Case report

Chronic thromboembolic pulmonary hypertension in Behçet's disease: effectiveness of endarterectomy

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ABSTRACT

Behçet's disease is a systemic vasculitis characterised by recurrent mouth and genital ulcers and uveitis. About 25% of patients suffer from vascular involvement. We describe a patient with Behçet's disease who suffered recurrent pulmonary embolism and developed severe chronic thromboembolic pulmonary hypertension. The patient was successfully treated with pulmonary endarterectomy that normalised pulmonary haemodynamics. Chronic thromboembolic pulmonary hypertension is a potential complication of Behçet's disease that may be amenable to pulmonary endarterectomy.

Case report

A 29-year-old male was diagnosed with Behçet's disease (BD) in 2002 in another hospital on the basis of four recurrent episodes of painful oral aphthae within 12 months, two episodes of left posterior uveitis, subsequent acne-like lesions and a positive skin pathergy reaction. Other entities such as sarcoidosis and systemic lupus erythematosus were appropriately ruled out. The patient was treated with colchicine 1 mg/day and prednisone 30 mg/day, which was tapered and discontinued within two years. Three years after diagnosis, the patient suffered right popliteal deep venous thrombosis with acute dyspnea and was diagnosed with massive bilateral pulmonary embolism (PE). Angio-computed tomography (CT) scan showed complete occlusion of the right lobar arteries and the left inferior lobar artery. Clinically, the patient remained in NYHA-functional class (FC) III. Echocardiography suggested severe pulmonary hypertension (PH) with an estimated systolic pulmonary artery pressure (sPAP) of 100 mmHg. Exhaustive thrombophilic study was negative and anticoagulation was started. However, the patient presented haemoptysis and oral anticoagulation was withdrawn. After two months without anticoagulation treatment, there was worsening of the FC and a second episode of PE was diagnosed. Angio-CT scan showed a new thrombosis in the middle lobar artery and segmental branches with marked venous pulmonary dilation without venous aneurysms. Prophylactic low molecular weight heparin and aggressive immunosuppressive therapy with high doses of methylprednisolone (1 g/day for 3 days, followed by a maintenance dose of 30 mg/day), and six monthly intravenous cyclophosphamide pulses (750 mg/m^2) were added. The patient remained in FC III and oxygen-therapy was started due to persistent hypoxemia. A new echocardiographic study showed an estimated sPAP of 85 mmHg, and bosentan (125 mg b.i.d.) was added at a centre without experience in pulmonary arterial hypertension. After 14 months, the FC remained unchanged and the patient was referred to our centre in October 2006 to evaluate further therapeutic options.

On admission, a ventilation-perfusion scan showed perfusion defects in both inferior lobes. Angio-CT scan showed complete occlusion of the right lobar arteries and left inferior lobar artery with signs of chronic thromboembolism in the segmental arteries and marked venous pulmonary dilation (Fig. 1A) which was confirmed by angiography. Transthoracic echocardiography showed severe right ventricular dilation and a sPAP of 80 mmHg. Pulmonary haemodynamics, arterial oxygenation and exercise tolerance are shown in Table I.

The patient underwent pulmonary endarterectomy (PEA) by median sterno-

tomy. The pulmonary arteries were enlarged, but no aneurysmatic lesions were identified. The abundant material resected from both sides was not especially friable or easily smashed, and no special difficulties were experienced in vascular suturing. In the histological analysis of pulmonary artery section, atherosclerotic changes with an organised thrombus were found. Surprisingly, neither signs of vasculitis nor inflammatory infiltrate were described. The patient had no postoperative complications. Two weeks after surgery, an angio-CT scan showed reperfusion of the majority of the lobar arteries with some residual thrombosis in the middle lobar artery and segmental branches. Additionally, the pulmonary arteries returned to normal diameter (Figure 1B). Ecochardiography suggested mild PH (sPAP of 46 mmHg). Oxygen-therapy and bosentan were discontinued. The patient was maintained on lifelong anticoagulation (with an international normalised ratio between 2 and 3) and immunosuppressive therapy with prednisone (7.5 mg/day) and mycophenolic acid (360 mg b.i.d). Fourteen months after surgery, the patient had a FC II, improved exercise tolerance with an increase of 180 meters in the distance covered in the 6-minute walk test and pulmonary haemodynamics within the normal range (Table I). After thirty-four months of follow-up no further thromboses were detected and the patient remained in FC II.

