

Endomyocardial fibrosis in Behçet's disease

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Abstract

Objective—To report on four patients with Behçet's disease associated with endomyocardial fibrosis involving the right or the left ventricle.

Methods—Charts of more than 350 patients with Behçet's disease were reviewed. Endomyocardial fibrosis was confirmed because of cardiac failure in three patients and incidentally discovered by histological examination of an operative specimen in one patient. Echocardiography displayed bright echogenic endocardium. Angiocardiography showed a reduced ventricular size. Electron beam computed tomography demonstrated a low density area involving the endocardium. Magnetic resonance imaging showed a mass of intermediate intensity on T1 weighted images. Diagnosis of endomyocardial fibrosis was based on histological study of a biopsy specimen in one patient and of an operative specimen in three.

Results—Six other similar cases of endomyocardial fibrosis complicating Behçet's disease were previously reported in the medical literature. Endomyocardial fibrosis predominantly involved the right ventricle. It can be considered a feature of Behçet's disease because: (a) no other cause was discovered; (b) arteritis, valvulopathy, and intraventricular thrombus were closely linked, and (c) all patients with endomyocardial fibrosis had vasculo-Behçet pattern.

Conclusion—Endomyocardial fibrosis may be the sequelae of vasculitis involving endocardium or myocardium, or both and complicated with intraventricular thrombosis. Behçet's disease should be added to the list of causes of endomyocardial fibrosis.

(*Ann Rheum Dis* 1997;56:205-208)

Behçet's disease (BD) is a systemic vasculitis,¹ which can rarely be associated with endomyocardial fibrosis. We describe four patients with endomyocardial fibrosis out of a series of 350 patients with BD.

Case reports

CASE NO 1

A 34 year old Algerian man had recurrent oral and genital aphthae, thrombophlebitis, and uveitis. In 1982, right sided cardiac failure occurred. Cardiac catheterisation and angiography showed an abnormal tricuspid valve that was attributed to Ebstein's disease.

Bilateral iliac thrombophlebitis occurred after catheterisation. BD was suspected. Anticoagulants, prednisone (60 mg/d) and colchicine (1 mg/d) were started. In April 1984, he was admitted to our department. Physical examination disclosed murmur of tricuspid regurgitation and signs of right sided cardiac failure. Chest radiography showed cardiomegaly. Electrocardiography disclosed first degree atrioventricular block, right atrial and ventricular hypertrophies. Echocardiography displayed bright echoes in the right ventricular inflow tract, the papillary muscles and the apex and a downward displacement of the septal and anterior leaflets of the tricuspid valve. A second catheterisation found a pressure drop from the right atrium to the ventricle with no evidence of diastole. Angiocardiogram showed a stenotic and pulled downward tricuspid valve and a large right ventricular filling defect. Histological study of an endomyocardial biopsy specimen disclosed a dense fibrous tissue extending to the myocardium. Digitalis and diuretics were added. The patient remained asymptomatic until he was lost to follow up after his return to Algeria 17 months later.

CASE NO 2

A 32 year old French woman had recurrent oral and genital aphthae, and polyarthritis that were attributed to BD. During her first pregnancy in 1984, paroxysmal atrial tachycardia occurred, which was attributed to mitral valve prolapse. During her third pregnancy in 1989, she suffered from transient facial palsy and aphasia. Carotid ultrasound examination and brain computed tomography were normal. Echocardiography showed an enlarged left atrium and a severe mitral regurgitation. An operation in July 1990 disclosed an ulcerated endocarditis affecting the left ventricle, the anterior mitral leaflet, and extending to the anterior and posterior papillary muscles and associated with intraventricular mural thrombus. A mitral annuloplasty was done. Histological examination showed a dense fibrous tissue with neovessels, moderate mononuclear, and polynuclear infiltrate centred on fibrinous or calcified areas. With more than six years follow up, she is asymptomatic with low dose aspirin and colchicine.

CASE NO 3

A 24 year old Turkish man was admitted to our department in March 1992 for fever, weight loss, and recurrent oral and genital aphthae. BD has been treated with cyclophosphamide (100 mg/d) and prednisone (40 mg/d) since

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Accepted for publication
17 December 1996



Figure 1 Electron beam computed tomography: low dense apical area involving the right ventricle.



Figure 2 Four chamber bidimensional end diastolic echocardiogram: bright echoes in the right ventricular endocardium.

