Cholesterol Embolism after Cardiac Catheterization Mimicking Infective Endocarditis

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Abstract

We present a 65-year-old man with rheumatic combined valvular heart disease showing persistent fever 3 weeks after diagnostic cardiac catheterization. Infective endocarditis was strongly suspected from the clinical course, however, serial blood cultures were negative. Transesophageal echocardiography, done to investigate vegetation, revealed multiple mobile plaques in the descending aorta. Administration of both steroid and simvastatin improved both symptoms and renal function. Cholesterol embolism should be considered to be one of the possible causes of low-grade fever after cardiac catheterization especially in patients with anticoagulation.


Key words: cholesterol embolism, complications, cardiac catheterization, transesophageal echocardiography

Introduction

Cholesterol embolism is a progressive disease resulting in renal failure if unrecognized and untreated. Early diagnosis is important as well as prevention. It is an uncommon but grave complication of arteriography and vascular surgery. Thrombolyis and anticoagulation are also predisposing factors in patients with severe atherosclerosis (1–3). Here, we report a patient showing persistent low grade fever after cardiac catheterization, who was found to have cholesterol emboli by multiple mobile plaques detected by transesophageal echocardiography.

Case Report

A 65-year-old ex-smoker with rheumatic combined valvular heart disease was admitted because of persistent fever and deteriorating renal function 3 weeks after cardiac catheterization. He had a history of open mitral commissurotomy and aortic commissurotomy at the age of 45. At that time, his medication was warfarin potassium (2 mg/day), Ca-antagonist (Nifedipine 40 mg/day), and diuretics (Furosemide 40 mg/day). His C-reactive protein level had been elevated to as high as 0.5–2.0 mg/dl in the recent few years.

Aortography performed 3 weeks earlier had demonstrated grade 3/4 aortic regurgitation; calculated aortic and mitral valve areas were 2.3 cm$^2$ and 1.2 cm$^2$, respectively. Coronary angiography demonstrated 75% stenosis at the mid-portion of the left anterior descending artery.

On physical examination, his heart rate was 90 beats/min and irregular, blood pressure 130/60 mmHg, and temperature was 38.0°C. A grade 2/6 systolic murmur at 4LSB, a grade 2/6 diastolic blowing and rumbling murmur at the apex were heard. Ejection click and opening snap were heard as well. Osler nodes, and splinter hemorrhage were not detected. Ophthalmologic examination did not disclose any abnormalities.

Laboratory tests showed increased peripheral white blood cells 13,500/mm$^3$ with eosinophils of 3,308/mm$^3$ (24%). Hemoglobin was 11.9 g/dl, platelets 41.1×10$^4$/mm$^3$, and total protein 7.1 g/dl. Liver enzymes were within normal ranges. Serum creatinine was increased at 2.1 mg/dl from 1.5 mg/dl one month earlier. Total cholesterol was 169 mg/dl, LDL cholesterol 99 mg/dl, HDL-cholesterol 76 mg/dl, and triglyceride was 54.8 mg/dl. Fasting blood glucose was 98 mg/dl and hemoglobin A1c was 5.8 %. C-reactive protein was 10.7 mg/dl. Prothrombin time (PT) was 19.9 seconds, PT-INR 2.79, and activated partial thromboplastin time (aPTT) was 48.9 seconds. Hypocomplementemia was not detected. Autoantibodies to neutrophil cytoplasmic antigens were negative. Chest CT scan, done to investigate the origin of

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fever, did not show any remarkable findings. Infective endocarditis was strongly suspected from the clinical course. However, serial blood cultures were negative and there was no vegetation found by transthoracic echocardiography.

Transesophageal echocardiography, done to investigate vegetation, did not disclose vegetation, but multiple mobile plaques were detected in the descending thoracic aorta (Fig. 1). Due to findings of multiple mobile plaques along with persistent eosinophilia and deteriorating renal function after cardiac catheterization, cholesterol embolism was diagnosed clinically. Three days after the diagnosis, that is, thirty-five days after cardiac catheterization, blue toe signs developed on the bilateral feet, then disappeared after several days.

