Endomyocardial fibrosis in Behçet’s disease

Du Le Thi Huong, Bertrand Wechsler, Thomas Papo, Dominique de Zuttere, Olivier Bletry, Anne Hernigou, Annick Delcourt, Pierre Godeau, Jean-Charles Piette

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 endocardium. Angiocardiography showed a reduced ventricular size. Electron beam computed tomography demonstrated a lowdense 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 patients.

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) arthritis, valvulopathy, and intraventricular thrombus were closely linked, and (c) all patients with endomyocardial fibrosis had vasculo-Behçet pattern.

Conclusion—Endomyocardial fibrosis may be the sequela 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.

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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. Digitalics 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
December 1991. He complained of hemothysis, 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 the 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 stared. 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 inflow 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 x 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 infow 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 x 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 x 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 series12 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. Angiography 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,
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. Since that study, six other cases have been described. Three cases were only briefly mentioned. 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, endomyocardial fibrosis was revealed by cardiac failure. It should be pointed out that echocardiography found only valvulopathy in one case. Angiography showed a ventricular pseudotumoral filling defect in another case. 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

<table>
<thead>
<tr>
<th>Age, sex</th>
<th>Signs of Behçet’s disease</th>
<th>Vascular involvement</th>
<th>Involved cavitary</th>
<th>Cardiac failure</th>
<th>Valvulopathy</th>
<th>Diagnostic procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Oral aphthae, genital aphthae, uveitis, pseudofolliculitis, skin hyperirritability</td>
<td>Phlebitis</td>
<td>Right ventricle</td>
<td>Present</td>
<td>Tricuspid</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Case 2</td>
<td>Oral aphthae, genital aphthae, pseudofolliculitis, skin hyperirritability, arthritis</td>
<td>Stroke</td>
<td>Left ventricle</td>
<td>Absent</td>
<td>Mitral</td>
<td>Surgery</td>
</tr>
<tr>
<td>Case 3</td>
<td>Oral aphthae, genital aphthae, pseudofolliculitis, arthritis</td>
<td>Phlebitis, arthritis</td>
<td>Right ventricle</td>
<td>Present</td>
<td>Tricuspid</td>
<td>Surgery</td>
</tr>
<tr>
<td>Case 4</td>
<td>Oral aphthae, uveitis, pseudofolliculitis, skin nodules, arthritis</td>
<td>Phlebitis</td>
<td>Right ventricle</td>
<td>Present</td>
<td>Tricuspid</td>
<td>Surgery</td>
</tr>
<tr>
<td>Case 5</td>
<td>Oral aphthae, genital aphthae, pseudofolliculitis, skin nodules, skin hyperirritability, arthritis</td>
<td>Phlebitis, Right atrium and ventricle</td>
<td>Present</td>
<td>Tricuspid</td>
<td>Necropsy</td>
<td></td>
</tr>
<tr>
<td>Case 6</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Necropsy</td>
</tr>
<tr>
<td>Case 7 and 8</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Necropsy</td>
</tr>
<tr>
<td>Case 9</td>
<td>Oral aphthae, genital aphthae, skin nodules and pustules, arthritis</td>
<td>Right ventricle</td>
<td>Present</td>
<td>Absent</td>
<td>Necropsy</td>
<td>Surgery</td>
</tr>
<tr>
<td>Case 10</td>
<td>Oral aphthae, genital aphthae, uveitis, skin hyperirritability, arthritis</td>
<td>Left ventricle</td>
<td>Absent</td>
<td>Mitral and aortic</td>
<td>Biopsy</td>
<td></td>
</tr>
</tbody>
</table>

ND=not determined.
Despite its rarity, endomyocardial fibrosis can be considered a feature of BD because: (a) no other cause of endomyocardial fibrosis was discovered; (b) arteritis, valvulopathy, endomyocardial fibrosis and intraventricular thrombus were closely linked, and (c) in all patients, the disease had a typical vasculo-Behçet 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. Furthermore, other systemic diseases as Churg Strauss syndrome, periarthritis nodosa, and hypereosinophilic-like syndrome may be associated with endomyocardial fibrosis. Hypereosinophilia has not been reported in BD 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. One patient with endomyocardial fibrosis had mitral and aortic endocarditis that rapidly improved with prednisone. Valvulopathy was also associated with arteritis in four patients without endomyocardial fibrosis. Intraventricular thrombus was reported in 11 patients with BD of whom half had associated pulmonary arteritis or endocarditis or endomyocarditis without endomyocardial fibrosis. All our patients and other published cases had in common a history of venous or arterial occlusion. This defines the vasculo-Behçet’s pattern of which frequency ranges from 3.6% to 46% of the patients with BD.

We conclude that endomyocardial fibrosis in BD may be a sequela of endocarditis or myocarditis, 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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