

Acute myocardial infarction and ascending aortic aneurysm in a child with Behçet's disease

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A 12-year-old boy with a history of recurrent aphthous ulcerations and cutaneous erythema nodosum suddenly experienced chest pain. Together, the symptoms and a positive skin pathergy test established a diagnosis of Behçet's disease. An acute extensive anterior myocardial infarction was based on electrocardiography and a cardiac computed tomography confirmed an ascending aortic aneurysm. Coronary angiography showed mural irregularity and a 50% constriction in the first diagonal artery. Following treatment with urokinase, corticosteroids, colchicine, and aspirin, most symptoms gradually improved. There were no complications noted at the one-year follow-up evaluation. Myocardial infarction is a rare event in children with Behçet's disease; treatment with corticosteroids and colchicine can result in regression of concomitant aneurysm.

Key words: Behçet's disease, myocardial infarction, aortic aneurysm, child.

Behçet's disease, which most commonly occurs in Asia and the Mediterranean, is a recurring systemic inflammatory syndrome of unknown etiology. Different organs and systems can be involved. In 1937, Hulusi Behçet, a Turkish dermatologist, first described the disease as a triad consisting of oral and genital ulcerations and ocular lesions. The primary pathology is a vasculitis affecting the skin and joints, and the pulmonary, gastrointestinal, urinary, and nervous systems¹. Cardiovascular involvement, known as cardio-Behçet's disease, has also been reported, although it is very rare in children. It is estimated that the rate of vascular or cardiac involvement varies from 7 to 29%² and mortality occurs in up to 20% of those patients with marked vascular involvement³. We report herein a case of Behçet's disease in a boy who developed an ascending aortic aneurysm and had an acute extensive myocardial infarction.

Case Report

On 5 August 2005, a 12-year-old boy with an acute anterior myocardial infarction was referred to our hospital. He suffered chronically

from recurrent aphthous lesions and cutaneous erythema nodosum during the past eight years. He was admitted to another hospital three days earlier because of severe, sustained chest pain. At that hospital, his electrocardiogram revealed ST segment elevation in leads I, aVL, and V₁₋₆. Echocardiography showed a ventricular apex aneurysm. In addition, laboratory tests showed elevation of plasma total creatine kinase (CK), CK-MB isoenzyme (CK-MB), and troponin I. On the basis of these data, the boy was diagnosed with an acute extensive anterior myocardial infarction. Aspirin, vitamin C, dopamine, and dobutamine were initiated and thrombolytic therapy with 300,000 IU urokinase (10,000 IU/kg) was administered within 1 hour. The boy's symptoms improved and the hemodynamic status gradually stabilized. Because of the rarity and complexity of the case, the physicians in the local hospital referred the boy to our center for further evaluation. The physical examination showed several mandibularis papulopustular lesions (Fig. 1), multiple aphthous ulcerations (the largest of which was approximately 4×4 mm), peri-



Fig. 1. Papulopustular lesions involving the lower jaw.

anal erythema nodosum, and exanthema papulosum at the previous injection site. On chest auscultation, the heart sounds were blunt and both of the lung fields were clear. Further laboratory tests were obtained and the results were as follows: C-reactive protein, 43.2 mg/L; erythrocyte sedimentation rate, 38 mm/hr; CK, 850 U/L; CK-MB, 165 U/L; troponin I, 3.58 ng/ml; and anti-cardiolipin IgG/IgA titers, positive. Titers of anti-cardiolipin IgM, anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, rheumatoid factor, lupus erythematosus cell, anti-dsDNA, anti-ssDNA, anti-Sm, HLA-B26, and HLA-B51 were all negative.

