Case report

Acute coronary syndrome and late stent failure in a patient with Behcet's syndrome

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The present case report describes the occurrence of an acute coronary syndrome and of a post-percutaneous coronary intervention complication in a patient with Behcet's syndrome. An active phase of this syndrome, through an increased oxidative stress and reduced nitric oxide availability, could explain both an early myocardial infarction as well as an infarction following late in-stent re-occlusion. This complication can be very difficult to treat.

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Introduction

Behcet's syndrome is a chronic multisystem inflammatory disorder; clinical features typically include oral and genital ulcers, skin lesions and uveitis[1]. In addition, vascular complications, such as arterial and deep vein thrombosis, aneurysm formation and thrombophlebitis, may develop in about 25% of patients; the predominant lesion is vasculitis, affecting both the vessel wall and the perivascular tissues[1,2].

This report describes the occurrence of an acute coronary syndrome and the post-percutaneous coronary intervention (PCI) complications in a patient with Behcet's syndrome.

Case report

A 37-year-old male with Behcet's syndrome and no usual coronary artery disease risk factors was admitted to our Coronary Care Unit (CCU) for an anterior ST-segment elevation myocardial infarction. The diagnosis of Behcet's syndrome was posed at the age of 33 years on the basis of recurrent oral ulcers (major aphthous), eye lesions (anterior uveitis and retinal vasculitis in the right eye) and skin lesions (inferior limb erythema nodosum) in accordance with the criteria proposed by the International Study Group for Behcet's Disease in 1990[3]. The patient was receiving specific treatment with colchicine and prednisolone.

Immediate coronary artery angiography showed occlusion of the proximal left anterior descending (LAD) coronary artery and normal right and circumflex coronary arteries. LAD primary percutaneous transluminal coronary angioplasty (PTCA) and stent implantation were successfully performed 1 hour after symptom onset. Abciximab (0.25 mg/kg intravenous bolus and 12-hour infusion at 0.125 μg/kg/min) was administered immediately before PCI. Complete ST-segment resolution was observed at the post-primary PCI electrocardiogram (ECG) (Fig. 1A). The patient remained asymptomatic and in Killip class 1 during CCU observation. At the echocardiographic examination, the left ventricular ejection fraction was 63% and akinesis of the mid anterior wall, of the apical anterior wall and of the apical septum was found. The peak value of troponin I was 18.36 ng/ml and the peak value of the creatine kinase-MB mass was 42.34 ng/ml. The patient was discharged on a therapeutic regimen including beta-blockers, aspirin and 4-week ticlopidine.

Fifteen days later, the patient was referred to the Internal Medicine Department of our Hospital for nodular skin lesions on the left lower limb related to vasculitis and left deep femoral vein thrombosis, detected at color Doppler echography. Unfractionated heparin was administered intravenously, and gradually substituted by oral warfarin to achieve a target INR of 2.5. The patient's clinical conditions improved.

