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CASE REPORT

Reversible Cardiomyopathy, What Should the Clinicians Keep in Mind? A Case Report

Abdulmajeed A. Alzahrani [a,*], Saud A. Bahaidarah [b], Zuhair N. Al-Hassnan [c], Gaser A. Abdelmohsen [b,d]

[a] Cardiac Surgery Division, Department of Surgery, King Abdulaziz University Hospital, P.O.BOX: 80215, Jeddah, 21589, Saudi Arabia
[b] Pediatric Cardiology Division, Department of Pediatrics, King Abdulaziz University Hospital, P.O.BOX: 80215, Jeddah, 21589, Saudi Arabia
[c] Center of Genomic Medicine, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia
[d] Pediatric Cardiology Division, Department of Pediatrics, Kasr Al Ainy School of Medicine, Cairo University, 99 El-Manial St., Cairo, 11451, Egypt

Abstract

Primary carnitine deficiency (PCD) is an autosomal recessive disorder characterized by decreased carnitine levels essential for Beta oxidation in various organs, including the heart. Early diagnosis and treatment of PCD can revert cardiomyopathy. A 13-year-old girl presented with heart failure due to dilated cardiomyopathy and severe cardiac dysfunction; following L carnitine treatment, the patient's clinical conditions improved, and cardiac functions returned to normal within weeks. Investigations revealed PCD; regular L carnitine has been provided, all cardiac medications are discontinued, and the patient is doing well. We believe PCD should be ruled out in every patient with cardiomyopathy.

Keywords: Primary carnitine deficiency, Dilated cardiomyopathy, Carnitine supplementation, Case report

1. Introduction

L-carnitine is a hydrophilic amino acid of which about 75% is derived from meat and dairy products, and the remainder is produced endogenously [1]. It is vital for transporting long-chain fatty acids into mitochondria for beta-oxidation. Different enzymes, such as carnitine palmitoyl transferase I (CPT I), carnitine-acylcarnitine translocase (CACT), and carnitine palmitoyl transferase II (CPT II), aid in the transport of long-chain fatty acids across mitochondrial membranes. This process could be altered if these enzymes are impaired [2] (Fig. 1).

Primary carnitine deficiency (PCD) is a rare autosomal recessive disorder with an estimated incidence between 1/40 000 and 1/120 000 [3]. Many PCD patients remain asymptomatic or have dilated cardiomyopathy. If PCD is not identified and L-carnitine is not administered, heart failure may worsen and eventually result in death, while early diagnosis and treatment are associated with complete recovery of cardiomyopathy [4]. This report described a 13-year-old girl with heart failure and dilated cardiomyopathy who recovered entirely after receiving empirical L carnitine. Written consent is obtained, and the local ethical committee approved the case report.

2. Case report

A 13-year-old girl was diagnosed with Dilated Cardiomyopathy (DCM) after experiencing chest pain and shortness of breath when she was seven years old. Although she was compliant with various

Abbreviation: PCD, Primary carnitine deficiency,

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* Corresponding author.
E-mail address: abdulmajeedabdullah305@gmail.com (A.A. Alzahrani).

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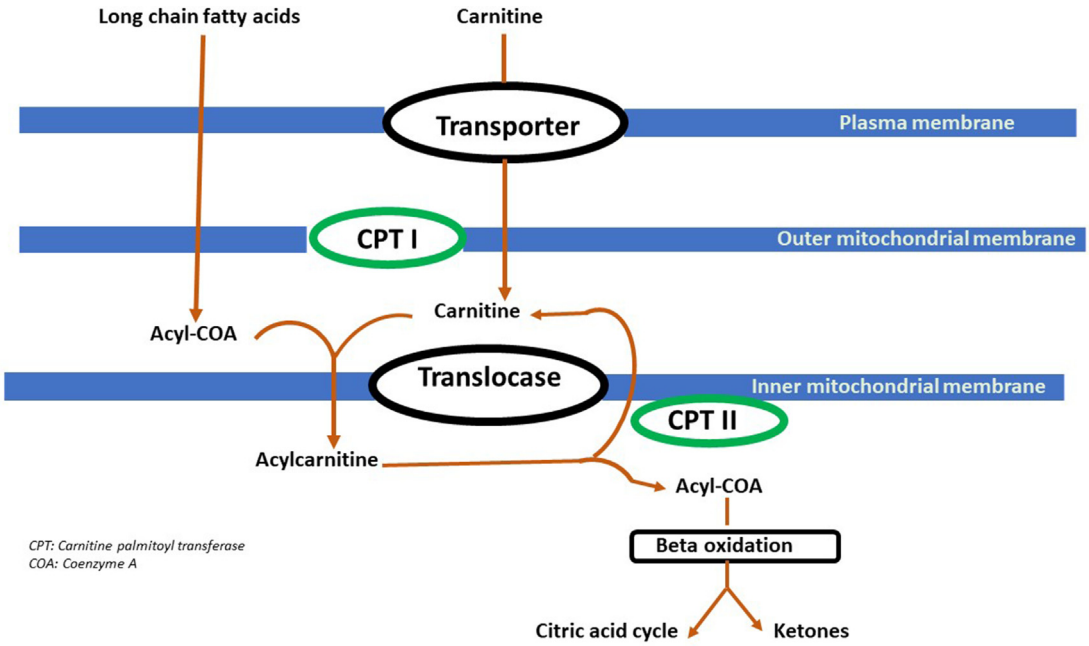

