A 19-year-old Man with Myocardial Infarction and Sitosterolemia

Shingo Katayama, Toru Satoh, Takashi Yagi, Nobuyoshi Hirose*, Yasuo Kurita, Toshihisa Anzai, Yasushi Asakura, Tsutomu Yoshikawa, Hideo Mitamura and Satoshi Ogawa

Abstract

This is a case report of a 19-year-old man who presented with acute myocardial infarction with obstruction of one coronary artery and rapid progression to three vessels in 8 months. He was proved to have sitosterolemia, a rare hereditary disease with plant sterol storing, resulting in juvenile coronary artery disease. Atherosclerotic complications can be preventable by administration of bile acid-binding resin, after the correct diagnosis is made. We introduce this disease with a review of the literature.

Key words: juvenile myocardial infarction, plant sterol, cholestyramine, xanthomatosis

Introduction

We encountered a very rare case of sitosterolemia with xanthomatosis, a lipid metabolism abnormality causing devastating juvenile coronary atherosclerosis. It is inherited in an autosomal recessive manner, and only about 50 families with the disease have been reported in the literature (1), because this genetic mutation rarely occurs and many cardiologists, who often see these patients for the first time, have little knowledge of this preventable disorder and miss the diagnosis.

Sitosterol is a plant sterol, which is poorly absorbed from the intestine and excreted readily, though some enters the body (2). A genetic defect disorganizes this mechanism and increases blood plant sterol with accumulation in blood vessels, resulting in xanthomatosis of tendons and atherosclerotic plaques in arteries.

Case Report

A 19-year-old Japanese man was taken by ambulance to our hospital because of nausea and severe chest oppression, while doing his cleaning job, on March 12, 2001. He had experienced the symptoms for one hour when he stopped working and took a rest. He had no prior history of chest oppression, and no past medical history of note. He had smoked one pack of cigarettes a day for 3 years even though he was a teenager (smoking is prohibited for teenagers in Japan). His father had died suddenly in his 40s, despite showing few abnormalities on physical check-up every year. On physical examination, he looked agonal. Blood pressure was 104/60 mmHg, pulse 86/min, regular. Consciousness was alert and well oriented. Height was 169 cm, weight 57 kg, and body mass index (BMI) 20. There was no anemia, jaundice or jugular venous distension. The apex beat was not felt. A fourth heart sound was audible. Lungs were clear. No pretibial edema, cyanosis or clubbing was noted. Exanthomas on both elbows and slight thickening of the Achilles tendons (Fig. 1) were found. Electrocardiogram showed ST elevation in leads II, III, V5, V1, V2, V3, and V5 with ST depression in leads I, V1, V3 to V6 (Fig. 2). Chest X-ray was normal (cardiothoracic ratio: 54%) with no
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Figure 1. Achilles tendon. Slight thickening of the Achilles tendon (25 mm) is noted.

Figure 2. Electrocardiogram on first admission. ST elevation in leads II, III, V6, V7, V8 and reciprocal ST depression in leads I, V4, V5 to V6 are shown, indicating acute inferior and right ventricular infarction.

Figure 3. Right coronary arteriographic findings on first admission. The right coronary artery is occluded in the proximal portion (arrow).

Figure 4. Left coronary arteriographic findings on first and second admissions. Left: Left coronary arteriographic findings on first admission. Stenosis is not observed in the left coronary artery (arrow). Right: Left coronary arteriographic findings on second admission. Severe stenosis is apparent in the proximal left coronary artery (arrow).

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Clinical course was good and he was discharged 2 weeks later. We scrutinized the possible etiologic diseases causing juvenile myocardial infarction, such as familial hypercholesterolemia, homocysteinemia, disseminated intravascular coagulation, anti-phospholipid antibody syndrome, protein C deficiency, protein S deficiency, anti-thrombin III deficiency, collagen disease, Kawasaki’s disease, rheumatic fever and Marfan’s syndrome. About one month after discharge, his beta-sitosterol level was proved to be high at 98.6 μg/ml, indicating sitosterolesmia. He did not return to hospital for follow-up after discharge and thus, did not take
cholestyramine, which is the optimal treatment for this disease.

He started to notice chest pain again on heavy exertion two weeks after discharge. It had steadily increased, and he was readmitted to hospital for prolonged chest pain on November 15, 2001. ECG only showed old inferior myocardial infarction. Serum total cholesterol and LDL-cholesterol were elevated this time to 310 mg/dl and 243 mg/dl, respectively and the serum triglyceride level of 121 mg/dl and HDL-cholesterol level of 50 mg/dl were within the normal range. Coronary angiography revealed a right coronary artery stenosis (#3) of 90%, left anterior descending arterial stenoses of 99% (#6) and 90% (#7) and circumflex arterial stenoses of 90% (#11) and 90% (#13) with diffuse coronary calcification (Fig. 4), showing extraordinarily rapid progression of the coronary arterial lesions over 8 months. Balloon angioplasty with stent implantation successfully ameliorated all the stenoses with the aid of a Rotablator and directional coronary antherectomy. He recovered uneventfully.