Electrocardiogram showed pathologic Q waves in leads I, aVL, and V₂₋₆, with ST segment elevation in leads V₁₋₅ (Fig. 2). Echocardiography

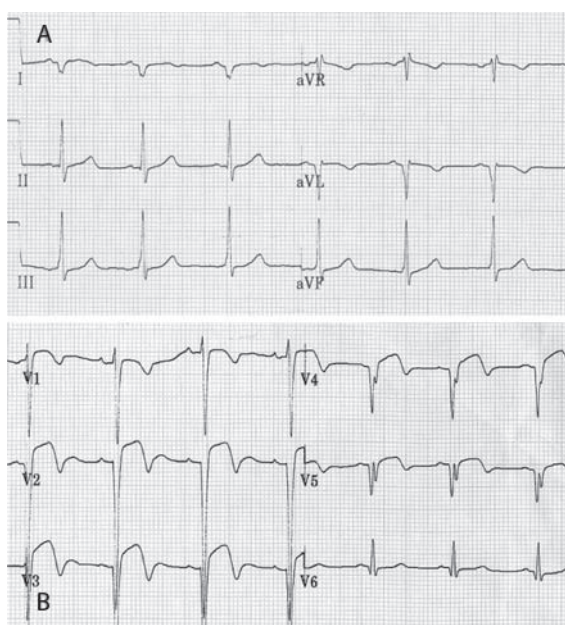


Fig. 2. ECG three days after the episode of chest pain.

revealed a left ventricular apex aneurysm and a cardiac ejection fraction of 55%. A focal aneurysm in the ascending aorta above the left aortic sinus was confirmed by cardiac spiral computed tomography (Fig. 3). Coronary arteriography and left ventriculography were performed six days after the episode of chest pain. Mural irregularity and 50% constriction of the first diagonal artery were demonstrated, and the other coronary branches were normal on coronary arteriography (Fig. 4). A left

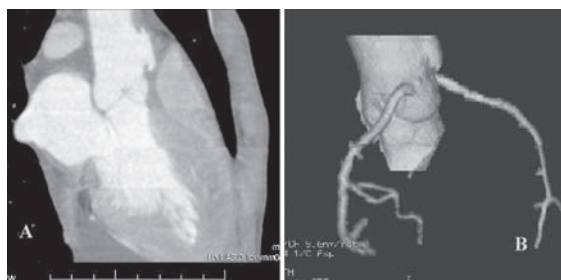


Fig. 3. Three-dimensional reconstructive computed tomography demonstrated a focal aneurysm in the ascending aorta. Both main coronary arteries were normal.

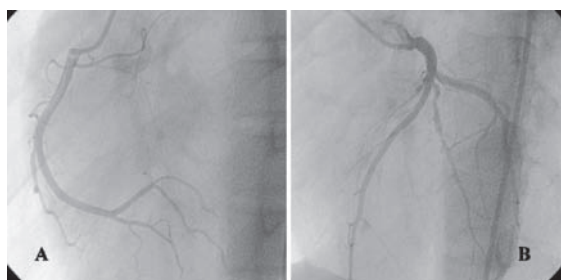


Fig. 4. Coronary artery angiogram. The right coronary artery was normal (A) and the first diagonal artery had a mural irregularity (B).

ventricular apex ventricular aneurysm was identified by left ventriculography (Fig. 5). Radiographs of the patient's knee joints were normal. Skin biopsy of the peri-anal erythema nodosum exhibited hyperplasia of the horny layer with no liquefactive degeneration of the stroma cell layer (Fig. 6). Immunoglobulin and complement deposition were not detected by direct immunofluorescence. Pathergy testing was performed and a single papulopustular lesion, approximately 6 mm x 6 mm, appeared at the puncture point after 24 hours.

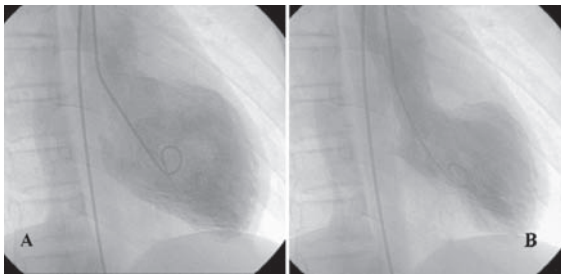


Fig. 5. A 30° right anterior oblique left ventriculograph in end-diastole (A) and end-systole (B) showed apical hypokinesia.

