

Case report

Chest pain in patients with undiagnosed Behçet's disease

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ABSTRACT

Behçet's disease (BD) is a systemic inflammatory disease having a chronic and prolonged course with 4 major symptoms: oral and genital ulcerations, eye disease and cutaneous manifestations, as well as other multisystem involvements. Arterial involvement is a comparatively rare complication in BD and coronary lesions are extremely rare.

We report here two cases of BD presenting as myocardial infarction (MI) with coronary artery aneurysm (CAA), with good improvement after immunosuppressive therapy.

Introduction

Behçet's disease (BD) is a systemic inflammatory disease having a chronic and prolonged course with 4 major symptoms: oral and genital ulcerations, eye disease and cutaneous manifestations, as well as other multisystem involvements such as arthropathies, central nervous system involvement, gastrointestinal ulceration and thrombosis of major vessels (1).

The vascular system is often involved, most frequently on the venous side, with disorders such as superficial thrombophlebitis and deep venous thrombosis. Arterial involvement is a relatively rare complication in BD and coronary lesions are extremely rare (2).

We report here two cases of BD presenting as myocardial infarction (MI) with coronary artery aneurysm (CAA).

Case 1

A 24-year-old male without any medical history, smoker of 1 packet of cigarettes per day, came to our emergency room. He had had retrosternal pain radiating to his left shoulder, and worsening on inspiration and change of position. He did not complain of nausea, vomiting, sweating or weakness but he had had these pains for at

least 2 months and had not consulted. On first physical examination at the emergency room, his pulse rate and blood pressure were 95 bpm and 90/60 mmHg. Heart auscultation revealed mild muffled sound, pericardial friction and systolic mitral murmur; chest x-ray showed cardiomegaly; maximal total creatine kinase was 1754 units/l; electrocardiogram (ECG) showed Q waves of necrosis in the inferior leads. He was admitted with the diagnosis of MI and received isosorbide dinitrate, aspirin, and a beta blocker. His past history revealed recurrent episodes of bifocal ulcers treated symptomatically and an episode of deep venous thrombosis treated with heparin relayed by acenocoumarol. He did not have any risk factors for coronary artery disease. The physical examination at the department showed genital scars and pseudofolliculitis on his back. The Pathergy test was positive. The patient was diagnosed with BD according to the criteria of the International Study Group for Behçet's Disease (3). He had had a cardiac ultrasound which showed a circumferential pericardial effusion, a severe akinesia at the inferior territory, mitral regurgitation and an impairment of the left ventricular ejection function. Coronary arteriography showed an aneurysm three centimeters wide, sitting in segment 2 of right coronary artery associated to an upstream stenosis (Fig. 1). Pulse therapy was performed using methylprednisolone at a dose of 1 gr per day for 3 days followed by 1mg/kg/day of prednisone associated to 6 bimonthly and 5 monthly pulses of cyclophosphamide and colchicine. Control coronary arteriography realised at the sixth pulse of cyclophosphamide showed an improvement of the aneurysm size (Fig. 2). The myocardial scintigraphy revealed a precarious viability of the

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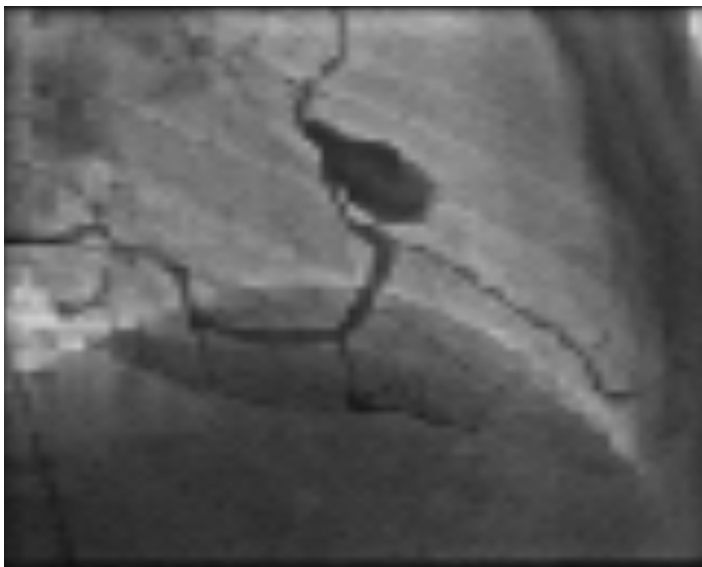


