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# Primary Carnitine Deficiency: Rare Cause of Paediatric Dilated Cardiomyopathy, Often Underdiagnosed

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**Abstract** **Case Report**

Primary carnitine deficiency (PCD) is an autosomal recessive disorder of fatty acid beta-oxidation. Which results from a defect in the transport of carnitine and is one of the rare treatable etiologies of metabolic cardiomyopathies. Affected patients may present with acute metabolic decompensation in infancy or severe cardiomyopathy in childhood. There have also been reports of dramatic sudden infant death syndrome. Early disease detection and treatment with L-carnitine can be lifesaving. We present in this report, a severe case of decompensation of previously undiagnosed dilated cardiomyopathy in a 14-year-old boy, who presented to the pediatric emergency department with acute heart failure, initially suspected to be viral myocarditis. Chest x-ray showed cardiomegaly, echocardiographic findings included hypokinetic dilated cardiomyopathy with reduced ejection fraction at 22%, the respiratory multiplex PCR came back in favor of a SARS-CoV-2 infection, Laboratory test results showed hepatic failure and a low rate of free and total plasma carnitine. His clinical condition deteriorated rapidly, with the onset of cardiogenic shock leading up to his death in the intensive care unit before carnitine therapy was initiated. The aim of this case report is to highlight the importance of searching for a metabolic cause, particularly primary carnitine deficiency, for early treatment and improved prognosis of the disease.

**Keywords:** Carnitine deficiency, dilated cardiomyopathy, metabolic disorder.



## BACKGROUND

Dilated cardiomyopathies (DCM) are the most common cardiomyopathies in children and are a leading cause of acute heart failure and a major indication for heart transplantation. The etiologies are diverse and only one-third are identified at the time of diagnosis, although two-thirds are classified as idiopathic [1]. 11% of DCM cases are metabolic, wish primary carnitine deficiency (PCD) is the most common cause [2].

We report on a particular case because of the age of onset, the clinical presentation, and the dramatic course of the disease leading to the death, of a previously healthy 14-year-old child who developed cardiogenic shock and toxic hepatitis secondary to previously undiagnosed dilated cardiomyopathy due to primary carnitine deficiency, which was revealed by the SARS-CoV-2.

## CASE REPORT

An early adolescent male was admitted to our department with acute heart failure. In the family history, the mother died of an undocumented heart disease. The history of his illness goes back to a week before his hospitalization by the installation of a productive cough, pain of the right hypochondrium, vomiting, and fever. After 4 days, it was complicated by dyspnea on exertion. Initial clinical examination revealed polypnea of 50 cycles/min, blood pressure of 110/70 mmHg, heart rate of 140 beats/min, oxygen saturation of 90% (room air), jugular venous distention, congestive hepatomegaly, enlarged and displaced apex beat, galloping sound, and 2/6 systolic murmur at the apex. Lung auscultation revealed bilateral crepitus rales. Chest x-ray showed cardiomegaly at 0.64 (Figure 1), echocardiographic findings included hypokinetic dilated cardiomyopathy with reduced ejection fraction (EF=22%), reduced shortening fraction (FS=10.6%), left ventricular end-diastolic (LVED) of 8.67 cm (Figure 2), mitral regurgitation grade II, and tricuspid insufficiency grade II (Figure 3). The patient's electrocardiogram (ECG)

showed ventricular extrasystoles. Laboratory test results showed microcytic hypochromic anemia at 9 g/dl, hepatocellular insufficiency with ASAT at 5436 IU/L, ALAT at 2692 IU/L, TP at 19%, factor V at 9.3%, blood sugar at 0.8g/dl, procalcitonin at 0.57 ng/ml, CRP at 17.9, sed rate at 5 mm/h. D-dimer at 31.3%, troponin at 155.28 ng/L, BNP at 1758. 20 pg/ml. The toxicological evaluation was negative. The viral serologies HAV, HBV, and HCV were negative. In front of this clinical picture, the diagnosis of viral myocarditis was first evoked, the respiratory multiplex PCR came back in favor of a SARS-CoV-2, In view of the mother's history of heart disease, a metabolic cause was also sought, and the result was a primary carnitine deficiency (PCD) with a low rate of free and total plasma carnitine at 5 µmol/L and 8 µmol/L, respectively. The treatment initiated was symptomatic with vitamin K, furosemide, captopril, and digoxin. The child underwent cardiogenic shock during his hospitalization, was transferred to the ICU, and died before carnitine therapy was initiated.