Fig. 1. Acyl–Carnitine cycle. Showing the Acyl-carnitine cycle with enzymes and transporters involved in the metabolism of long-chain fatty acids for beta-oxidation and energy production. CPT: carnitine Palmitoyl transferase, COA: Coenzyme A.

heart failure medications, her symptoms did not improve. At the age of 13 years, she had gastroenteritis, which exacerbated her heart failure symptoms. During that time, she presented to the emergency room with progressive dyspnea (NYHA IV) and orthopnea. She was born to a consanguineous couple at term after a normal pregnancy. Prenatal, natal, and postnatal histories were unremarkable. The family history revealed that her mother died of a sudden cardiac death at the age of 27 years, in her second month of pregnancy, despite having no known diseases. The patient's eight-year-old brother is asymptomatic.

Examination revealed tachypnea (respiratory rate was 35/minute), orthopnea, tachycardia (heart rate was 120/minute), and hypotension (Blood pressure was 77/45 mmHg). Cardiac examination revealed S3 and S4 gallop, soft apical systolic murmur with bilateral basal chest crackles. The patient had average growth and psychomotor development with a normal neurological examination. Chest x-ray revealed cardiomegaly, and echocardiography revealed dilated left ventricle with severe dysfunction (EF 25%) (Fig. 2 A-B). The patient was admitted to the pediatric intensive care unit and discharged after stabilization. The patient was discharged home on furosemide, spironolactone, enalapril, digoxin, carvedilol, and L carnitine. On follow-up, we were surprised as the cardiac function and patient exercise tolerance returned to near normal. At this time, we thought about reversible cardiomyopathy. The patient was not on L carnitine before, and with this dramatic response after adding L carnitine, PCD was highly suspicious. The patient lived in a rural area with limited access to a specialized hospital, and our country did not have a nationwide newborn screening program for PCD then. Therefore, a blood sample was sent for plasma acylcarnitine analysis. The result showed extremely low free carnitine at 0.28 μmol/L (normal 6-72 μmol/L). A genetic test by whole exome sequencing detected a previously reported homozygous pathogenic variant (c.395G > A; p. W132Ter) in the SLC22A5 gene, which confirmed the diagnosis.

Therefore, the oral L-carnitine supplementation was initiated at 750 mg twice daily, then increased to 900 mg three times per day based on the plasma carnitine level, and all other medications were discontinued. The patient had regular follow up in the last three years and is asymptomatic with good cardiac function (Fig. 2 C-D).

3. Discussion

Cardiomyopathy is a potentially fatal disease within two years of diagnosis. Only one-third of cases of cardiomyopathy in children have a definitive etiology; the remaining two-thirds are classified

