Visual Disturbance due to Carotid Artery Thrombosis in a Patient with Familial Hypercholesterolemia; Response to Surgical Thrombectomy

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Abstract

A 48 years-old Japanese man suffered from marked xanthomas on ankles, knees, hand fingers, and foot joints due to insufficient control of serum hypercholesterolemia despite low density lipoprotein (LDL-C) absorptive therapy followed by treatment with potent anti-hypercholesterolemic agents. He had undergone surgical resection of xanthoma on the knee, foot and hand finger joints. Treatment with simvastatin returned the serum total cholesterol levels to nearly normal levels, followed by marked fluctuations. He subsequently experienced transient right-visual disturbance, and roentogenographic examination was performed. The patient was diagnosed as right-common carotid artery thrombosis. After the thrombectomy of the right-common carotid artery, his visual power was markedly improved.

Key words: familial hypercholesterolemia, xanthoma, carotid artery thrombosis, visual disturbance

Introduction

Familial hypercholesterolemia (FH) is a genetic disorder associated with severe hypercholesterolemia, atherosclerosis and xanthomas on various sites (1, 2). The etiology of FH is thought to be reduced numbers of low density lipoprotein (LDL) receptor especially in the liver, and endothelial tissue damage of vessels could be induced by oxidized LDL cholesterol. FH is a very rare disease affecting homozygous individuals, who are present in the general population at a frequency of one per million people, and also heterozygous individuals at a frequency of one per five hundred people. The former has a poor prognosis and seldom live beyond age 15 years despite combined heart and liver transplantation. The latter have a fairly good life style experience usually reaching their 80's by lowering a serum level of LDL-C due to reduced cholesterol intake and medication to lower serum cholesterol level. However, cardiovascular manifestations are often observed in coronary and carotid arteries and aortae (3, 4). We reported here an interesting case of heterozygous FH with right-carotid artery thrombosis followed by visual disturbance.

Case Report

A 63 years-old Japanese male patient is reported. He was found to have subcutaneous tumors around bilateral elbows, hand fingers, wrists, knees, and ankles followed by thickness of achilles tendons. These tumors were the size of hens eggs, and interfered walking and writing. In 1980, periarticular tumors were diagnosed as xanthoma and were resected. He was treated for hypercholesterolemia, but medication was discontinued because of drug-induced skin eruption. On April 19, 1983, he visited our outpatient clinic at Jikei Medical University Hospital. He showed giant periarticular xanthoma such as ping-pong ball-sized nodules on the knees, chicken egg-sized nodules on the elbows, and bean-sized nodules on the backs on his hands and ankles (Fig. 1). The serum levels of total cholesterol and triglyceride were 357 and 60 mg/dl, respectively. In March 1984, xanthomas on the knees and ankles were resected followed by treatment with tocopherol nicotinate, clinofibrate and melinamide because of persisting hypercholesterolemia. The cholesterol-lowering agent nicomol was also administered, and the serum total cholesterol level remained near 400 mg/dl. In December 1987, low density lipoprotein cholesterol (LDL-C) adsorption therapy was started twice a month for 6 months. This therapy induced a marked reduction in the serum level of total cholesterol, but this effect disappeared quickly one or two days after this treatment, and there was no reduction in the size of periarticular tumors. In July 1989, simvastatin was also administered at 20 mg a day, and the serum level of total chole-
terol was reduced from 408 to 289 mg/dl with no influence on the serum level of triglyceride followed by a slight increase in the serum level of HDL-C. Although abnormal lipid metabolism was partially improved by simvastatin, the patient complained of orthostatic dizziness, and mitral valve calcification was observed by echocardiogram examination. For further control of the serum cholesterol level, cholestyramine was co-administered at a dose of 18 g a day with simvastatin; consequently the serum cholesterol level was markedly reduced to an almost normal level.