The clinical course in this case is shown in Fig. 2. Administration of corticosteroids (prednisolone 20 mg/day) and simvastatin improved the symptoms, eosinophilia and gradually renal function.

Discussion

Cholesterol embolism is caused by occlusion of small arteries due to cholesterol crystals derived from eroded atherosclerotic plaques of the aorta or large feeder arteries. Several reports have demonstrated that risk factors for the development of atherosclerosis, such as older age, male sex, diabetes, hypertension, and cigarette smoking, are the same as risk factors for developing cholesterol embolism (1–3).

In addition, several studies have demonstrated an important role of inflammation in atherosclerosis (4). Fukumoto et al showed that increased plasma C-reactive protein is an independent predictor of cholesterol embolism (5). The present patient showed a slightly elevated C-reactive protein level (0.5–2.0 mg/dl) over the recent several years. There is a possibility that persistent inflammation might have been related to atherosclerosis or the occurrence of cholesterol emboli in this patient.

Angiographic procedures, vascular surgery, anticoagulation, and thrombolytic therapy are reported to be precipitating factors for cholesterol embolism. Angiographic procedures and vascular surgery may disrupt plaques on the wall of the vessels. Anticoagulation and thrombolytic therapy may prevent the formation of a protective thrombus overlying complex plaques (1–3). In this patient, infective endocarditis was initially suspected from the combination of persistent low-grade fever associated with combined valvular heart disease. However, cholesterol embolism should be considered as one of the possible causes of low-grade fever after cardiac catheterization especially in patients receiving anticoagulation.

Along with increased longevity comes an increased possibility for complications by valvular heart disease and atherosclerosis. The number of patients similar to this case may continue to increase since there are many elderly patients being treated for atrial fibrillation with anticoagulation.

The clinical manifestations of infective endocarditis result from not only infection and embolization of bland or septic fragments of vegetations but also an antibody response to the infecting organism with subsequent tissue injury caused by deposition of preformed immune complexes or antibody-complement interaction with antigens deposited in tissues (6). On the other hand, the presence of cholesterol crystals within the vascular lumen is reported to trigger a characteristic localized inflammatory and endothelial vascular reaction, that is to say, vasculitis-like reaction (7). Therefore, the
common feature that infective endocarditis and cholesterol embolism share is the immunological mechanism that mediates organ injury. Both diseases have nonspecific symptoms and the threat of multisystem involvement (8). Therefore, cholesterol embolism should be considered in the differential diagnosis when infective endocarditis is suspected.

The diagnosis of cholesterol embolism is sometimes difficult because symptoms are nonspecific and it develops several weeks after predisposing factors, such as angiography. In addition, renal biopsy or skin biopsy cannot always detect cholesterol crystals (1–3). In the present case, severe mobile plaques that were not detected by CT or aortography were detected by transesophageal echocardiography. Cholesterol embolism was diagnosed by clinical findings showing the presence of multiple mobile plaques along with persistent eosinophilia and deteriorating renal function after cardiac catheterization. Transesophageal echocardiography is more useful than CT, aortography, or other methods for detecting dynamic findings such as mobile plaques (9). Transesophageal echocardiography should be considered as a diagnostic procedure if cholesterol embolism is suspected.

Because immunological factors are involved in the progression of cholesterol emboli, corticosteroid therapy has been utilized to reduce the inflammatory response (10, 11). In addition, statin is also a possible treatment because it not only decreases plasma cholesterol levels, but also reduces systemic inflammation or stabilizes atherosclerotic plaques in the wall of vessels (12). In the present case, administration of corticosteroids and simvastatin improved symptoms, eosinophilia and renal function. However, several recent reports showed that corticosteroids were not effective for some patients with cholesterol emboli (10, 11). Further studies are needed to investigate the therapeutic strategies for cholesterol embolism.

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