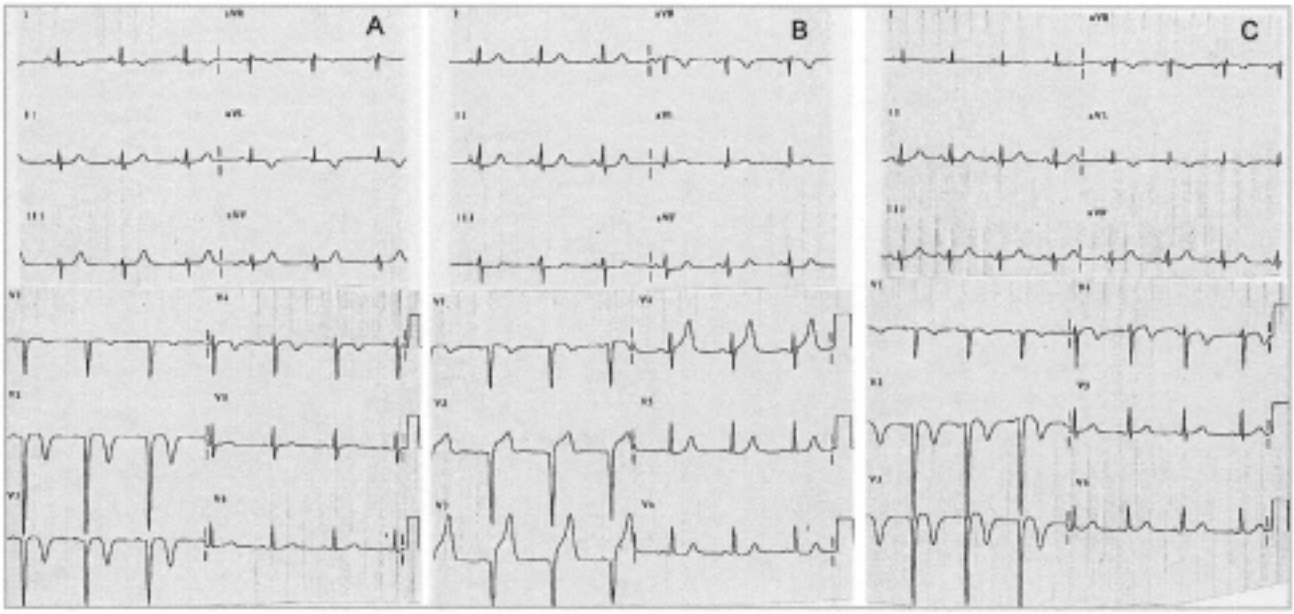

Figure 1. *The post-primary percutaneous coronary intervention ECG* (A) *shows QS complexes in leads V_1-V_3 and inverted symmetrical T waves in leads I, aVL and V_1-V_4. The following ECG* (B) *shows slope-elevation of the ST segments and high and wide T waves in leads V_2-V_4; note the "normalized" T waves in leads I and aVL. ECG* (C) *shows ST-segment resolution and T wave inversion in leads aVL and V_1-V_4.*

Twenty-five days after the acute anterior myocardial infarction and primary PCI, the patient presented with chest pain. ECG showed ST-segment elevation in the anterior leads (Fig. 1B). Urgent coronary artery angiography revealed stent failure with proximal LAD coronary artery reocclusion (Fig. 2). PTCA was immediately performed, obtaining a good initial result; a few minutes later, however, stent reocclusion was observed; multiple balloon insufflations were unsuccessfully attempted. Thus, additional stenting within the region of in-stent reocclusion was performed and a persistent and complete re-opening of the LAD coronary artery was achieved (Fig. 2). The post-PCI ECG showed ST-segment resolution (Fig. 1C) and was similar to the first post-primary PCI ECG (Fig. 1A). During CCU observation, the patient remained asymptomatic. Echocardiographic examination did not show new wall motion abnormalities of the left ventricle. A moderate increase of cardiac troponin I and of the total creatine kinase serum levels were observed.