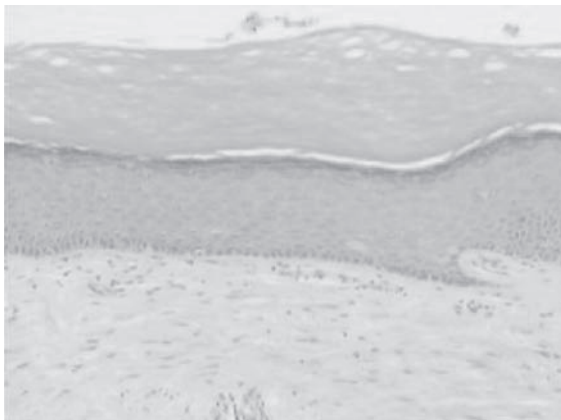


Fig. 6. Histologic changes characteristic of cutaneous erythema nodosum. (HE stain×20).

The boy was diagnosed with Behçet's disease, acute myocardial infarction, and an ascending aortic aneurysm. Methylprednisolone at a dose of 300 mg (10 mg/kg/d) for three days was initiated, followed by once-daily oral prednisone (1.0 mg/kg/d). Colchicine (0.5 mg/d, twice a day), aspirin (10 mg/kg/d, once a day), carvedilol, and captopril were started once the diagnosis of Behçet's disease and acute myocardial infarction were confirmed. With these therapies, the boy's oral aphthous ulcerations resolved within three days and the peri-anal erythema nodosum gradually improved. Plasma CK and CK-MB levels declined and returned to normal within five days, and the troponin I activity returned to normal within seven days of admission. On the fifteenth day following the episode of chest pain, the boy was discharged home and the therapy was continued. One month following discharge, the boy returned for re-evaluation. He felt well and his ECG recording showed pathologic Q waves in the precordial leads with T wave inversion (Fig. 7). Five months later, the

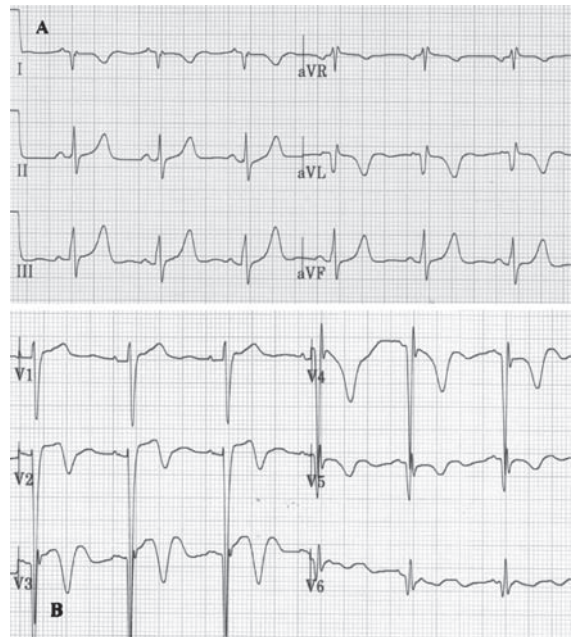


Fig. 7. ECG one month after treatment.

boy underwent a re-examination of computed tomography showing that the ascending aortic aneurysm had regressed (Fig. 8). At the one-year follow-up visit, the boy was still under treatment with aspirin and a maintenance dose of prednisone and was doing well. He did not experience further episodes of chest pain or other thrombotic events. There were no new aphthous ulcerations or cutaneous erythema nodosum, but the acne-like papules in the lower jaw had recurred at the time of the follow-up visit.

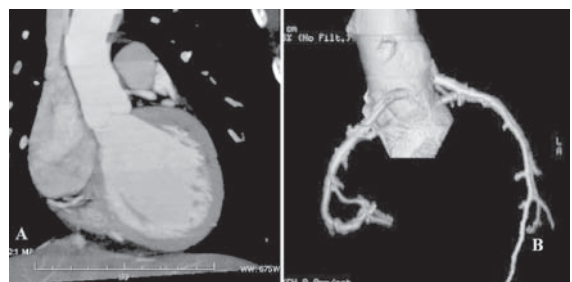


Fig. 8. Follow-up study with computed tomography confirmed that the aneurysm had regressed.

Discussion

Behçet's disease is a systemic, multi-system vasculitis with no specific serum markers. Its diagnosis is made according to the diagnostic criteria recommended by the International

Study Group for Behçet's disease⁴. Specifically, the diagnosis of Behçet's disease requires the presence of recurrent oral ulcerations, along with two of the following criteria: (a) recurrent genital ulcerations, (b) eye lesions, (c) skin lesions, and (d) a positive skin pathergy test (i.e., pustule formation 24-48 hours following a skin prick). In the present case, the diagnosis of Behçet's disease was based on recurrent oral aphthous ulcers, cutaneous erythema nodosum, and a positive pathergy test.