**Discussion**

This case report is aimed at introducing a rare but preventable disease, sitosterolemia, which causes juvenile coronary atherosclerotic lesions.

The diagnosis of sitosterolemia was made one month after this patient’s discharge but necessary treatment was not performed soon, since the patient thought that regular visits to the hospital were not necessary and was thus he was not able to receive the appropriate treatment. Eight months later, severe unstable angina pectoris made him come to hospital. The coronary angiography showed severe three vessel stenosis, which was not seen at the first visit, and was successfully treated with percutaneous coronary intervention including directional coronary antherectomy. A planed coronary intimal specimen demonstrated atherosclerotic plaque and calcification typical of the findings of hypercholesteromic plaques. This extraordinary rapid progression of the coronary pathology proves the dreadfulness of this disease, though it can be prevented by reducing the intake of plant sterols and administration of bile acid-binding resin.

He was 19 years old when he suffered an acute myocardial infarction. We ruled out several diseases causing juvenile coronary atherosclerosis such as familial hypercholesterolemia, homocysteinemia, disseminated intravascular coagulation, anti-phospholipid antibody syndrome, protein C deficiency, protein S deficiency, anti-thrombin III deficiency, collagen disease, Kawasaki’s disease, rheumatic fever and Marfan’s syndrome. After eliminating these diseases, we assumed that he developed the disease as a result of early-onset smoking and an atherosclerotic diathesis judging from the fact that his father had died suddenly in his 40’s. However, one month after our diagnosis, we reached the diagnosis of sitosterolemia as we suspected the disease and examined its presence using high performance liquid chromatography. This is a disease that is never diagnosed unless it is suspected.

Sitosterolemia is a rare autosomal recessive disease of the lipid metabolism causing juvenile atherosclerosis with xanthomatosis. Its exact prevalence is not known because a significant number of cases are left undiagnosed. There have been about 50 families with the disease reported in the medical literature (1). The cause of the disease is increased absorption of unsaturated plant sterols such as sitosterol, campesterol, cholestanol and stigmastanol, failure of tissue recognition between cholesterol and sitosterol, and failure of plant sterol excretion, resulting in tissue deposition of these sterols (2). Plant sterol absorption is normally near 4%, but it is increased to 40–60% in patients with sitosterolemia. The blood sitosterol pool is 15–20 times larger in the afflicted than in the normal population, indicating the existence of decreased plant sterol excretion (3). Most patients show xanthomatosis over multiple tendons including the elbows and Achilles tendons, and in the earlobes and subcutaneous tissues. Plant sterols tend to accumulate in the lipoprotein-rich tissues such as the liver and coronary arteries, resulting in juvenile coronary artery disease (4). Men are inclined to suffer from coronary stenosis earlier than women. When sitosterol accumulates in the erythrocyte membrane, hemolytic anemia ensues. Only one case of familial spinal xanthomatosis with sitosterolemia was reported in which plant sterol was stored in the dentate ligaments of the spine (5). Differential diagnoses include other lipid storage diseases such as familial hypercholesterolemia, familial defective apoB100, and pseudo familial hypercholesterolemia. In sitosterolemia, LDL-cholesterol is elevated in about half the adult cases as in this case and in almost all the cases in children (6). High LDL-cholesterol in these sitosterolemic patients is caused by increased cholesterol absorption and decreased excretion in addition to abnormal plant sterol metabolism. Considering that the level of sitosterol was mild to moderately elevated in this patient, the severe coronary atherosclerotic lesions are also ascribed to high LDL-cholesterol. Cutaneous xanthomas are thought to be caused by accompanying hypercholesterolemia in sitosterolemia because they are decreased in size by dietary cholesterol restriction (7). Pseudo familial hypercholesterolemia is reported to be associated with or identical to sitosterolemia.

It is advocated that sitosterol should be measured routinely in cases of juvenile hypercholesterolemia (8). The final diagnosis is made by measuring serum sterol by gas chromatography or high-performance liquid chromatography (9) and demonstrating a high titer. The genetic defect in sitosterolemia has been identified. Specific proteins, sterolin-1 and sterolin-2, in the intestine work together and restrict plant sterol absorption. Mutation in the DNA that produces the ABC transporter family, which is related to plant sterol absorption, has been found in sitosterolemic patients (10). Missense mutations
have been found only in Asian patients (11). We plan to examine these abnormalities in the present patient. Treatment (12) consists of restricting food containing plant sterols such as plant oils, various kinds of seeds and chocolate. Cholestyramine is also effective to reduce plant sterol absorption by binding bile acids.

References