Journal of Clinical Lipidology (2017) ■, ■–■

Journal of Clinical Lipidology

Case Report

Acute myocardial infarction in a 25-year-old woman with sitosterolemia

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KEYWORDS:
Sitosterolemia;
Hypercholesterolemia;
Myocardial infarction;
Coronary artery disease;
ABCG8

Abstract: We report the case of acute myocardial infarction in a 25-year-old woman with sitosterolemia. She was treated using statins, but her low-density lipoprotein cholesterol (LDL-C) levels did not decrease appreciably. Genetic analysis revealed mutations in the ABCG8 gene. Ezetimibe treatment was initiated, and her LDL-C levels decreased substantially. Sitosterolemia must be considered in the differential diagnosis of familial hypercholesterolemia in case of early onset cardiovascular disease patient with high LDL-C.

A 25-year-old Japanese woman was presented to the emergency department of our hospital with acute onset of chest pain at rest in December 2013. She had no history of obesity, diabetes, smoking, or hypertension, but she did have hypercholesterolemia. Her electrocardiogram showed ST elevation in leads II, III, $_{a}V_{F}$, and V_{1}. On the basis of the electrocardiogram findings and results of blood tests and echocardiography, we suspected acute myocardial infarction, which is considered to be extremely rare in young women.

We performed emergency coronary angiography, which revealed total occlusion at the proximal segment of the right coronary artery (Fig. 1A). After thrombectomy using a catheter system was completed, intravascular ultrasonography revealed plaque rupture in the affected segment without any specific features of spontaneous coronary artery dissection. Finally, her right coronary artery was revascularized using bare metal stents (S-Stent; 3.5 × 11 mm and 3.0 × 28 mm; Fig. 1B). Optical coherence tomography revealed a signal-poor region with poorly delineated borders beneath a thin homogenous band in the unaffected segment of the right coronary artery, indicating the presence of another lipid-rich plaque. Although this patient had no family history of severe dyslipidemia or coronary artery disease, we initially diagnosed familial hypercholesterolemia on the basis of her elevated low-density lipoprotein cholesterol (LDL-C) level (220 mg/dL) and Achilles tendons thickness of 14 mm according to the diagnostic criteria established by the Japan Atherosclerosis Society.[1] Rosuvastatin (20 mg/d) was prescribed but did not reduce her LDL-C level adequately.

A part of this study has been supported by the grant from the Mochida Memorial Foundation.

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Submitted June 7, 2017. Accepted for publication October 20, 2017.

1933-2874/
https://doi.org/10.1016/j.jacl.2017.10.017

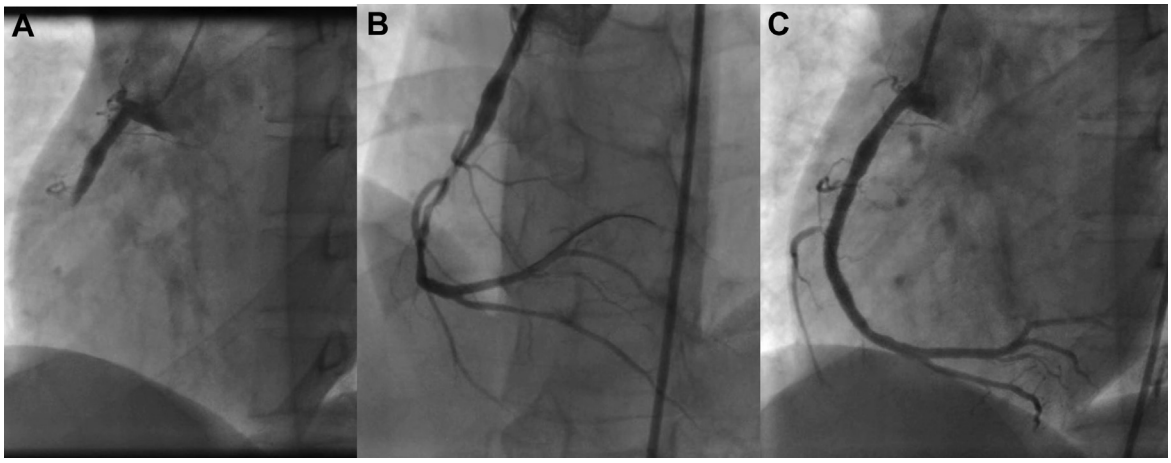

Figure 1 Emergency coronary angiography and percutaneous coronary intervention. (A) Initial right coronary artery angiogram. (B) After thrombectomy. (C) Final angiogram.