Fig. 1. Aneurysm three centimeters in diameter sitting in segment 2 of right coronary artery.

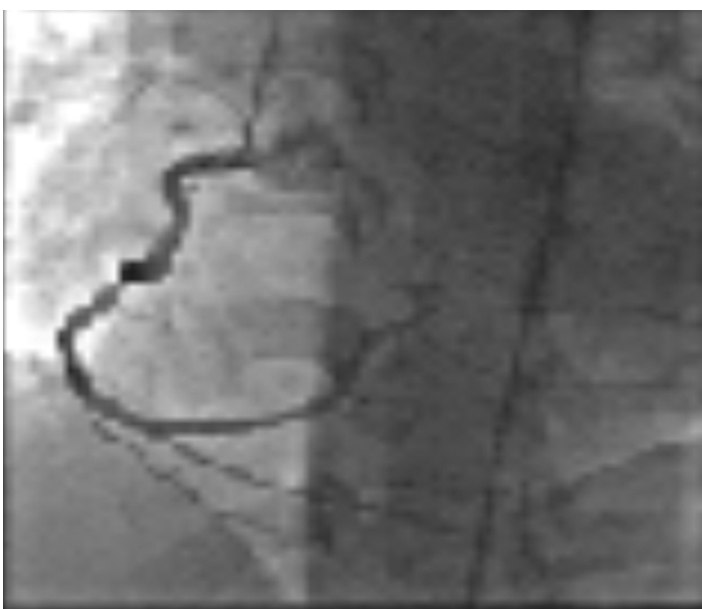


Fig. 2. Improvement of the size of the aneurysm at 6 months.

inferior wall. Cyclophosphamide was relayed by azathioprine. The patient was lost from sight for six months and stopped the treatment by himself. He started complaining of headache with early morning vomiting. We authorised a cerebral MRI which revealed a cerebral thrombophlebitis. He was hospitalised and pulses of methylprednisolone were performed associated to an adequate anticoagulation. We reintroduced azathioprine. A control angiography showed an intraventricular thrombus (Fig. 2) which, six months later, on a cardiac ultrasound control, had disappeared. The patient is now regularly seen in our outpatient clinic.

He is treated with azathioprine and a low dose of prednisone. He still complains of an exertional dyspnea.

Case 2

A 28-year-old male with no medical history, smoker of 1 packet of cigarettes a day, was admitted to our hospital with severe chest pain. On physical examination, he was afebrile, with a pulse rate of 90 bpm and blood pressure of 130/70 mmHg. An examination of the cardiovascular system showed normal results. On admission, the CRP level was 50 mg/l, the white blood count was 14,000 elements/ μ l and the erythrocyte sedimentation rate (ESR)

