Case Report

Marked Regression of Aortic Plaque by Intensive Cholesterol-Lowering Therapy
— A Case of Cholesterol Embolism

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A 65-year-old man with rheumatic combined valvular heart disease showed a persistent fever after cardiac catheterization. He was diagnosed with cholesterol embolism due to multiple mobile plaques in the descending thoracic aorta by transesophageal echocardiography (TEE) along with persistent eosinophilia, deteriorating renal function, and blue toe sign. He was treated with intensive cholesterol-lowering therapy for 3 years, resulting in marked regression of the aortic plaque on TEE.


Key words: Aortic plaque, Intensive cholesterol-lowering therapy, Transesophageal echocardiography

Introduction

Recently, atheromatous plaque of the aorta has been regarded as a potential source of emboli¹-². Catheterization is the most common trigger event for the development of cholesterol emboli³-⁴.

Previous reports have demonstrated that coronary plaque regressed with intensive cholesterol-lowering therapy⁵-⁶; however, few reports have examined the relationship between cholesterol-lowering therapy and the regression of aortic plaque⁷-⁹. Here, we report a case of cholesterol embolism that showed marked regression of aortic plaque after intensive cholesterol-lowering therapy.

Case Report

A 65-year-old man with rheumatic combined valvular heart disease had a history of open mitral commissurotomy and aortic commissurotomy at the age of 45. He gradually began to feel dyspnea on effort (NYHA II-III) and transthoracic echocardiography showed deterioration of valvular heart disease; therefore, cardiac catheterization was performed. A few days after cardiac catheterization, a persistent fever developed along with progressive renal failure, blue toe sign, and eosinophilia.

On transesophageal echocardiography (TEE), severe atheromatous plaque with ulceration and multiple mobile plaques were detected in the descending thoracic aorta (Fig. 1A). Due to the existence of multiple mobile plaques along with persistent eosinophilia, deteriorating renal function after cardiac catheterization, and blue toe sign, cholesterol crystal embolism was suspected. Peripheral white blood cells were 13,500/mm³ with eosinophils of 3,308/mm³ (24%), and total cholesterol was 169 mg/dL, LDL-cholesterol 99 mg/dL, HDL-cholesterol 76 mg/dL, and triglyceride was 54.8 mg/dL.

Corticosteroids (prednisolone 20 mg/day) and simvastatin 5 mg/day were started and the symptoms, eosinophilia, and renal function gradually improved. Corticosteroids were tapered and finally stopped 1 year later. Simvastatin was stopped because liver enzymes increased to four times the normal range; therefore, probucol 500 mg/day and colestimide 1.5...
g/day were administered instead of simvastatin. After 3 years, total cholesterol fell from 169 to 109 mg/dL and LDL-cholesterol from 99 to 72 mg/dL (Fig. 2). Follow-up TEE, performed 3 years after initial TEE, showed marked regression of multiple mobile plaques in the descending thoracic aorta (Fig. 1B). The aortic plaque area measured at the maximal level on the descending aorta on the transverse view of TEE was 1.52 to 0.63 cm². The large mobile plaques disappeared and only small mobile plaques remained.

**Discussion**

In this case of cholesterol embolism, marked regression of atheromatous plaque in the aorta was observed after lipid-lowering therapy using statins, probucol, and colestamide. As shown in this case, TEE is a more powerful tool to detect dynamic findings such as mobile plaque than CT or MRI.

The diagnosis of cholesterol embolism is difficult because the symptoms are nonspecific and it develops several weeks after predisposing factors. Detecting mobile plaque in the aorta by TEE helps to make a diagnosis of cholesterol embolism. There is no curative treatment for cholesterol embolism. Discontinuing anticoagulant therapy and administration of corticosteroids have been reported to be effective for improving symptoms and renal dysfunction. Intensive cholesterol-lowering therapy with statins and LDL apheresis is another possible treatment for cholesterol embolism. Statins may also be effective because they not only decrease plasma cholesterol levels, but also reduce systemic inflammation and stabilize atherosclerotic plaque in the vessel wall. In the present case, anticoagulation could not be stopped because of atrial fibrillation and mitral stenosis. Administration of prednisolone and simvastatin improved the symptoms and renal function.

Previous reports using intravascular ultrasound demonstrated that coronary plaque regressed with intensive cholesterol-lowering therapy with statins; however, there have been few reports about the regression of aortic plaque. In the present case, marked regression of aortic plaque was detected using TEE. Simvastatin was stopped because the patient's liver enzymes increased, and therefore probucol 500
mg/day and colestimide 1.5 g/day were administered instead of simvastatin. In spite of the normal lipid profiles at baseline, the amount of aortic plaque significantly regressed after administration of intensive cholesterol-lowering therapy for 3 years. We believe that not only statin treatment for 1 year but also the combination of probucol and colestimide treatment for 2 years contributed to plaque regression. The regression of aortic plaque was likely induced by the lipid-lowering and anti-atherosclerotic effects of statins and probucol. Several reports have demonstrated that statins and probucol have anti-atherosclerotic effects independent of their lipid-lowering effects\cite{12-14}. Wu et al.\cite{15} reported that probucol inhibits compensatory remodeling and promotes lumen loss associated with atherosclerosis in apolipoprotein E-deficient mice. Probucol decreased the plaque area, expression of vascular cell adhesion molecule-1, and proliferation of intimal cells, resulting in delayed macrophage accumulation in the vessel. Probucol also decreased the production and activity of matrix metalloproteinases-2 and -9, independent of the plasmin protease system, and this was associated with the inhibition of expansive remodeling, resulting in lumen loss.

Some mobile structures in the descending aorta observed on TEE might have been thrombi, but anticoagulation was continued and well controlled several years before cholesterol embolism occurred. In addition, intimal flaps are generally considered as mobile structures attached to the aorta; however, in this case, there was little possibility that all of the structures were intimal flaps for the following reasons. First, the morphology of the structures was mass-like. Second, follow-up TEE showed that the aortic wall thickness had also regressed. Third, there were no areas suspected of aortic dissection in the regions observed by TEE. Some atheromatous plaque may have been disrupted and disappeared from the wall of the aorta; however, no embolic symptoms or signs appeared during the follow-up period. Therefore, we considered that severe aortic plaque markedly regressed after intensive cholesterol-lowering therapy.

**Conclusion**

We report a case of cholesterol embolism in which the aortic plaque was markedly regressed after intensive cholesterol-lowering therapy.

**Acknowledgements**

We appreciate the kind advice of Professor Hide-nori Arai, Department of Human Health Sciences,
Kyoto University Graduate School of Medicine, Kyoto, Japan.

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