Dilated cardiomyopathy in celiac disease : role of carnitine deficiency

N. Uslu[1], H. Demir[1], T. Karagöz[2], I.N. Saltik-Temizel[1]

(1) Section of Gastroenterology, Hepatology and Nutrition, (2) Department of Pediatrics, Section of Cardiology, Hacettepe University, Faculty of Medicine, Ankara, Turkey.

Abstract

Celiac disease (CD) is an immune-mediated enteropathy in genetically susceptible persons and the disease can present with manifestations in the intestine and in organs outside the gut. An increased prevalence of CD in patients with idiopathic dilated cardiomyopathy or secondary cardiomyopathy and some other cardiac disorders has been reported. Here is described a case of dilated cardiomyopathy in a patient with CD and secondary carnitine deficiency. Dilated cardiomyopathy due to carnitine deficiency may occur in CD patients and carnitine deficiency may present not only at the time of diagnosis of CD but it may also develop during gluten-free diet, particularly in patients with fast weight gain and without carnitine supplementation. (Acta gastroenterol. belg., **2010**, 73, **530-531**).

Key words : celiac disease, carnitine, children, cardiomyopathy.

Introduction

Celiac disease (CD) is an immune-mediated enteropathy in genetically susceptible persons perpetuated by the daily-ingested gluten cereals, and characterized with inflammation of the intestinal mucosa along with hyperplasia of the crypts and atrophy of the villi. CD presents with manifestations in the intestine and in organs outside the gut (1). An increased prevalence of CD in patients with idiopathic dilated cardiomyopathy or secondary cardiomyopathy and some other cardiac disorders has been reported (2-11). We herein describe a case of dilated cardiomyopathy in a patient with celiac disease and secondary carnitine deficiency.

Case report

A six-year old girl with chronic diarrhea, vomiting and loss of weight for six months was admitted to hospital for edema and tetany. She was pale, apathic and had malnutrition (height and weight below -2 SD), pretibial edema, clubbing, and abdominal distention. Laboratory evaluation revealed anemia (hemoglobin : 7.5 g/dL – normal range 11.5-15.5), hypoalbuminemia (1.8 g/dL – normal range 4.0-5.3) and hypocalcemia (4.9 mEq/L – normal range 8.8-10.5), positive antigliadin (AGA) IgA and IgG (48.4 IU/mL – normal range 0-23 and 53.3 IU/mL – normal range 0-28, respectively) and anti-endomysial antibodies (EMA) (++- normal range : negative). Small bowel biopsy showed villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes representing celiac disease (Marsh type 3a). Celiac disease was diagnosed and a gluten-free diet (GFD) was initiated. Diet included 120% of calories recommended for age and weight. She also received calcium, potassium, trace elements (magnesium, zinc), iron, vitamin B12, folic acid and vitamin E. Her weight increased by 24.2% after the diagnosis till the second admission, two months after, because of dyspnea, palpitation and cyanosis. Echocardiographic examination showed advanced left ventricular dilatation with atrioventricular septum deviation to the right, an ejection fraction of 46% (normal value > 60%). Supportive treatment with digoxin, furosemide and captopril was started with the diagnosis of dilated cardiomyopathy. No further evidence was shown for systemic hypertension, ischemic heart disease or systemic infections and there was no history of cardiotoxic medication. There was no family history of any cardiac disease, either. Serum total carnitine level was very low as 0.5 µmol/L (normal : 0-60) and carnitine was added to the treatment. After seven months of GFD and carnitine supplementation diastolic and systolic functions were within normal limits on echocardiographic evaluation. Two years after the diagnosis while she was still on GFD all treatments were stopped as serum carnitine level was within normal levels (27.52 µmol/L) as well as cardiac functions. For the last 5 years having a strict GFD she has been followed up with negative AGA and EMA, normal cardiac functions, and normal serum carnitine levels with height and weight appropriate for her age.

