Left ventricular noncompaction in primary systemic carnitine deficiency: A rare association

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ABSTRACT

Left ventricular noncompaction (LVNC) is a rare phenotype of dilated cardiomyopathy. We report a child with primary systemic carnitine deficiency having associated LVNC.

Keywords: Cardiomyopathy, carnitine deficiency, left ventricular noncompaction

INTRODUCTION

Left ventricular noncompaction (LVNC) is a rare form of dilated cardiomyopathy and is usually associated with genetic mutations involving sarcolemmal proteins or ion channels. We report an 11-year-old girl with LVNC with associated primary systemic carnitine deficiency, with improvement in left ventricular ejection fraction following carnitine supplementation.

CASE REPORT

An 11-year-old girl was referred in view of reduced exercise tolerance at school as compared to peers, which was first found 6 months prior, and was progressively increasing. She also had one episode of drowsiness 1 year back, at which time she was noted to have hypoglycemia, and was managed conservatively. She was first born to a third-degree consanguineously married couple, with no history of spontaneous abortions or sudden cardiac deaths.

On examination, she did not have any dysmorphism or neurocutaneous markers. Cardiovascular examination showed cardiomegaly, with normal jugular venous pressure and no evidence of murmur. Rest of the systemic examination was unremarkable.

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Chest radiograph showed cardiomegaly with cardiothoracic ratio of 0.62 [Figure 1], while electrocardiogram showed evidence of left ventricular hypertrophy with volume overload [Figure 2]. Echocardiography showed dilated left ventricle with evidence of noncompaction, along with mild left ventricular dysfunction (ejection fraction – 52%) [Figure 3].

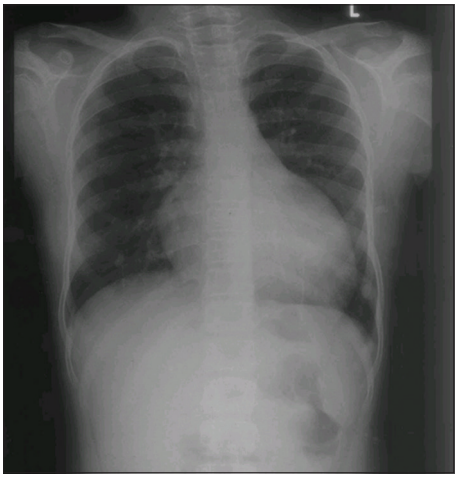

Figure 1: Posteroanterior chest radiograph showing cardiomegaly

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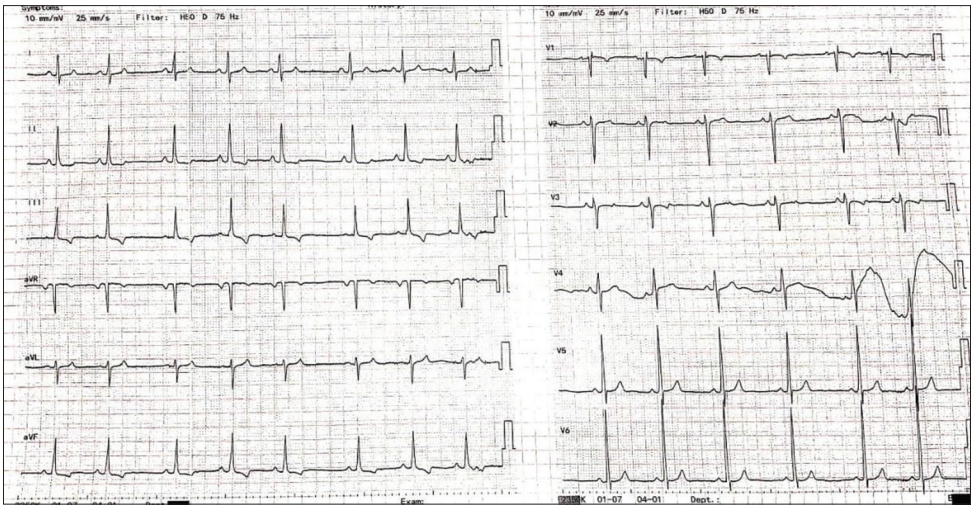