level was 20mm/h. ECG showed negative T waves in inferior leads. Maximal total creatine kinase was 2300 Units/l and cardiac ultrasound showed akinetic motion of the inferior wall. A non-ST-elevation myocardial infarction was diagnosed and a thrombolytic therapy was immediately administered. This early strategy relieved the chest pain and we did not notice any modification in the ECG. Coronary arteriography showed a partial thrombotic aneurysm in the circumflex artery. The patient received an anti ischaemic treatment (beta blockers, inhibitor of angiotensin converting enzyme) with an appropriate anticoagulation. Coronary arteriography showed a 2.6-centimeter wide aneurysm, sitting in the circumflex artery. His past history revealed recurrent episodes of bifocal ulcers treated symptomatically and an episode of anterior uveitis treated by local steroids. He had also genital scars, pseudofolliculitis at the trunk and the pathergy test was positive. The diagnosis of BD was based on bifocal ulcers, skin and ocular lesions according to the diagnosis criteria of BD from the international study group for BD. Pulse therapy was performed using methylprednisolone at a dose of 1 gr per day for 3 days followed by 1mg/kg/day of prednisone associated to 6 monthly pulses of cyclophosphamide. Control coronary arteriography realized at the sixth cure of cyclophosphamide showed that the aneurysm had disappeared. Cyclophosphamide was relayed by azathioprine. Cardiac ultrasound control was normal. The patient is now regularly seen in our outpatient clinic. He is being treated with azathioprine, colchicine, captopril, metoprolol and acenocoumarol, is now completely asymptomatic and his last ophthalmologic examination revealed sequels of anterior uveitis.

Discussion

Large venous or arterial lesions occur in about 25% (7–38%) of patients with BD. Vascular lesions are most likely to involve the venous system; however, arterial lesions are the greater risk, seen in 1.5–2.2% of patients, often as a rapidly expanding aneurysm which is the most notable arterial abnormality (2–4–5–6).

Tab. I. Behçet syndrome presenting as coronary artery aneurysm and myocardial infarction.

	Gender	Age	Infarct type	Coronarographic findings	Treatment	Evolution
Kaseda (1982) (13)	F	39	Posterior MI	Rupture of an aneurysm of the RC. Occlusion of the RC. Stenosis of the LAD.	Haematoma evacuation	Residual angina
Bowles (1985) (14)	F	22	Anterior MI	LAD aneurysm Occlusion of the first septal	Steroids Hydroxychloroquine	Sudden death
Bletry (1988) (15)	M	32	Threat syndrome	LAD and circumflex false aneurysm LAD stenosis	Anticoagulant Angioplasty Surgery	Residual angina Sudden death
Chakroun (1989) (16)	M	33	Threat syndrome	Aneurysm of the RC ruptured	Angioplasty Surgery Steroids	Asymptomatic
Rolland (1993) (17)	M	29	Anterior MI	LAD aneurysm	Steroids	Asymptomatic
Lopez (2000) (18)	M	27	Pectoris angina	LAD aneurysm	Surgery	Remission
Arishiro (2006) (19)	M	33	Inferior MI	Stenosis RCA Aneurysm RCA	Thrombolytic therapy PCI Steroids, Anticoagulant	Asymptomatic
Cuisset (2007) (20)	M	27	Non-ST elevation MI	LAD Aneurysm	Aspirine Clopidogrel Colchicine	Asymptomatic
Dogan (2006) (21)	M	67	Pectoris angina	Giant, saccular aneurysm of the left main CA stenotic lesions in the left anterior descending artery and the RCA	coronary bypass surgery.	
Lee (2007) (22)	M	45	MI	Unruptured Valsalva aneurysm compressing the proximal LAD	Surgery	Remission
Jin (2008) (23)	M	34	MI	Compression of coronary arteries by a sinus of valsalva aneurysm		
Case 1	M	24	MI	Aneurysm RCA	Thrombolytic agents Steroids Immunosuppressive agents Aspirine	Remission
Case 2	M	28	Inaugural inferior MI	Aneurysm circumflex artery	Thrombolytic agents Steroids Immunosuppressive agents Aspirine	Remission

VF: ventricular fibrillation; LAD: left anterior descending artery; MI: myocardial infarction; PCI: percutaneous coronary intervention; M: male, F: female.

Cardiac abnormalities in patients with BD include pericarditis, myocarditis, endocarditis with valvular regurgitation, intracardiac thrombosis, endomyocardial fibrosis, coronary arteritis with or without myocardial infarction (MI), and aneurysms of the coronary arteries or sinus of Valsalva (7, 8).

