Cluster Differentiation-36 Deficiency Type 1 and Acute Coronary Syndrome Without Major Cardiovascular Risk Factors

——Case Report——

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A 45-year-old man without major coronary risk factors, including hypertension, diabetes mellitus, smoking, hypercholesterolemia, hyperuricemia, or a family history of early cardiovascular disease, presented with acute coronary syndrome. Angiography showed thrombus formation in segment 7 of the left anterior descending coronary artery, and percutaneous coronary intervention was successful after implantation of a bare metal stent. Scintigraphy showed the absence of 123I-β-methyl-iodophenyl pentadecanoic acid accumulation in the myocardium. Flow cytometric analysis of platelets and monocytes showed the absence of cluster differentiation (CD)-36 expression. These findings are consistent with a diagnosis of CD36 deficiency type 1, which might be associated with cardiovascular disease. The patient had no apparent major coronary risk factors except for insulin resistance and an abnormal lipoprotein profile. The findings suggest that in this case the CD36 deficiency type 1 was the pathogenic mechanism of acute coronary syndrome relative to insulin resistance and modification of the lipid profile. (Circ J 2007; 71: 166–169)

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were diagnosed with CD36 deficiency type 2. Table 2 shows the blood biochemical data at the outpatient clinic. The fasting concentration of insulin was 24.6 IU/ml and the homeostasis model assessment ratio (HOMA-R) was 8.7, suggesting insulin resistance. Furthermore, the lipoprotein profile on polyacrylamide gel electrophoresis analysis showed 37% high-density lipoprotein (HDL), 42% LDL, 12% very LDL and 9% midband. In contrast, concentrations of other lipids such as total cholesterol, triglyceride (TG), HDL, apo/lipoprotein, remnant-like particles (RLP)-cholesterol, lipoprotein (a), and platelet function including thrombin-antithrombin III complex, plasminogen activator inhibitor 1, thrombomodulin and p-selectin were normal, although the patient had been medicated with calcium channel antagonists, nitrates and antiplatelet agents.

Discussion

CD36 is a multifunctional membrane glycoprotein that is expressed on platelets, monocytes, and endothelial cells. A CD36 deficiency is a hereditary disease that occurs in 0.3–0.5% of Japanese patients with various heart diseases, including cardiomyopathy, ischemic heart disease and valvular disease. CD36 deficiency can be diagnosed via myocardial scintigraphy with BMIPP, an analog of LCFA, in which a CD36 deficiency type 1 (no expression of CD36 on platelets or monocytes) manifests as the complete absence of tracer accumulation in the myocardium and a CD36 deficiency type 2 (positive expression of CD36 on monocytes but not on platelets) manifests as reduced tracer accumulation in the myocardium. The present patient was diagnosed with a CD36 deficiency type 1. The CD36-nega-
al reported that CD36 regulates the secretion and clearance of intestinal lipoproteins and that a CD36 deficiency results in hypertriglyceridemia in postprandial and fasting states. The lipid profiles of our patient were normal except for the presence of a “midband” in the lipoprotein fraction that indicates RLP, lipoprotein (a) and modified LDL. “Midband lipoproteins” are reportedly related to carotid arteriosclerosis and coronary artery diseases including coronary artery spasm. Although concentrations of RLP and lipoprotein (a) were normal in the present patient, they might represent one cause of ACS. Moreover, a CD36 deficiency is associated with insulin resistance. An increased fasting insulin concentration and HOMA-R indicated that the patient had insulin resistance. Because insulin resistance is associated with metabolic syndrome, which is linked to atherosclerotic cardiovascular disease, his disorder might be related to ACS. Adiponectin, an adipose-tissue-specific collagen-like protein, is an important antiatherogenic, anti-diabetic, and anti-inflammatory protein. Therefore, it is negatively related to metabolic syndrome based on insulin resistance. Indeed, Hong et al showed that the adiponectin concentration in ACS patients is significantly lower than that in those with normal coronary arteries. However, in our case the adiponectin concentration in the present patient was similar to that of patients with normal coronary arteries, which might be because we tested blood samples collected from the patient while he was stabilized with medication. Further examination is required. An in vitro study has showed that CD36 is necessary for myristic acid-stimulated endothelial nitric-oxide synthesis through adenosine monophosphate kinase but not through the PI-3 kinase/Akt pathway. Because patients with a CD36 deficiency type I do not express CD36 in myocardial capillary endothelial cells, endothelial nitric oxide synthesis might be decreased, thus leading to ACS.

Despite differences in the platelet expression of CD36 in patients with this inherited disorder, the relationship between CD36 expression and abnormal platelet function, as well as coagulation, remains unclear. Platelet functions after taking antplatelet agents, coagulation indices and bleeding time were normal in the present patient at the first emergency event. Thus, the possibility of this patient having had a previous abnormality in platelet functions cannot be denied.

Although Shiraishi et al found from a multicenter study that tobacco smoking, hypercholesterolemia and a family history are the most common risk factors for cardiovascular diseases in young Japanese adults, this 45 year-old patient had neither these nor any other major risk factors, such as diabetes mellitus and hypertension.
Taken together, CD36 deficiency might represent a new risk factor for the development of ACS in association with insulin resistance and modified lipid profiles.

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References