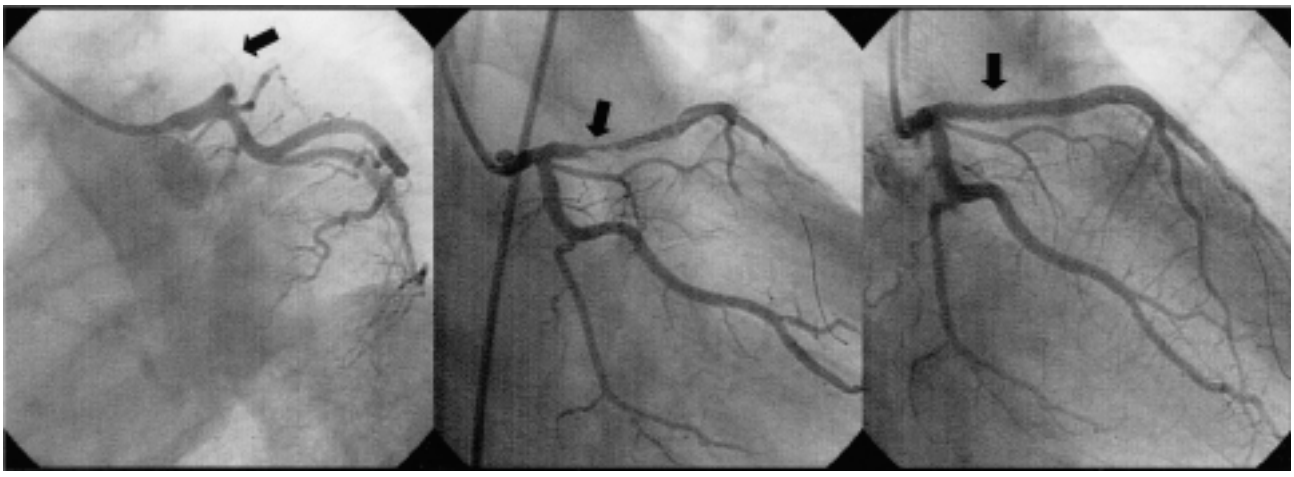

Figure 2. *Angiographic views of the left coronary artery. The caudal 25° left anterior oblique 45° view* (left panel) *shows in-stent occlusion* (arrow) *in the proximal left anterior descending coronary artery. The caudal right anterior oblique projection* (mid panel) *shows left anterior descending coronary artery reopening with a residual pronounced narrowing* (arrow) *after angioplasty. Complete left anterior descending coronary artery reopening* (right panel, arrow) *was achieved by additional stenting of the in-stent reocclusion. An angioplasty guidewire may be seen with its tip in the first diagonal branch.*

Discussion

The etiologic mechanisms underlying vascular injury in Behcet's syndrome are not well understood. The presence of vascular endothelial dysfunction was suggested but not proven in some studies reporting increased serum concentrations of the indirect markers of vascular injury, such as plasminogen activator inhibitor-1, von Willebrand factor and thrombomodulin[4,5]. According to recent studies, activated leukocytes may cause vascular damage in Behcet's syndrome; in particular, neutrophils generate high levels of oxygen-derived free radicals causing endothelial cell lysis *in vitro*[6,7]. Other authors found elevated concentrations of lipid peroxidation products, but did not succeed to elucidate the relation between oxidative stress mechanisms and vascular injury[8].

A role for oxidative stress in the pathophysiology of Behcet's syndrome is strongly supported by a recent report[9] in which the vascular endothelial function, impaired in basal conditions, rapidly improved following the intravenous administration of vitamin C, an antioxidant that scavenges superoxide anion radicals. In this study, the vascular endothelial function was investigated by evaluating the brachial artery flow-mediated dilation, which is mainly influenced by the release of endothelial nitric oxide[9,10]. An increased oxidative stress may explain the vascular injury in Behcet's syndrome; oxygen-derived free radicals react with nitric oxide and reduce its availability[11]. However, an additional role for inflammatory cytokines, antiendothelial cell antibodies or vasoconstrictors underlying endothelial dysfunction cannot be excluded[12].

In the patient admitted to our CCU, a 37-year-old male without any usual coronary artery disease risk factors, a reduced activity of nitric oxide[9], the major endothelium-derived vasodilator, might have led to vasoconstriction, platelet aggregation and monocyte adhesion, which, in turn, may have contributed to the observed clinical events: the progression of coronary artery disease, thrombotic occlusion and the onset of an acute coronary syndrome.

Furthermore, late stent failure occurred in this patient. "Stent failure" is defined as late if the event (death, myocardial infarction or angiographically documented stent vessel occlusion) occurs during days 15 to 30[13]. While angiographic factors and the procedural success are considered as independent risk factors for early (first 14 days) events, clinical variables such as the patient's age and a reduced left ventricular function are associated with late events[13]. In patients with a 4-week ticlopidine, in addition to chronic aspirin, regimen, late stent failure is a rare event (0.5%); patients younger than 65 years and with a normal left ventricular function have an event rate of only 0.1%[13]. In our patient, a young male with a satisfactory left ventricular ejection fraction, the clinical presentation of occlusive in-stent restenosis was an ST-segment elevation acute myocardial reinfarction. Acute coronary syndromes occur more frequently in patients with in-stent restenosis than in those with restenosis without stenting[14]. Neointima formation and thrombosis may have determined the in-stent restenosis and recurrent reocclusions during the last PCI[15]. These findings, along with the vasculitis and deep vein thrombosis with which the patient presented 10 days earlier, may be consistent with an active phase of Behcet's syndrome, endothelial dysfunction and a higher susceptibility to vascular injury. In this clinical subset of patients, additional stenting within the region of the in-stent restenosis could yield a better angiographic result compared with PTCA alone.

This case report suggests that the vascular complications of Behcet's syndrome may include acute myocardial infarction and stent failure, independently of the usual coronary artery disease risk factors. An increased oxidative stress and a reduced nitric oxide activity could explain these myocardial ischemic events. In-stent reocclusion may be very difficult to treat.

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