When studying 807 patients with BD, Geri *et al.* found 52 (6%) patients with cardiac abnormality, and cardiac involvement was the first feature of BD in 17 (32.7%); among these patients, 9 (17.3%) had myocardial infarction, and 1 (1.9%) had myocardial aneurysm (7). Coronary involvement is quite rare in BD and its prevalence is about 0.5% (9).

About 34 cases of MI associated to BD have been reported previously; some

of them have had normal coronary (6 cases) and some have had abnormalities: stenosis (21), aneurysm (9), false aneurysm in the culprit artery (1-2, 10-13).

We have described here two patients with BD revealed by myocardial infarction (MI) due to Coronary aneurysm. To our knowledge, CAA and MI occurring as a presenting feature of the disease have been reported in 11 cases. These cases are listed in Table I (14-24).

The patients are generally young, usually male, without vascular risk factors, except smoking for some of them. MI in this case should be regarded as a clinically significant complication because it often leads to a poor prognosis (25). Twenty percent of the patients die

within months or years after myocardial infarction, often due to a direct complication of coronary artery disease. The prognosis is also influenced by the type of lesions: occlusive or aneurismal. In fact, aneurysms are more serious because of the risk of rupture and recurrence in the stitches of arterial bridges (10).

To determine the existence of myocardial perfusion defects caused by coronary microvascular dysfunction in BD, and to evaluate coronary arterial distribution and left ventricular systolic function by gated single-photon emission computed tomography (SPECT), Kaya *et al.* studied 23 patients with BD and 20 healthy controls. They conclude that myocardial perfusion and

function are disturbed because of influenced coronary microvasculature in BD, and CAG is frequently observed to be normal. Gated SPECT is a non-invasive reliable method that simultaneously evaluates the existence, extent and severity of myocardial ischemia or infarction and the wall movements in cardio-Behçet (26).

Appropriate therapeutic approach in a patient with acute MI, aneurysm and BD is currently not clear. Some authors report using a high dose of corticosteroids, some using thrombolytic agents, and some doing primary percutaneous coronary intervention (PCI). Quite few published reports have addressed PCI for patients with coronary aneurysm in BD. In all of these cases, restenosis and/or aneurysm formation emerged at follow up for coronary arteriography (27, 28).

Thus, Ozeren *et al.* recommended that surgical intervention for aneurysm in BD is only indicated in patients with a growing aneurysm, acute rupture or severe ischaemia (29).

However, many problems can arise after surgical treatment, such as ruptured stitches and occlusion of the vascular joints (30).

The use of immunosuppressive therapy is essential in patients with BD and arterial lesions. Geri *et al.* found that a complete remission of cardiac involvement is possible when treated by oral anticoagulants, immunosuppressive agents, and colchicine (8).

These data were confirmed in the recent study of Saadoun *et al.* the use of immunosuppressive agents (OR, 3.38; 95% CI, 0.87–13.23) led to complete remission (6).

There are no controlled data on evidence of benefit from uncontrolled experience with anticoagulants in the management of arterial aneurysm in BD, and more controlled trials are needed.

In this context, anticoagulation should be discussed case by case by weighing the advantages and disadvantages of each patient.

We did not attempt coronary intervention and decided on a conservative treatment including antithrombotic agents, colchicine, corticosteroids and immu-

nosuppressive therapy. The two patients recovered and there were no complications during the follow-up period.

The prognosis of cardiac involvement in BD is poor; and improves with oral anticoagulation, immunosuppressive therapy, and colchicine (6, 8).

Conclusion

Acute myocardial infarction and coronary aneurysm has a high mortality and morbidity especially in young patients with BD; so, it is essential to show careful attention in the diagnosis and the treatment of this vascular complication, even in the absence of known risk factors.

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