

—Report on Experiments and Clinical Cases—

Behçet's Syndrome Associated with Acute Myocardial Infarction

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Abstract

We report here a case of Behçet's syndrome. The patient was suddenly affected by chest pain during the clinical course of the disease and developed abdominal pain and melena after 5 weeks. The diagnosis of acute anteroseptal myocardial infarction was made on the basis of the electrocardiography findings, and many perforated ulcers were confirmed in specimens of the resected colon. Coronary angiography showed constriction by 50% of the left anterior descending artery. There were no atherosclerotic changes. Pulse therapy was performed using sodium methylprednisolone succinate at a dose of 1,000 mg for 3 days, followed by oral administration of prednisolone at a dose of 60 mg/day, leading to improvement of all the symptoms after 3 weeks. The electrocardiogram findings at that time were normal. Prompt resolution of the symptoms provided by corticosteroid therapy supports the conclusion of previous studies that myocardial infarction in Behçet's syndrome may possibly be due to vasculitis of the coronary arteries.

In Behçet's syndrome, myocardial infarction is rare but should be considered as one of the most important lesions that determine the prognosis.

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Key words: Behçet's syndrome, myocardial infarction, coronary angiography

Introduction

Behçet's syndrome is a systemic inflammatory disease having a chronic and prolonged course with the appearance of 4 major symptoms: oral and genital ulceration, eye disease and cutaneous manifestations, as well as other multisystem involvement such as large joint arthropathies, central nervous system involvement, gastrointestinal ulceration and thrombosis of major vessels^{1,2}.

The vascular system is often involved, most frequently on the venous side, with disorders such as superficial thrombophlebitis and deep-vein thrombosis^{2,3}. Arterial involvement is a relatively

rare complication in Behçet's syndrome².

We report here a Behçet's syndrome patient who developed acute myocardial infarction with constriction of the left anterior descending artery.

Case report

A 44-year old man had fevers of 40°C, erythema nodosum-like lesions on the extremities (**Fig. 1**) and large joint arthropathies of 2 weeks' duration. A skin biopsy specimen showed moderate infiltration of neutrophils and lymphocytes in the dermis and around the blood vessels of the subcutaneous fat tissue. There was no image of necrotizing vasculitis. No evidence of immunoglobulin or complement

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Fig. 1 Infiltrating erythema on the finger (an arrow).

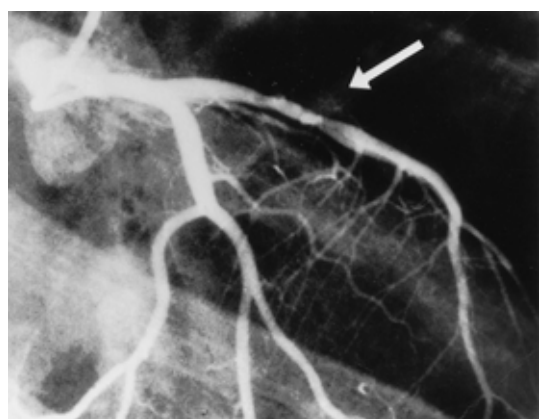


Fig. 2 Coronary angiography. Mural irregularity and constriction by 50% are confirmed in the left anterior descending artery (an arrow).

deposition by direct immunofluorescence was obtained. Oral ulceration, acne-like papules and pustules on the back and extremities and epididymitis had occasionally appeared since he was in his thirties. Eye symptoms and genital ulceration were not observed.

Laboratory studies revealed a leukocyte count of $25,300/\text{mm}^3$ with 92% segmented neutrophils, erythrocyte sedimentation rate 90 mm in the first hour, C-reactive protein 29.3 mg/dl and total hemolytic complement 45.6 IU/ml. Tests for rheumatoid factor, lupus erythematosus cells, antinuclear factor, cryogloblins and circulating immune complexes by the C1q binding assay were negative. Multiple determinations of serum cholesterol and triglycerides were within normal limits. The prothrombin time, the antithrombin III



Fig. 3 Specimen of resected colon. Many ulcers and perforations are confirmed.

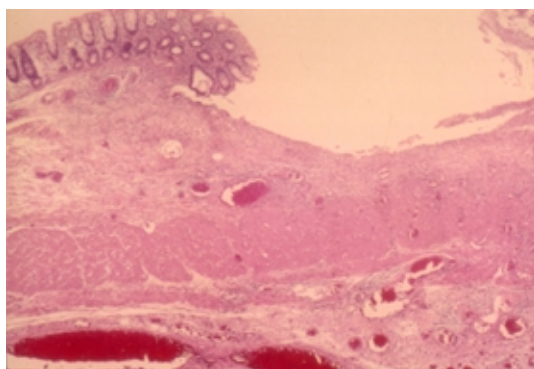


Fig. 4 Histology of resected colon. The deep ulcer from the lamina propria to the serosa with non-specific inflammation. No vasculitis is found. (HE stain $\times 4$)

level, partial thromboplastin time and thrombin time were also normal. The euglobulin lysis time was > 24 h, plasma fibrinogen 700 mg/dl and the fibrin degradation products level 20 ug/ml. HLA typing was A 2, A 24, B 7, B 39, Cw 7, DR 1. Other hematologic and biochemical parameters, routine urine and stool examination, and a radiograph of the chest and abdomen showed no abnormalities. Renal biopsy revealed no abnormality.