In the summer of 1997, he complained right visual disturbance. Ocular examination showed reduced retinal blood flow, and mild arteriosclerosis in the eye ground. Moreover, the visual field was completely destroyed in the right-side eye. Cervical echogram and enhanced magnetic resonance image (MRI) examination showed the severe stenosis of the right common carotid artery. Furthermore, bilateral carotid angiography showed severe stenosis of the right common carotid artery (Fig. 2). In contrast, left-carotid angiography showed slightly reduced common artery circulation. Furthermore, abdominal aneurysm was observed near the saddle branch. Thrombectomy of right-common carotid artery was performed 3 days after the onset of right visual disturbance, and the blood flow was significantly improved followed by correction of the visual field.

Discussion

We reported here a case of FH showing macroangiopathy of common carotid artery, and abdominal artery, and marked xanthoma of cutaneous lesions requiring re-operations, especially on achilles, elbows, hand fingers and eyelids. Unfortunately no information was available concerning familial inheritance and no blood examinations of his family members was carried out. However, he showed marked abnormalities in lipid metabolism. FH has been reported to be complicated by severe atherosclerosis especially in macro-vessels such as the coronary and carotid arteries, and aortae (5, 6). The present case was thought to be heterozygous FH as there was no evidence of the organ damages seen in homozygous cases (7). Lipid-lowering agents such as clofibrate, and nicomol, and LDL-apheresis were used to treat severe hypercholesterolemia, but he showed a transient reduction of serum level of total cholesterol in response only to the latter. In contrast, combined LDL-apheresis and lipid lowering drug therapy has been shown to produce regression of coronary thrombosis in patients with FH. However, right-common carotid arterial thrombosis occurred in our patient despite various treatments (8, 9).

This patient complained of visual disturbance seventeen years after diagnosis of FH, and was diagnosed as having common carotid artery thrombosis. Surgical resection of the common carotid arterial thrombus was performed, and the visual disturbance disappeared. Many kinds of arterial thrombosis have been reported in patients with FH. In fact, the present case was shown to have an aneurysm of the abdominal aorta, and left-common carotid atherosclerosis by echography and enhanced MRI. The decreased blood flow in the right common carotid artery had been confirmed before the operation. Recently this patient has infrequently complained left visual dis-
turbance. Therefore, careful follow-up examination is necessary to detect re-onset of arterial thrombosis in various sites (10, 11). For this purpose, such patients are generally treated with anti-platelets, anti-coagulants and prostaglandin derivatives.

Atherosclerosis in the present case was treated by controlling the serum level of total cholesterol, but it is also essential to maintain optimal diet control. However, there are limits in the degree to which restriction can regulate the serum level of total cholesterol.

There are many kinds of lipid-lowering agents such as clinofibrate, cholestyramine, resins, and HMG-CoA reductase inhibitors for treating patients with hypercholesterolemia. Before the development of HMG-CoA reductase inhibitors, the serum level of total cholesterol could not be significantly reduced in patients with FH (12). In fact, the present case showed only about a 10% reduction of serum level of total cholesterol in comparison with that prior to HMG-CoA reductase inhibitor treatment. However, we administered cholestyramine, and the serum level of total cholesterol was further reduced 280 mg/dl to 230 mg/dl. HMG-CoA reductase inhibitors and cholestyramine have different modes of action for the lowering serum lipid level. However, the precise reasons for the effectiveness of co-treatment with these two kinds of medications are not clear. As the long-term prognosis of the present case is fairly poor due to generalized atherosclerosis, strict control of the serum level of LDL-C by medications and diet control are necessary.

In conclusion, here we report a rare case of FH, with visual disturbance due to thrombosis of the common carotid artery. This patient still has atherosclerosis, careful follow-up study is required. For this purpose, the patient is being treated with fluvastatin to promote reduction of the serum level of LDL-C and oxidants, which may play a role in the development of atherosclerosis. Coronary atherosclerosis is the most significant risk factor in the present case; and therefore it is necessary to carefully monitor the circulatory system.

References