Vascular involvement is a very important feature in Behçet's disease, since it is one of the major causes influencing the clinical course of the disease, often causing serious complications and death. Vascular involvement occurs mostly as superficial thrombophlebitis, deep vein thrombosis, venous collateralization, arterial aneurysm, and occlusion⁵. Myocardial infarction in Behçet's disease is infrequent and has been documented in only a few cases in the literature.

Myocardial infarction is a rare event in a child with Behçet's disease. According to the literature, Kawasaki disease, hypoplastic coronary arteries, and congenital coronary anomalies comprise the basic underlying diseases leading to myocardial infarction in children⁶. To the best of our knowledge, there have been no reported cases of children with a myocardial infarction associated with Behçet's disease. Hattori and Kawana⁷ reviewed the English literature published between 1980 and 2000 and found that myocardial infarction in Behçet's disease was rare, with only 10 cases thus far, all of whom were young adults 22 to 39 years of age. Coronary arteries were severely occluded or coronary aneurysms had ruptured in these 10 cases. In 2004, Iyisoy⁸ reported an adult with a myocardial infarction and Behçet's disease; coronary angiography showed total occlusion of the left anterior descending artery after the first diagonal artery. In most cases, it appears a coronary artery abnormality leads to myocardial infarction in Behçet's disease. In the case we studied, only the first diagonal artery appeared to be involved with vasculitis and the other coronary branches were normal. Correlation of the ECG pattern with the site of coronary obstruction early in the course of myocardial infarction has been investigated before. Isolated obstruction of the first diagonal artery results in changes

localized to leads I and aVL and rarely involves the precordial leads^{9,10}. Extensive anterior myocardial infarction is always caused by left anterior descending coronary artery occlusion. Was the coronary artery occluded in our case? As the hypercoagulable state of Behçet's disease is well known, it is conceivable that the left anterior descending coronary artery was once occluded by a thrombus, which may have already dissolved by thrombolytic therapy when the boy underwent coronary angiography.

To date, the precise pathogenic mechanism underlying the thrombotic tendency in Behçet's disease is not known. Although there is compelling evidence linking anti-phospholipid antibodies to the thrombotic events in patients with systemic lupus erythematosus, an association with Behçet's disease has not been established¹¹. Vasculitic endothelial cell activation, increased neutrophil chemotaxis, and activated fibrinolytic kinetics are thought to play crucial roles in the thrombotic process¹²⁻¹⁴. Hemostatic investigations have shown findings not specific for Behçet's disease, but consistent with both activation of coagulation system and fibrinolytic activity, reflecting endothelial activation and/or injury. It has been suggested that the activation of endothelial cells by perivascular infiltrates composed of activated mononuclear cells and neutrophils is the origin of the thrombotic tendency in Behçet's disease¹⁵.

Several different therapeutic approaches have been suggested for the management of myocardial infarction in patients with Behçet's disease. Hattori and Kawana⁷ reported a patient with Behçet's disease undergoing myocardial infarction and treated with corticosteroids. The authors reported that corticosteroid therapy led to an improvement in all symptoms. The other approach is the administration of fibrinolytic therapy during the early hours of an acute myocardial infarction. In patients with Behçet's disease and an intra-cardiac thrombus, thrombolytic or anticoagulant therapies are considered first-line treatments¹⁶. Some studies have reported a therapeutic approach with percutaneous transluminal coronary angioplasty in adult cases. In our patient, thrombolytic therapy was initiated and we believe that the thrombus in the coronary artery completely resolved. With the treatment of corticosteroids, colchicine, and aspirin, the boy's aneurysm decreased in size and he experienced no new thrombotic events.

In summary, myocardial infarction is a rare event in children with Behçet's disease. With corticosteroids and colchicine therapy, most symptoms of Behçet's disease improve, and in the case described herein, the aortic aneurysm shrunk dramatically. The boy was satisfactorily responsive to corticosteroids, colchicine, and aspirin, but further follow-up studies should be done.

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