Hypertrophic Cardiomyopathy With Type I CD36 Deficiency

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CD36 is a multifunctional membrane-type receptor glycoprotein that reacts with oxidized low-density lipoprotein and long-chain fatty acid (LCFA). A patient presented with hereditary hypertrophic cardiomyopathy (HCM) and type I CD36 deficiency (neither platelets nor monocytes expressed CD36) but showed no myocardial LCFA accumulation. CD36 was expressed in the capillary endothelial cells of the cardiac muscle of a control subject, while the patient's myocardial capillary endothelial cells were completely CD36-negative. These results suggest that type I CD36 deficiency is closely related to hereditary HCM and lack of myocardial LCFA accumulation. (Jpn Circ J 1998; 62: 541–542)

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CD36 is a multifunctional membrane type receptor glycoprotein that reacts with thrombospondin, collagen, oxidized low-density lipoprotein and long-chain fatty acid (LCFA). LCFA is one of the major cardiac energy substrates; hence, LCFA metabolism may have an important role in cardiac diseases. We present here a patient with hereditary hypertrophic cardiomyopathy (HCM) and type I CD36 deficiency who showed no myocardial LCFA accumulation.

Case Report

A 57-year-old man presented with a history of exertional chest oppression and shortage of breath for 1 year. His brothers had been diagnosed as having HCM; one brother had died suddenly at the age of 17 years old. Normal plasma concentrations of lactate dehydrogenase, creatine kinase, pyruvic acid and carnitine isoenzyme fraction were noted. The results of a bicycle-ergometer lactate test were normal. Electrocardiography showed left ventricular hypertrophy; echocardiography revealed a slightly dilated left ventricle with decreased systolic function (ejection fraction of 39%). Endomyocardial biopsy samples from the left ventricle showed marked cellular hypertrophy, fibrosis and abnormal arrangement of myofibers (disarray). We analyzed the CD36 expression in the patient's blood cells using a flow cytometer and he had type I CD36 deficiency (neither platelets nor monocytes expressed CD36), while the patient's myocardial capillary endothelial cells were completely CD36-negative. These results suggest that type I CD36 deficiency is closely related to hereditary HCM and lack of myocardial LCFA accumulation.

Discussion

LCFA is one of the major cardiac energy substrates, and therefore understanding LCFA metabolism may help in elucidating the mechanisms of various cardiac diseases. CD36 is a multifunctional integral membrane glycoprotein that acts as a receptor for thrombospondin, collagen, oxidized low-density lipoprotein and LCFA. The incidence of type II CD36 deficiency (monocytes express CD36 but platelets do not) is relatively high: about 3% of the Japanese population and 0.3% of the USA population. However, the incidence of type I CD36 deficiency is estimated to be much lower than that of type II.

Although mutations of the ß-myosin heavy chain, troponin T and ß-tropomyosin have been reported to be involved in HCM, the genetic abnormalities are still unknown in many cases of this disease. Some patients with end-stage HCM may have left ventricular dilation (dilated phase HCM) and there is clinical and experimental
evidence of a relationship between a shift in myocardial substrate utilization and cardiac hypertrophy. In 8 (1.1%) of 700 patients who underwent myocardial BMIPP scintigraphy at our clinic, there was no BMIPP accumulation in the heart and all 8 patients (2 patients with HCM, 1 with dilated cardiomyopathy and 5 with other heart diseases) showed type I CD36 deficiency. Tanaka et al indicated that a high proportion (39%) of patients with HCM showed type I or II CD36 deficiency. If CD36 is the myocardial LCFA transporter and altered myocardial LCFA uptake is related to the pathogenesis of HCM, the association of CD36 deficiency with HCM is reasonable. Cardiac muscle tissue is highly oxidative and catabolizes LCFA as a source of energy. Glucose is the major energy substrate in the fetal heart, whereas LCFA utilization is limited. During the early postnatal period, a marked increase in LCFA utilization occurs, and ultimately LCFA becomes the chief myocardial energy substrate. If myocardial LCFA uptake does not function normally and stress occurs, serious sequelae such as sudden death may occur.

Although we could not perform a family study in the patient reported here, another family showed type I CD36 deficiency in the mother, son and daughter (unpublished data). Present patient who had hereditary HCM and type I CD36 deficiency showed no myocardial LCFA uptake, although myocardial perfusion was normal. Our results suggest that type I CD36 deficiency is closely related to hereditary HCM and lack of myocardial LCFA accumulation.

References