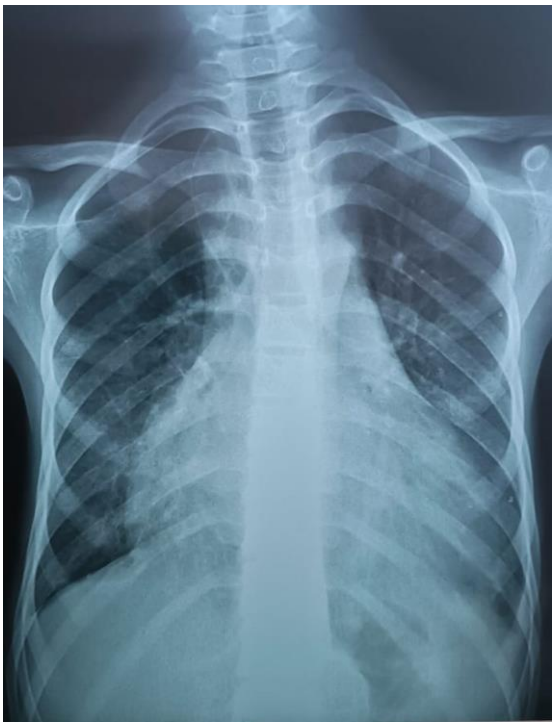

**Figure 1: Chest x-ray showing the cardiomegaly**

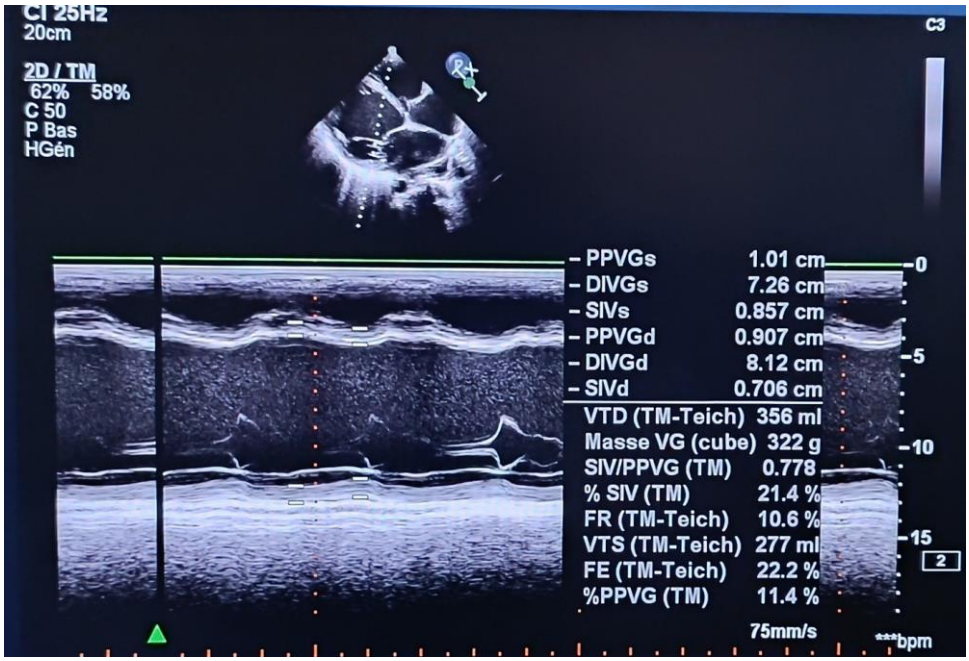


**Figure 2: Transthoracic echocardiography: TM mode demonstrating severely enlarged left ventricle (LEVD: 8.67cm) with poor systolic function (EF: 22%)**