December 1991. He complained of hemoptysis, headaches, and arthralgias. Physical examination disclosed murmur of tricuspid regurgitation, signs of right sided cardiac failure, and bilateral papillary oedema. Brain resonance magnetic imaging showed superior sagittal and right lateral sinus thrombosis. Electrocardiography showed right atrial hypertrophy and incomplete right bundle branch block. Thoracic computed tomography and angiography disclosed bilateral pulmonary aneurysms. Echocardiography displayed a severe tricuspid regurgitation and bright echoes in interventricular septal endocardium. Electron beam computed tomography showed a 5 mm thick low dense area surrounded by linear calcifications involving pulmonary infundibulum (fig 1). Catheterisation demonstrated impairment of right ventricular systolic and diastolic functions. Low dose aspirin and colchicine treatment was started. In December 1993, echocardiography, catheterisation, and computed tomography showed an increased thickness of intraventricular mass. At operation in August 1994, a marked ulcerated endocarditis involved the in flow tract, the apex, and the anterior papillary muscle, and extended to the tricuspid valve, which appeared both stenotic and incompetent with fusion of the septal leaflet. Resection of endomyocardial fibrosis and tricuspid annuloplasty were done. Histological examination showed a 50 × 40 mm dense fibrous tissue with numerous calcifications, scarce neovessels and inflammatory cells that extended to the myocardium. The patient is asymptomatic with low dose prednisone, azathioprine, and anticoagulants after two years of follow up.

CASE NO 4

A 27 year old Algerian man suffered from recurrent uveitis and oral aphthae, and polyarthralgias. In June 1992, he complained of progressive exertion dyspnea. Physical examination disclosed oedema of the face and neck, venous jugular distension, and prominent superficial venous collateral flow. Electrocardiography showed right atrial hypertrophy. Echocardiography disclosed an enlarged right atrium, severe narrowing of the in flow tract and the middle part of the right ventricle. Bright echoes were seen within the inferior and the middle parts of the right ventricular endocardium (fig 2). Catheterisation showed no

gradient between the right atrium and ventricle. Angiogram disclosed superior vena cava thrombosis and right ventricular filling defect. Electron beam computed tomography showed a 10 × 20 mm low dense mass that blocked the middle part of the right ventricle and involved the endocardium in front of the interventricular septum and the anterior part of the pulmonary infundibulum. Cardiac magnetic imaging showed a mass of intermediate signal intensity on T1 weighted images (fig 3). Vascular ultrasonographic examination showed bilateral jugular and left sub-clavian thrombosis. At operation in December 1992, the inferior part of the tricuspid valve was blocked by a fibrous tissue that filled the half inferior part of the inflow tract. Endomyocardial fibrosis was excised. Histological examination found a 50 × 30 mm dense fibrous tissue with inflammatory infiltrate and numerous vessels that extended to the myocardium. The endocardium surface was abraded in some places with anchored mural thrombi (fig 4). Azathioprine (150 mg/d), prednisone (10 mg/d), colchicine (1 mg/d), and anticoagulants were started. The patient was in remission when he was lost to follow up after returning to Algeria six months later.

Discussion

Cardiac manifestations are found in 1-5% of the patients in clinical series^{1,2} and 16.5% of the cases in the Japanese autopsy registry.³ They consist of cardiomegaly, endocarditis or pericarditis and less commonly of myocardial infarction and myocarditis. Association of endomyocardial fibrosis and BD seems extremely rare. Since our previously reported case no 1,⁴ we have seen three other similar patients. Symptoms consisted of cardiac failure in patients nos 1 and 3. Endomyocardial fibrosis was incidentally discovered by systematic echocardiography in patient no 4 and at operation in patient no 2 although not detected by echography. Endomyocardial fibrosis appeared as a brightly echogen pseudotumour. Angiocardiography showed a reduced ventricle size. Linear calcifications surrounding fibrosis were seen by electron beam computed tomography and magnetic resonance imaging in patient no 4 and demonstrated by histological examination in patient no 2. Endomyocardial fibrosis involved the right ventricle in patients no 1, 3,



Figure 3 Magnetic resonance imaging: intermediate signal intensity mass on T1 weighted image occupying the middle part of the right ventricle.



Figure 4 Histological examination of the operative endomyocardial fibrosis specimen (Haematein eosin safran, original magnification $\times 5$): dense fibrous tissue with neovessels, granulocytes, mononuclear cells and fibroblasts infiltrate and anchored thrombus.

and 4 and the left ventricle in patient no 2. It appeared as a dense fibrous tissue with neovessels and various degree of endocardial inflammation consisting of granulocytes and mononuclear cells infiltrate that could extend to the myocardium. In all cases, valvular dysfunction was related to extension of endomyocardial fibrosis to leaflets and papillary muscles.