Discussion

This case represents a patient with CD, secondary carnitine deficiency and dilated cardiomyopathy. There have been some case reports and population studies describing the association of CD and cardiomyopathy (idiopathic or any other forms). Curione *et al*. (2) examined 52 idiopathic dilated cardiomyopathy patients for CD and found that three of them had CD and suggested that prevalence of CD in dilated cardiomyopathy patients was high. In another study conducted in Italy

Correspondence to : Nuray Uslu, M.D., Fellow in Pediatric Gastroenterology and Nutrition, Hacettepe University, Faculty of Medicine, Department of Pediatrics, Section of Gastroenterology, Hepatology and Nutrition 06100, Ankara, Turkey. E-mail : nurayu@hacettepe.edu.tr

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642 patients encountered in the waiting list for heart transplantation were evaluated and 1.9% were EMA positive while EMA positivity was 0.35% for the control group supporting the results of the previous study (3). Frustaci *et al*. (4) evaluated 187 patients with myocarditis and found that nine (4.4%) of them had CD. In another study 283 adult patients with inherited or sporadic dilated cardiomyopathy, 418 relatives, and 2000 healthy blood donors were screened for anti-human-tissue-transglutaminase (anti-h-tTG) Ig A and Ig G and EMA. The higher prevalence of CD in patients with sporadic or inherited dilated cardiomyopathy was found (7). Carnitine levels of the patients were not evaluated in any of these studies.

Several mechanisms have been proposed for the development of cardiomyopathy in CD. Abnormalities of intestinal permeability in patients with CD may lead to increased systemic absorption of some luminal antigens or infectious agents which may cause myocardial damage through immune-mediated mechanisms (12). It has also been suggested that myocardial injury may occur as a result of an immune response directed against an antigen present in both the myocardium and the small intestine (4,7). In a study, patients with myocarditis and CD had detectable anti-cardiac antibodies supporting the immune-mediated mechanism (4). Although requiring further confirmation it has also been suggested that cardiomyopathy may be another atypical presentation of CD (7).

Chronic malabsorption is common in CD leading to deficiencies of vitamins, minerals and trace elements. Chronic malabsorption may lead to cardiomyopathy secondary to nutritional deficiencies including thiamine, riboflavin, magnesium, calcium, selenium and carnitine (5,9,13). Carnitine is an important semi-essential quarternary ammonia derivative which is necessary for the transport of long-chain fatty acids across the inner mitochondrial membrane for β oxidation. A decrease in serum concentrations of total carnitine has been observed in children with CD (13,14) and in patients presenting with dilated cardiomyopathy associated with CD (9) as in our patient. Also it has been shown that GFD leads to a progressive increase in serum level of carnitine in patients with dilated cardiomyopathy and CD (9).

Our patient presented with symptoms and signs and laboratory findings of malabsorption. She did not have any further evaluation for cardiac functions during her first admission to the hospital as she did not have any symptoms of heart failure and cardiomyopathy and carnitine level was not measured, either. At her second admission she had symptoms of heart failure due to dilated cardiomyopathy. Carnitine level of the patient was evaluated and found to be low. During the time course between the diagnosis of celiac disease and occurrence of dilated cardiomyopathy her weight increased by 24.2%. This fast weight gain might have caused further decrease of serum carnitine level as a reason for dilated cardiomyopathy. After GFD with carnitine supplementation improvement in cardiac functions was observed. Also after the cessation of carnitine therapy carnitine deficiency did not reocur as the patient complied strict GFD during five-year follow up. It has been observed that GFD has a critical role for improvement of cardiac functions for patients with dilated cardiomyopathy (4, 6,15) as in our patient. We think that the improvement of cardiac functions of the patient by the concomitant GFD and carnitine supplementation supported our diagnosis of both gluten enteropathy and secondary carnitine deficiency.

In conclusion, clinicians should also be aware of dilated cardiomyopathy due to carnitine deficiency. It should be kept in mind that carnitine deficiency may be present not only at the time of diagnosis of CD but it may also develop during GFD, particularly in patients with fast weight gain and without carnitine supplementation.

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