Based on these findings, the patient was diagnosed with incomplete Behçet's syndrome.

During exacerbation of systemic and cutaneous symptoms, the patient suddenly suffered an attack of severe chest pain lasting more than 30 minutes. He was diagnosed with acute anteroseptal myocardial infarction on the basis of the electrocardiogram findings: ST segment elevation in leads V_1 through V_5 . In coronary angiography, mural irregularity and constriction by 50% were confirmed in the left

anterior descending artery (**Fig. 2**). No abnormal findings were noted in any other branches of the coronary artery. At that time, pathological laboratory findings included white blood cell counts $13,500/\text{mm}^3$, serum glutamic-oxaloacetic transaminase $1,288 \text{ IU/l}$ and creatine kinase $1,175 \text{ U/l}$. The patient was not overweight and had no history of hypertension, hyperlipidemia or diabetes mellitus. There were no risk factors for coronary artery disease present other than smoking one pack of cigarettes a day.

Two days after angiography, sterile pustules on the erythematous base appeared at the site of catheter insertion on the upper arm. After 1 week, this pustulation was followed by the formation of a tender restiform induration over a length of 8 cm in the subcutaneous area. The pulse of the forearm disappeared and the diagnosis of arterial thrombosis was made.

After 6 weeks, the patient developed sudden pain in the lower abdomen and melena with fever. Accordingly, emergency laparotomy was performed. The resected bowel specimen had 3 perforations as large as $3.5 \times 5.0 \text{ cm}$, and many deeply pitted ulcers with a size of $1.0 \times 1.5 \text{ cm}$ were observed in the region of the ileocecum to the transverse colon (**Fig. 3**). Histopathologic studies confirmed deep ulcers extending to the muscularis externa, cellular infiltration with coexistence of lymphocytes and neutrophils and deposits of fibrin in the lamina propria of the periphery and base of the ulcers. No epithelioid granuloma nor necrotizing vasculitis were found (**Fig. 4**). Myocardial infarction as well as multiple intestinal ulcers was thus included among the symptoms of Behçet's syndrome.

Pulse therapy was performed using sodium methylprednisolone succinate at a dose of 1,000 mg for 3 days, followed by oral administration of prednisolone at a dose of 60 mg/day, leading to improvement of all the symptoms after 3 weeks. The electrocardiogram findings at that time were normal.

Discussion

In the present patient, the diagnosis of incomplete Behçet's syndrome was made because oral

ulceration and skin lesions, such as erythema nodosum and acne-like pustules, as major diagnostic criteria, and multiple arthralgias as a minor criterion repeatedly appeared for about 15 years. The development of pustular reaction followed by arterial thrombosis at the site of catheter insertion after angiography was considered to be a state of pathergy, a peculiar hyperirritability reaction to needle puncture^{1,2}. These clinical findings also fulfilled the criteria for Behçet's syndrome proposed by an international study group⁴. In addition, development of epididymitis and hematologic and histopathologic studies yielding non-specific inflammatory findings suggested a diagnosis of Behçet's syndrome.

Multiple intestinal ulcers and perforation were recognized from the ileocecum to the transverse colon. Histological examination of the ulcers revealed a characteristic tendency for pitting from the lamina propria to the serosa with non-specific inflammation. No granulomas, necrosis or microvascular injury as pathognomotic features of other bowel diseases were found. These findings were consistent with features of intestinal lesions in Behçet's syndrome.

Myocardial infarction was also included in the symptoms of Behçet's syndrome for the following reasons: i) physical findings of atherosclerosis on examination were absent; ii) there were no risk factors for coronary artery disease present other than the habit of smoking; iii) the age of onset was young; iv) myocardial infarction occurred at the same time with exacerbation of other systemic and cutaneous symptoms; v) coronary angiography revealed only one mural irregularity and constriction, and the other angiographic images were very clear and differed from that of atherosclerotic myocardial infarction.

Myocardial infarction in Behçet's syndrome is rare with only 10 cases reported so far in the English literature since 1980⁵⁻¹⁴; these 10 patients developed myocardial infarction at a relatively young age (22~39 years, average 29.5 years), and 6 had no eye involvement, as in our case. In the vascular lesions, aneurysm was found in 5 patients^{6,8,9,13,14}, and occlusion and obstruction were found in 7 patients^{5,6,8-11,14}. All reported cases were

severe, due to proximal occlusions of the coronary artery or rupture of a coronary aneurysm. Complication of myocardial infarction and multiple intestinal ulcers at the same time as in our case was seen in only one case¹¹.

Coagulation disorders due to anticardiolipin antibodies or abnormal response of the vascular endothelial cells have been assumed to be involved in cardiovascular manifestations of Behçet's syndrome^{15,16}. Other investigators have also estimated that the coronary artery occlusion in Behçet's syndrome is possibly due to vasculitis of the coronary arteries^{5,7,8,12,13}. There has been a report that histopathologically confirmed destructive changes of the coronary artery consistent with arteritis⁵. In the present case, prompt resolution of the symptoms provided by corticosteroid therapy and absence of atherosclerotic changes in cardioangiography as well as no thrombotic tendency in laboratory tests support the latter studies.

In conclusion, myocardial infarction is a rare event in Behçet's syndrome, but should be regarded as a clinically significant complication because it often leads to a poor prognosis.

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