Genetic testing using Sanger sequencing of the LDL receptor (*LDLR*) and proprotein convertase subtilisin/kexin type 9 gene did not reveal any responsible mutations. Therefore, we expanded the investigation to include other forms of recessively inherited dyslipidemia, such as sitosterolemia. Her serum plant sterol levels were remarkably high (sitosterol: 45.5 μg/mL, campesterol: 47.0 μg/mL, stigmasterol: no data). In addition, whole exome sequencing revealed missense (c.1256T>A) and splice-site mutations (c.694+5G>C) in the "adenosine triphosphate–binding cassette, subfamily G" member 8 (*ABCG8*) gene (Fig. 2). We made a definitive diagnosis of sitosterolemia. Furthermore, we investigated the genotype–phenotype relationship of her parents and her elder sister. We found that both mutations were associated with elevated serum plant sterol levels in a recessive manner (Fig. 3). On the basis of these findings, we prescribed ezetimibe (10 mg/d) which reduced her LDL-C level to 55.4 mg/dL, as expected.

Sitosterolemia is an extremely rare autosomal recessive condition caused by mutation in the ABCG5/ABCG8, characterized by increased absorption and decreased biliary and intestinal excretion of plant sterols and cholesterol, resulting in significantly elevated serum sterol levels.[2] Around 100 cases have been reported in the literature.[3] Figure 4 shows a schematic diagram of cholesterol and plant sterol pathways in sitosterolemia. Free cholesterol and plant sterols are mainly absorbed from the intestinal epithelium via the Niemann-Pick C1-like 1 (*NPC1L1*) transporter. Cholesteryl esters are formed by Acyl-CoA cholesterol acyltransferase-2. Both plant sterol and cholesterol are secreted into the intestinal lumen via the heterodimer *ABCG5/ABCG8*. The liver can take up chylomicrons via *LDLR*. The liver can synthesize cholesterol de

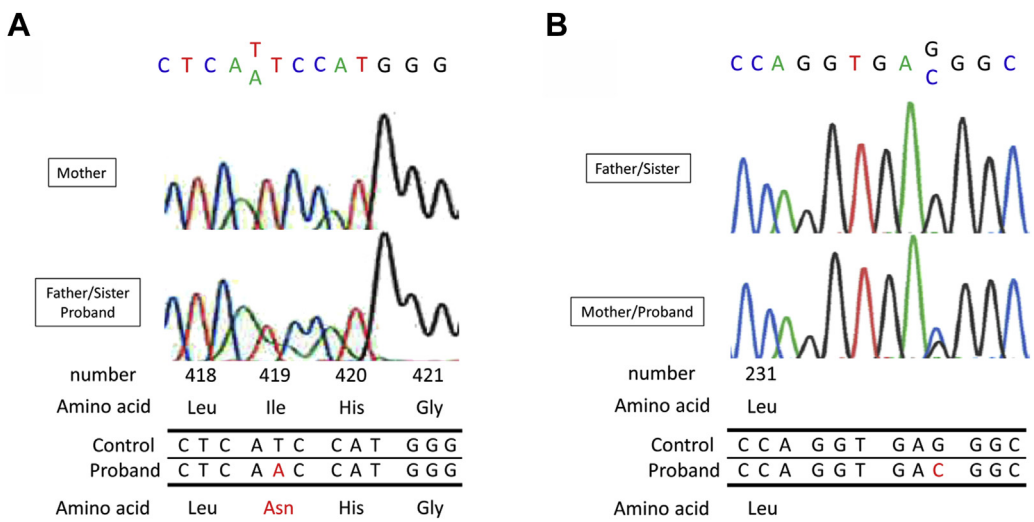

Figure 2 Gene mutations of the patient and immediate family members. (A) c.1256T>A or p.Ile419Asn (*ABCG8*). (B) c.694+5G>C (*ABCG8*).