Association of endomyocardial fibrosis and

BD was first described in 1977 at necropsy.⁵ Since that study, six other cases have been described.^{2-4 6 7} Three cases were only briefly mentioned.^{2 3} Endomyocardial fibrosis predominantly involved the right ventricle (table 1). One study quoted two cases of myocardial fibrosis out of 170 BD patients necropsies. In two detailed cases,^{6 7} endomyocardial fibrosis was revealed by cardiac failure. It should be pointed out that echocardiography found only valvulopathy in one case.⁷ Angiography showed a ventricular pseudotumoral filling defect in another case.⁶ No data concerning the echocardiographic, computed tomography, and magnetic resonance imaging aspects of endomyocardial fibrosis in BD are available in the medical literature.

Table 1 Main features of patients with Behçet's disease complicated by endomyocardial fibrosis

	Age, sex ethnic origin	Signs of Behçet's disease	Vascular involvement	Involved cavity	Cardiac failure	Valvulopathy	Diagnostic procedure
Case 1	34 years Male Algerian	Oral aphthae Genital aphthae Uveitis Pseudofolliculitis Skin hyperirritability	Phlebitis	Right ventricle	Present	Tricuspid	Biopsy
Case 2	32 years Female French	Oral aphthae Genital aphthae Pseudofolliculitis Skin hyperirritability Arthritis	Stroke	Left ventricle	Absent	Mitral	Surgery
Case 3	24 years Male Turkish	Oral aphthae Genital aphthae Pseudofolliculitis Arthralgias	Phlebitis, arthritis	Right ventricle	Present	Tricuspid	Surgery
Case 4	27 years Male Algerian	Oral aphthae Uveitis Pseudofolliculitis Skin nodules Arthralgias	Phlebitis	Right ventricle	Present	Tricuspid	Surgery
Case 5 Buge <i>et al</i> ⁶	45 years Male French	Oral aphthae Genital aphthae Pseudofolliculitis Skin nodules Skin hyperirritability Arthritis Central nervous system involvement	Phlebitis	Right atrium and ventricle	Present	Tricuspid	Necropsy
Case 6 Hamza ²	ND	ND	ND	ND	ND	ND	Necropsy
Cases 7 and 8 Lakhanpal <i>et al</i> ³	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND	Necropsy Necropsy
Case 9 El-Ramahi <i>et al</i> ⁶	30 years Male Saudi	Oral aphthae Genital aphthae Skin nodules and pustules Arthritis		Right ventricle	Present	Absent	Surgery
Case 10 Pena <i>et al</i> ⁷	35 years Male Spanish	Oral aphthae Genital aphthae Uveitis Skin hyperirritability Arthritis		Left ventricle	Absent	Mitral and aortic	Biopsy

ND=not determined.

Despite its rarity, endomyocardial fibrosis can be considered a feature of BD because: (a) no other cause of endomyocardial fibrosis was discovered⁸; (b) arteritis, valvulopathy, endomyocardial fibrosis and intraventricular thrombus were closely linked, and (c) in all patients, the disease had a typical vasculo-Beçet pattern. Intensive search for an alternative cause to endomyocardial fibrosis including parasitic infection, carcinoid tumour and other systemic disease, was negative. The idiopathic hypereosinophilic syndrome may be accompanied by skin, ocular, central nervous system, and vascular involvement.⁹ Furthermore, other systemic diseases as Churg Strauss syndrome, periarteritis nodosa, and hypereosinophilic-like syndrome may be associated with endomyocardial fibrosis.¹⁰ Hypereosinophilia has not been reported in BD¹ and none of our patients had an abnormal eosinophil count. Arteritis, valvulopathy, endomyocardial fibrosis and intraventricular thrombus were often associated. All our patients with endomyocardial fibrosis had valvulopathy and one had pulmonary arteritis. In the medical literature, all necropsy studies found intraventricular thrombi that covered endomyocardial fibrosis.^{5,6} One patient with endomyocardial fibrosis had mitral and aortic endocarditis that rapidly improved with prednisone.⁷ Valvulopathy was also associated with arteritis in four patients without endomyocardial fibrosis.¹¹ Intraventricular thrombus was reported in 11 patients with BD^{5,6,12-15} of whom half had associated pulmonary arteritis,^{6,13,14} endocarditis or endomyocarditis without endomyocardial fibrosis.¹⁵ All our patients and other published cases^{2,5,6} had in common a history of venous or arterial occlusion. This defines the vasculo-Beçet's pattern¹⁻³ of which frequency ranges from 3.6% to 46% of the patients with BD.

We conclude that endomyocardial fibrosis in BD may be a sequelae of endocarditis or myo-

carditis, or both, complicated with mural thrombus. Corticosteroids and anticoagulants or antiaggregants may deter development of endomyocardial fibrosis. If endomyocardial fibrosis is complicated by cardiac failure, surgical excision is successful in the short-term. BD should be considered as one of the causes of endomyocardial fibrosis.

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