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CASE REPORT

Dilated cardiomyopathy caused by plasma membrane carnitine transport defect

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It is recognized that dilated cardiomyopathy can be caused by metabolic disease, particularly mitochondrial cytopathies, glycogen storage disease and fatty acid β-oxidation deficiency. Primary carnitine deficiency (PCD; McKusick 212140) is an autosomal recessive disorder associated with a genetic defect in plasma membrane carnitine transport. It causes severe carnitine deficiency in muscle and heart and also blocks renal conservation of carnitine.

Half the recognized cases of PCD have never had an episode of fasting coma, but instead presented between 18 months and 4 years of age with cardiomyopathy. Without carnitine treatment this will lead to death in 2–3 years. Carnitine replacement has been effective in reversing the cardiac pathology in 3 weeks and is an important element in the diagnosis.

We report a case of a 6-year-old Chinese girl, the third child of nonconsanguineous parents. She has two healthy sisters (7 years old and 20 days old) and a brother who died at 18 months of age with acute dilated cardiomyopathy without any aetiology for the sudden disease.

In our index patient, the delivery, birth weight, stature and psychomotor development were normal. She was a healthy girl until 1 month before admission to our hospital, when she revealed dyspnoea, dizziness, generalized muscle

weakness and palpitations. On physical examination she had a very pale skin colour and polypnoea, but no heart murmur, hepatomegaly or swollen legs. Heart rate was 125/min and blood pressure 78/50 mmHg (normal). Chest radiography showed cardiomegaly and electrocardiography indicated left ventricular hypertrophy. Echocardiography showed left ventricular diastolic phase (LVDP) of 5.2 cm (normal 2.5–3.4), left ventricular E point septum distance (LVEPSD) 1.9 cm (normal <0.8), fraction shorting (FS) 11% (normal 28–35%), ejection function (EF) 25% (normal $>60\%$), very poor contractibility and mitral incompetence grade II.

Dilated cardiomyopathy was diagnosed and furosemide, digoxin and captopril were started. No clinical or echocardiographic improvement was observed. Plasma uric acid was 469 μmol/L (normal 140–340): C-reactive protein, glucose, glutamic-oxaloacetic and glutamic-pyruvic transaminases, creatine phosphokinase, lactic acid (fasting and after meal) and ketone bodies and organic acids in urine were normal. Total carnitine was very low (5 μmol/L; normal 25–61). Two control patients of the same age were also studied and the results showed normal levels: 49 μmol/L and 70 μmol/L, respectively.

After 3 weeks of treatment with oral carnitine, 100 mg/kg per day in two divided doses, the patient improved and could sit, walk and sometimes run in the ward corridor.

The echocardiogram showed remarkable changes after starting carnitine: LVDP 4.4 cm, LVEPSD 1.1 cm, FS 20%, EF 42%. The girl was discharged, and when re-examined after 6 weeks was asymptomatic with normal echocardiogram, ECG and chest radiograph.

After a few months of treatment, plasma total carnitine was 20 μmol/L. Carnitine supplementation was stopped for 1 week, after which plasma total carnitine had fallen to 8 μmol/L (reference range 25–61) and treatment was restarted. The rate of carnitine uptake in cultured skin fibroblasts (Dr J. Hammond, Royal Alexander Hospital for Children, Sydney, Australia) was 0.01 pmol/min per mg protein (control 1.15–1.50) confirming a defect in the plasma membrane carnitine transporter. Plasma carnitine concentrations were normal in both sisters.

The clinical evolution of this case is consistent with the diagnosis of PCD: family history of cardiomyopathy of unknown cause, hyperuricaemia, normal urinary organic acids, very low concentrations of free carnitine in plasma, and an excellent response to carnitine therapy. If PCD is being considered as a cause of dilated cardiomyopathy, carnitine therapy should be initiated without delay as diagnostic tests can still be performed after supplementation has started.

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