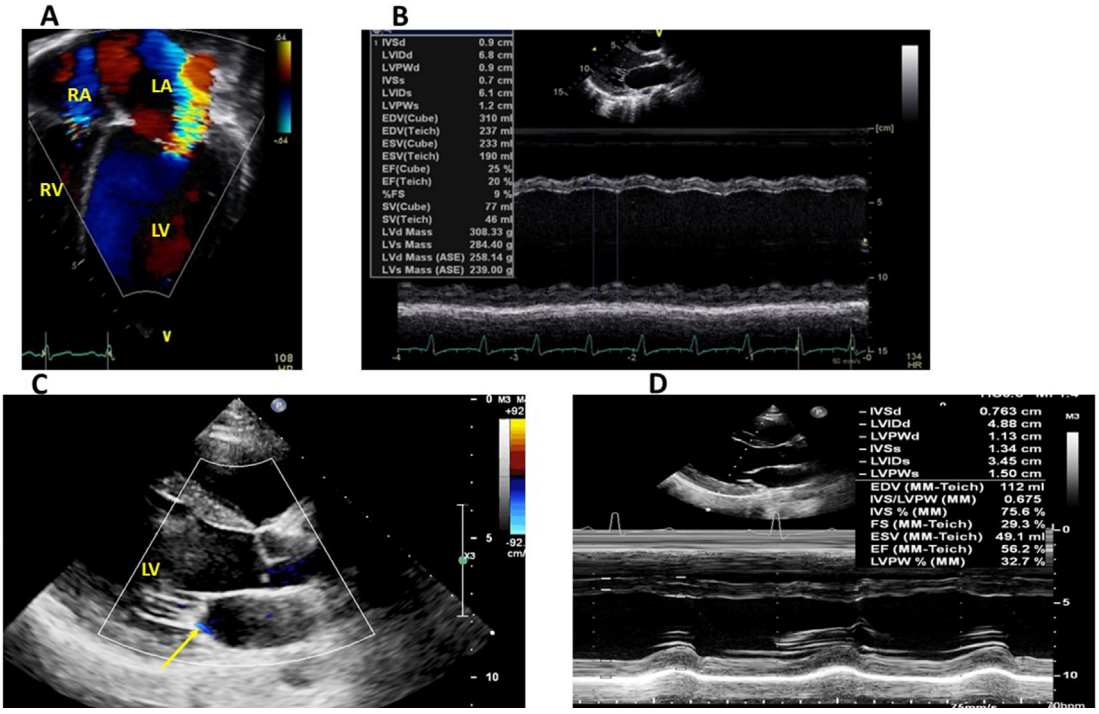

Fig. 2. Echocardiography before and after L carnitine treatment. A: Apical four-chamber view before L carnitine therapy showing dilated LV, with moderate-severe mitral valve regurgitation. B: M–mode before L carnitine therapy showing LV dilatation with severe systolic dysfunction. C: Parasternal long axis view after L carnitine therapy with the reverse remodeling of LV with trivial mitral regurgitation (yellow arrow). D: M–mode after L carnitine therapy showing normal LV size and function. LA: left atrium, LV: left ventricle, RV: right ventricle, RA right atrium.

as idiopathic. Without knowing a specific cause, specialized therapies cannot be started, which may contribute to poor outcomes [5].

Sudden death may be the primary clinical presentation of PCD; this could explain the sudden death of the patient's mother during pregnancy. As previously reported, clinical manifestations related to plasma carnitine deficiency in 51 patients identified 9 cases with cardiomyopathy. The other most frequent manifestations were hypotonia and failure to thrive [6]. An acute metabolic decompensation can be triggered by a catabolic event such as a viral infection [7]. The patient's cardiac symptoms worsened following an episode of acute gastroenteritis.

The average age of PCD onset is two years. However, it can occur at any age between two months and seven years. Older children often manifest with skeletal or cardiac myopathy, whereas infants typically present with hypoketotic hypoglycemia, hepatomegaly, and hyperammonemia with encephalopathy. Our patient had heart failure with no hypoketotic hypoglycemic encephalopathy symptoms or myopathy.

Tein et al. described 11 primary carnitine deficiency cases, all of which had cardiomyopathy. Carnitine therapy improved 8 cases within a month. Two remaining kids died in an acute episode before diagnosis and treatment. Because the last child was diagnosed at 3.5 months with only mild echocardiographic abnormalities, the clinical response to treatment was difficult to assess [8]. Our patient's rapid cardiac improvement also suggested a primary deficiency. These data and our case show the importance of screening children with cardiomyopathy for this disease and starting treatment immediately if suspicion is high.

Our patient needed high oral doses to maintain acceptable plasma levels. The recommended oral carnitine dose is 100–300 mg/kg per day for long-term treatment, and intravenous therapy is 100–400 mg/kg per day for life-threatening events [9]. It is essential to continue L carnitine therapy in these patients for life, as cessation of carnitine therapy can result in severe arrhythmia and heart failure symptoms as has been reported in 2 adult brothers with primary carnitine deficiency [10].

Finally, L-carnitine improved the patient's cardiac dysfunction, exercise capacity, quality of life, and her risk of sudden death is expected to decrease. To confirm PCD, a molecular workup must find biallelic SLC22A5 gene mutations.

4. Conclusion

A primary carnitine deficiency is a rare but treatable cause of cardiomyopathies. As soon as carnitine deficiency has been confirmed or suspected, a potentially life-saving regimen with carnitine at 100–400 mg/kg per day must be implemented. PCD should be immediately ruled out in each patient with cardiomyopathy. Family screening is highly advised to identify asymptomatic individuals at high risk.

Author contribution

Conception and design of Study: AAA, SAB. Literature review: AAT, ZNA, GAA. Acquisition of data: SAB, ZNA, GAA. Analysis and interpretation of data: AAA, SAB, ZNA. Research investigation and analysis: SAB, ZNA, GAA. Data collection: AAA, SAB, GAA. Drafting of manuscript: AAA, SAB, ZNA. Revising and editing the manuscript critically for important intellectual contents: SAB, ZNA, GAA. Supervision of the research: AAA, SAB, ZNA. Research coordination and management: SAB, ZNA, GAA.

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Conflict of interest

None declared.

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