

## Right ventricular dysfunction in thiamine-responsive megaloblastic anaemia syndrome: a case report

### CASE

A 20-year-old high school student was referred to our hospital with a diagnosis of Ebstein anomaly. He was the first child of consanguineous parents of Arab descent and was deaf and mute since he was 12 months old. At 18 months, he had been evaluated because of his pallor and increasing weakness, by which megaloblastic anaemia was noted. Considering bilateral sensorineural deafness, megaloblastic anaemia and mild hyperglycaemia, he was diagnosed as having thiamine-responsive megaloblastic anaemia (TRMA) syndrome. He has been receiving thiamine and folic acid since 18 months of age. There had been no overt diabetes mellitus requiring insulin and hyperglycaemia was controlled by dietary changes. Recent genetic studies by his haematologist confirmed the diagnosis. He mentioned the onset of diabetes in his father at the age of 30 years but reported no other family history of similar problems. He had a history of blood transfusions for haemoglobin concentrations as low as 4.5 g/dl. There was also an unclear history of syncope 4 years ago.

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

He was receiving vitamin B<sub>1</sub> (300 mg daily), vitamin B<sub>6</sub>, folic acid, furosemide, spironolacton and propranolol at the time of admission.

He had normal liver function tests and serum electrolytes except for fasting blood sugar 133 mg/dl. Haemoglobin

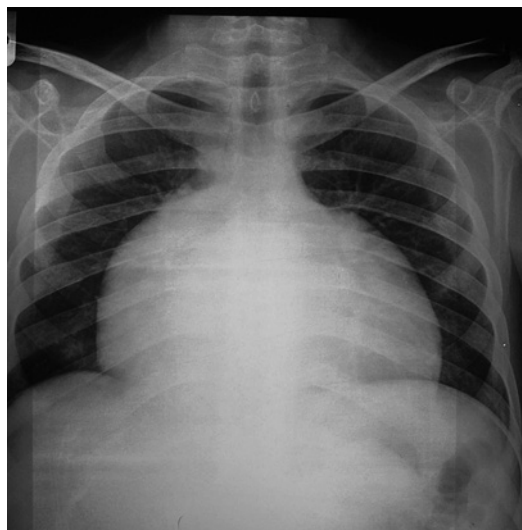


Figure 1

concentration was 11.2 g/dl, mean corpuscular volume 95 fl, retic count 0.5%, white blood cell count 6100 cells/ml and platelet count 224 000/ml. His serum iron (12.1 µmol/l), total iron-binding capacity (50 µmol/l) and ferritin (149 ng/ml) were in the normal laboratory range.

Chest x-ray showed cardiomegaly with right atrial and right ventricular (RV) enlargements (figure 1).

The 12-lead ECG showed baseline atrial fibrillation, right axis deviation and right bundle branch block (figure 2).

Transthoracic and transoesophageal echocardiography showed normal left ventricular size with mild to moderate dysfunction (left ventricular ejection fraction: 40–45%), severe RV enlargement and dysfunction, Huge right atrium with severe smoky pattern malcoapted tricuspid valve with severe low pressure regurgitation, moderate to severe pulmonary insufficiency and tricuspid septal leaflet displacement <8 mm/m<sup>2</sup> (figure 3).

