CASE REPORT

The recovery from dilated cardiomyopathy followed by hypertrophic cardiomyopathy, in the course of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase in infant

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Abstract

Dilated cardiomyopathy is one of the most common causes of the heart failure in childhood and can develop as a consequence of metabolic disorders such as fatty acid beta-oxidation disorders or amino acids metabolism disorders. In our report we present a case where in the course of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase the recovery from dilated cardiomyopathy resulted in hypertrophic cardiomyopathy.

Key words

Dilated cardiomyopathy, Gene mutation, Metabolic disease

1 Introduction

Dilated cardiomyopathy is one of the most common causes of the heart failure in childhood; despite the treatment, in most cases it has a progressive course. No specific treatment is available for most patients but dilated cardiomyopathy can develop as a consequence of metabolic disorders such as fatty acid beta-oxidation disorders, amino acids metabolism disorders and others in which the main principle of the treatment is a fat-reduced and fat modified diet [1].

We report a case where—in the course of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase—the recovery from dilated cardiomyopathy resulted in hypertrophic cardiomyopathy.

2 Case report

A 5-week-old girl was admitted to a pediatric intensive care unit due to the evolving cardiogenic shock with a severe impaired cardiac function.

She is the second child of non-consanguineous parents. The child was born in the 40th week of gestation, the birth weight being 3200g and the condition of the newborn was estimated to be 10 points in Apgar scale.

A few days before the admission to the pediatric intensive care unit she had more frequent vomiting and she refused feeding, without any infectious disease. At the admission because of cardio-respiratory failure she had to be put on mechanical ventilation. The thorax x-ray disclosed extensive cardiomegaly. The echocardiographical examination revealed a heart silhouette with a significant dilatation of the left ventricle and left atrium, a spherical left ventricle with global wall hypokinesis. The ejection fraction of the left ventricle was 20% (see Figure 1).

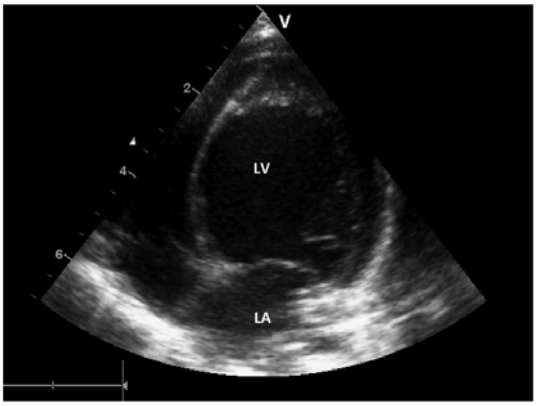

Figure 1. Cross sectional (two dimensional) echocardiogram reveals a significant dilatation of the left atrium and left ventricle at the age of 5 weeks. The estimated left ventricle ejection fraction at that time was about 20%.

The initial laboratory work-up revealed hypoglycemia without ketonuria, elevated liver enzymes. The metabolic work-up showed excretion of large quantities of 3-hydroxydicarboxylic acids and normal levels of total and free carnitine. Molecular analysis of the gene coding for mitochondrial trifunctional protein showed that the patient was homozygous for the 1528G>C mutation, and both mother and father were heterozygous. She was maintained on a low-fat diet that included medium-chain triglycerides as an energy source and provision of essential long-chain fats using the nasogastric tube feeding and on the standard heart failure treatment. After 60 days of the treatment, the child was discharged home.

During six months of the cardiological follow-up the child's condition remained stable. The echocardiography examination at the age of 7 months revealed the ejection fraction about 60%. Currently, the girl is 11 months old and does not show any signs of heart failure; she is physically active. Her last echocardiography examination (see Figure 2) unexpectedly revealed hypertrophic cardiomyopathy with hyperkinetic heart (the ejection fraction raised to 79%).

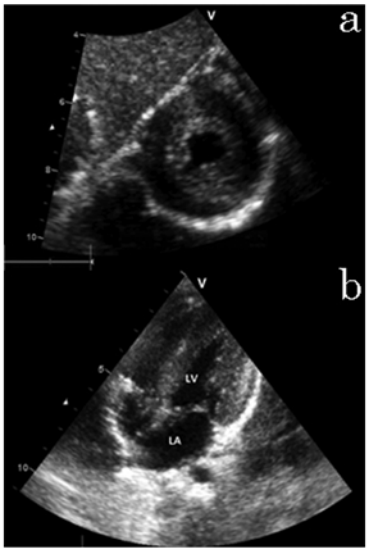

Figure 2. a. Short axis transthoracic echocardiographic image showing grossly thickened myocardium in the same child 6 months later. b. Apical four chamber echocardiographic image at the age of 11 months.

3 Discussion

As far as the available literature is concerned and up-to our knowledge this is the first report of the unusual recovery from dilated cardiomyopathy followed by hypertrophic cardiomyopathy in the course of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase.

The contemporary classification of cardiomyopathy includes different subtypes: dilated, hypertrophic, restrictive and others. This classification does not account for etiology. It focuses on similar pathophysiologic groups.

The deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase, also known as a trifunctional protein deficiency, is a rare inborn error of fatty acid metabolism. It is an autosomal recessive disorder caused by mutations in the hydroxyl-acyl-coenzym A dehydrogenase/3-ketoacyl-coenzym A thiolase/enoyl-coenzym A hydratase (trifunctional protein) alpha subunit (HADHA) gene [1].

A number of cases were described defining the key features of hypoketotic hypoglycemia and showing a wide variability in clinical presentation [2].

Patients with the trifunctional protein deficiency exhibit a wide clinical spectrum of disease with severe neonatal manifestations including cardiomyopathy and death, through moderate/severe infantile presentation with hepatic manifestations, to mild peripheral neuropathy with episodic rhabdomyolysis [1].

Cardiomyopathy is a frequent finding in fatty acid oxidation disorders [2-4] in deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase can be hypertrophic cardiomyopathy or, less frequently, dilated cardiomyopathy. The largest reported series of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase patients was described by Den Boer et al. [3] in 2002. Twenty one (42%) out of the 50 patients were said to have cardiomyopathy, although the type of cardiomyopathy was not reported. The second largest series of deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase patients was reported by Tyni et al. [4] in 1997.

Because there is a substantial variation in the clinical course of the disease even in siblings with the same molecular genetic defect, the genotype does not explain all the phenotypic variations in the deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase.

Our case is remarkable because we present an infant with deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase in whom both types of cardiomyopathies, dilated cardiomyopathy followed by hypertrophic cardiomyopathy, were disclosed in the course of that rare disease. It reveals that the incidence and pathophysiology of cardiac involvement in deficiency of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase is still poorly understood and multicenter studies should be conducted to clear it up.

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