracellular glucose metabolism and neuronal and neuromuscular transmission.

The TRMA Syndrome is believed to be caused by a frame shift mutation of the high-affinity thiamine transporter gene (SLC19 A2) with defective cellular transportation of thiamine and metabolic deficiencies in different tissues. Consanguinity and familial involvement has been described.^{1, 13} Diagnosis is based on the presence of bilateral sensorineural deafness, megaloblastic anemia, and non-type 1 diabetes with symptom onset being between infancy and adolescence.^{8, 18} Ocular involvement including retinal dystrophy, optic nerve atrophy, astigmatism, nystagmus and maculopathy, short stature, and cerebrovascular attacks have been described in some cases.⁸⁻¹²

Derangements in thiamine transport might lead to heart failure, myocardial hypotrophy, depressed contractility, and arrhythmias, perhaps in part due to a decrease in the calcium load and release from the sarcoplasmic reticulum.^{1, 15, 19}

Thirteen of the TRMA patients reported thus far in the existing literature had cardiac anomalies, including atrial fibrillation, atrial standstill, dextrocardia, secundum type atrial septal defects, Ebstein anomaly, endocardial cushion defects, and supraventricular tachycardias.^{1, 5, 14} In Ebstein patients, dysrhythmias are present on many occasions but might be more prevalent in teenagers or young adults.¹

High-dose thiamine might delay the onset or need for insulin in diabetes¹⁶ and correct anemia,¹ but there is no conclusive evidence for the prevention of hearing loss or cardiomyopathy and there is a possibility that alterations start even in intrauterine life. However, it is possible that earlier treatment may offer a better response.²

In this report, we presented a case of the TRMA Syndrome with severe RV dysfunction, moderate to severe PI, atrial dysrhythmia, and RBBB. Our patient, despite long-term thiamine administration, had developed severe RV failure and atrial fibrillation.

Conclusion

Currently, there are only recommendations for lifelong thiamine administration (25-75mg daily) in these patients, which should be commenced as early as possible. There should be at least annual monitoring of the efficacy of therapy by cardiac, hearing, and visual assessments and also through the laboratory indices of anemia and hyperglycemia.¹⁸

Conflict of Interest

No conflicts of interest have been claimed by the authors.

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