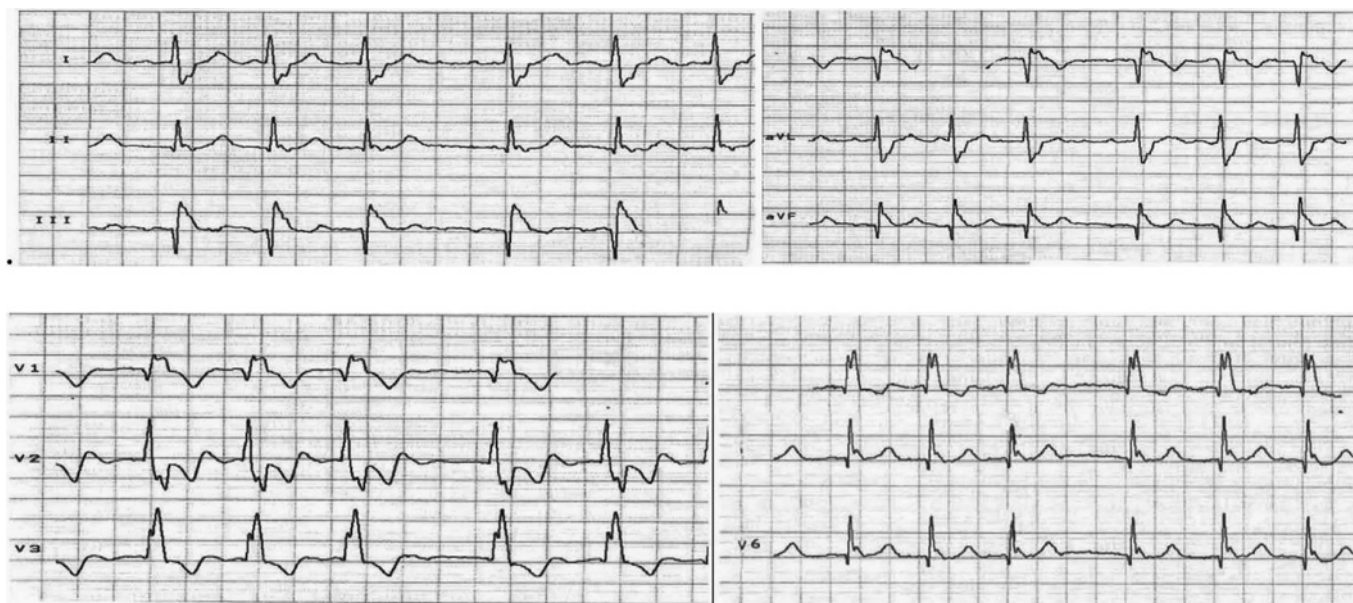


Figure 2

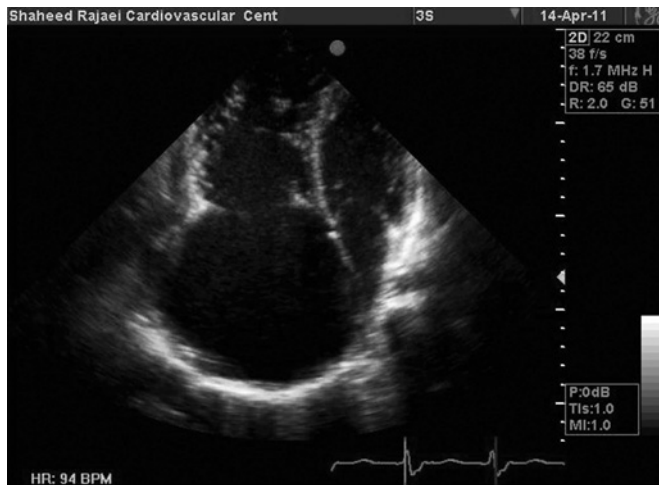


Figure 3

Catheterisation and saturation study showed no significant intracardiac shunt, pulmonary artery pressure 28/16 mm Hg, RV pressure 28/0–18, systemic arterial saturation 90% and pulmonary artery saturation 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 vitamin B supplementation for anaemia. Also, he has been prepared for cardiac transplantation in the near future.

## DISCUSSION

Thiamine (vitamin B<sub>1</sub>) is an essential micronutrient and cofactor for humans and its deficiency causes Beriberi (with neurological and cardiovascular involvement) and Wernicke–Korsakoff syndrome (with encephalopathy or psychotic features).<sup>1,2</sup> It is required for many anabolic and catabolic intermediary metabolism functions such as intracellular glucose metabolism and neuronal and neuromuscular transmission.<sup>2</sup>

TRMA syndrome or Rogers syndrome is a rare autosomal recessive genetic disorder; it is believed to be caused by a frame shift mutation of the high-affinity thiamine transporter gene (SLC19A2) resulting in defective cellular transportation of thiamine and metabolic deficiencies in different tissues. The gene responsible is located on chromosome 1q23.<sup>3–5</sup> Consanguinity and familial involvement have been described.<sup>3,6</sup>

Diagnosis is based on the presence of bilateral sensorineural deafness, megaloblastic anaemia and non-type 1 diabetes with symptom onset being between infancy and adolescence.<sup>4,7,8</sup> Ocular involvement including retinal dystrophy, optic nerve atrophy, astigmatism, nystagmus and maculopathy and short stature and cerebrovascular attacks have been described in some cases.<sup>4,9–13</sup>

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.<sup>3,14,15</sup>

Thirteen of the TRMA patients reported until now had cardiac anomalies including: AF, atrial standstill, dextrocardia, secundum type atrial septal defects, Ebstein anomaly, endocardial cushion defects and supraventricular tachycardias.<sup>3,16,17</sup> In Ebstein patients, dysrhythmias are present on many occasions but might be more prevalent in teenagers or young adults.<sup>3,16</sup>

High dose thiamine might delay the onset or need for insulin in diabetes and corrects anaemia,<sup>5,7,18</sup> but there is no conclusive evidence for the prevention of hearing loss or cardiomyopathy and there is the possibility that alterations start even in intra-uterine life. However, it is possible that with earlier treatment, there would be a better response.<sup>5,9,19</sup>

In this report, we present a case of TRMA with severe RV dysfunction, moderate to severe pulmonary insufficiency, atrial dysrhythmia and right bundle branch block. Our patient, despite long-term thiamine administration, had developed severe RV failure and AF.

## CONCLUSION

Currently, there are only recommendations for lifelong thiamine administration (25–75 mg daily) in these patients, which should begin as early as possible. There should be at least annual monitoring of efficacy of therapy by cardiac, hearing and visual assessments and also laboratory indices of anaemia and hyperglycaemia.<sup>8</sup>

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