Figure 2: 12 lead electrocardiogram showing sinus rhythm with left ventricular enlargement

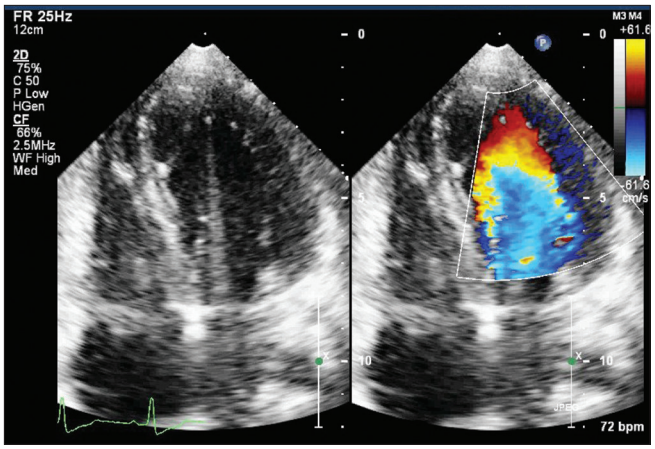

Figure 3: Transthoracic echocardiogram: long-axis modified four-chamber view showing the presence of trabeculations and deep intratrabecular recesses, with perfusion at end-diastole on Doppler echocardiography

In view of cardiomyopathy and one episode of hypoglycemia, inborn error of fatty acid metabolism was suspected. Tandem mass spectrometry showed low levels of free carnitine (0.3 μmol/l [normal 8–100]) and acylcarnitine (0.16 μmol/l [normal 8–150]), with normal levels of other acylcarnitines and amino acids. Next-generation sequencing revealed a homozygous pathogenic mutation of exon 5 of SLC22A5 gene (p.Glu317Ter) suggestive of primary systemic carnitine deficiency.

She was started on oral carnitine supplementation (100 mg/kg/day) along with enalapril and carvedilol. At 8 months of follow-up, there was significant improvement of exercise tolerance as well as left ventricular ejection fraction (62%).

DISCUSSION

The SLC22A5 gene is composed of 10 exons and has been mapped to the long arm of chromosome 5 and codes for a plasma membrane integral protein which acts a sodium-dependent high-affinity carnitine transporter.[1] Homozygous mutations result in systemic primary carnitine deficiency, which has a incidence of 1:40,000 newborns.[2] It is characterized by urinary loss of carnitine and reduced serum acylcarnitine levels, which lead to impaired fatty acid oxidation.[3] Manifestations usually include sudden death, episodic hypoketotic hypoglycemia, skeletal or cardiac myopathy, and Reye syndrome.[4] Supplementation with carnitine has been seen to improve symptoms.[5]

LVNC is a rare form of dilated cardiomyopathy, with an overall incidence of 0.12 children per 100,000 per year.[6,7] It is characterized by prominent trabeculae along the left ventricular endocardial border visible in end-diastole, which move synchronously with the thin compacted myocardial layer and deep intra-trabecular recesses, which demonstrate perfusion at end-diastole on Doppler echocardiography.[8] Associated genetic mutations described so far include those encoding nuclear envelope proteins, dystrophin-associated proteins, ion channels, and Notch signaling pathway.[9]

Systemic primary carnitine deficiency has been associated with myocardial disease but has been limited to dilated and hypertrophic cardiomyopathy.[10-12] In majority of these reports, carnitine supplementation has been found to have a favorable effect on myocardial function.[13]

In our patient, the episode of hypoglycemia was crucial in identifying the possibility of an underlying inborn error of metabolism, probably affecting the lipid metabolism pathway. Supplementation of carnitine resulted in improvement of the myocardial contractility as well as left ventricular ejection fraction.

CONCLUSION

Inborn errors of metabolism often manifest as inherited cardiomyopathies and require a high index of suspicion

for diagnosis. Supplementation of the appropriate micronutrient can help improve the outcome of these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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