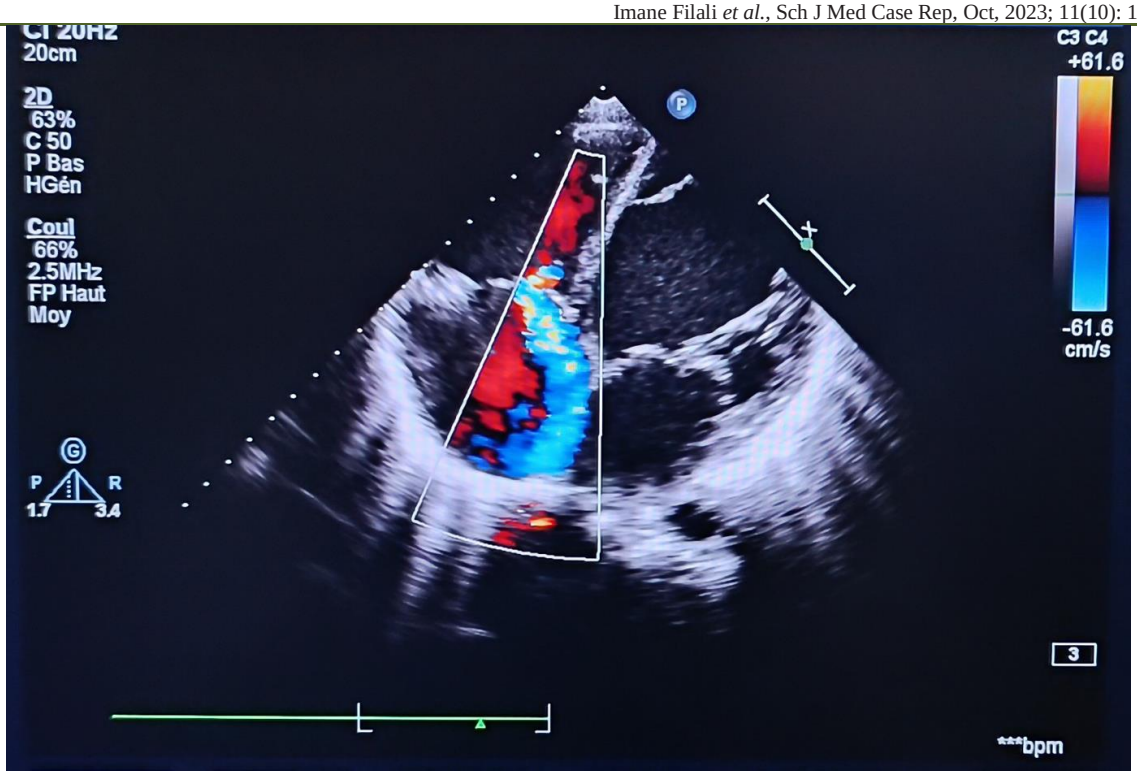


**Figure 3: Parasternal short-axis color Doppler echocardiographic view depicting large regurgitant jet of the tricuspid valve**

## DISCUSSION

DCM in children is a heterogeneous group of diseases whose etiology remains difficult to study, with a metabolic origin accounting for 4 to 11% according to studies [2-4], the main anomaly being a primary carnitine deficiency.

Primary carnitine deficiency is a rare condition with an incidence of one in 40,000 to one in 120,000 newborns [5], is an autosomal recessive disorder caused by a mutation in the SLC22A5 gene encoding the carnitine transporter OCTN2 [5, 6], The result is a defect in the transport of carnitine within cells and mitochondria. This leads to massive urinary losses and systemic carnitine depletion. Carnitine plays an essential role in the transfer of long-chain fatty acids into the mitochondria for subsequent β-oxidation; these fatty acids are essential energy substrates for the myocardium and other muscle tissues [7, 8].

The symptomatology is polymorphic, presenting mainly in childhood as hypoglycemic hypoketosis encephalopathy, muscle weakness, respiratory failure, digestive disorders, and heart failure secondary to cardiomyopathy [9]. Isolated cardiomyopathy in PCD in children is a late manifestation, usually appearing around the age of 4 years with a range of 1 to 7 years. Such a disease may be progressive and may cause sudden death before a diagnosis can be made [10]. In fact, cardiac events in apparently healthy patients have often been preceded by provocative events such as a minor infection or the initiation of pivalic acid-containing antibiotics, as in this report, where DCM was revealed by a coronavirus disease. Liver damage in primary carnitine deficiency is characterized by its onset during the neonatal period, up to 18 months. Clinically, it manifests as hypoglycemic episodes induced by prolonged fasting or trivial infection [3]. Hyperammonemia, hepatic cytolysis, and increased free fatty acids are also observed. In our case, the liver damage is more consistent with ischemic hepatitis which is secondary to congestive heart failure.

Heart failure during DCM due to primary carnitine deficiency does not respond to inotropes or diuretics. If the diagnosis is not made early and carnitine supplementation is not administered, progressive heart failure will eventually develop, leading to death [11].

## CONCLUSION

The low survival rate of children with primary carnitine deficiency, the late onset of clinical manifestations, and the frequency of sudden death in this category, highlight the importance of including primary carnitine deficiency screening in the national newborn screening program, the importance of a family investigation, and suggests that pediatricians should be on the lookout for the first clinical signs of the disease at an early age, rather than at a late stage when the prognosis is compromised, in order to initiate treatment, which is straightforward and has an excellent prognosis under carnitine treatment.

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