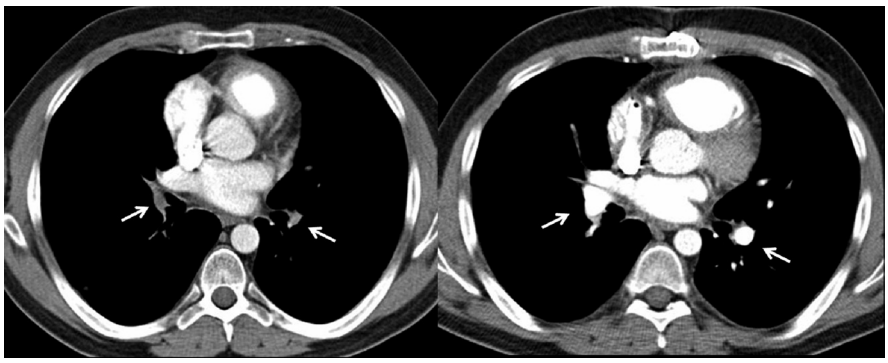

Fig. 1A. Axial multidetector computed tomography (MDCT) before (left image) and after (right image) pulmonary endarterectomy. Before surgery, there is occlusion and narrowing of right and left inferior lobar pulmonary arteries. After surgery, complete repermeabilisation (arrows) is shown. Pulmonary arteries returned to their normal diameter in the post-operative period.

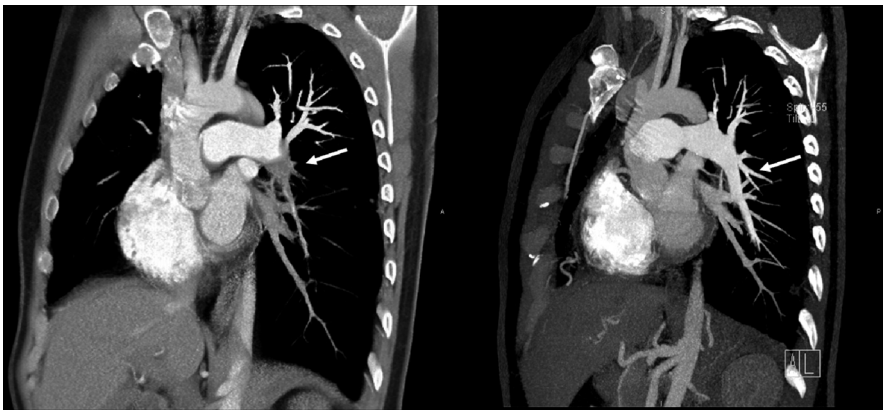

Fig. 1B. Saggital oblique MDCT reconstruction showing occlusion of left interlobar pulmonary artery (arrows) before pulmonary endarterectomy (left image) and current post-surgical arterial reconstruction (right image).

Table I. Pulmonary haemodynamics, arterial oxygenation and exercise tolerance, before and 14 months after pulmonary endarterectomy.

	Before surgery FiO_2 31%	Fourteen months after endarterectomy FiO_2 21%	Units
CO	4.46	5.12	L/min
CI	2.39	2.80	L/min/m^2
PAP (S/D/M)	69/17/34	29/6/14	mmHg
PCWP	NA	3	mmHg
PVR	NA	172	dyn/s/cm^5
Total PVR	609	218	dyn/s/cm^5
SVR	1505	1280	din/s/cm^5
PaO_2	57	64*	mmHg
SvO_2	69	71	%
6MWD	357 (52%)	540 (78%)	m (%pred)

FiO_2: inspiratory fraction of oxygen; CO: cardiac output; CI: cardiac index; PAP: pulmonary artery pressure (systolic/diastolic/mean); PCWP pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance; SVR: systemic vascular resistance; PaO_2: partial pressure of arterial oxygen; SvO_2: mixed venous oxygen saturation; 6MWD: six-minute walk distance.
*1 month after pulmonary endarterectomy.

Discussion

This case suggests that chronic thromboembolic pulmonary hypertension (CTEPH) (1) is a potential complication of BD that may be amenable to PEA.

Vascular involvement in BD has an estimated prevalence of 25% including venous and/or arterial thrombosis and arterial aneurysms (2). Pulmonary artery aneurisms are the most common pulmonary lesions in BD (3). Immunopathologic findings indicate that the underlying pathogenesis of pulmonary vascular involvement is a vasculitis that may result in thrombosis, infarction, haemorrhage or aneurysm formation. Pulmonary thrombosis in BD differs from classic pulmonary thromboembolic disease since arterial occlusion mostly results from *in situ* thrombosis complicating an underlying vasculitis rather than emboli (3). However, despite the high prevalence of venous thrombosis in BD, PE is rare, ranging from 1.5% to 4.6% (3, 4). Moreover,

BD has not been identified as a medical condition associated with or a risk factor for CTEPH (5).

Recent European League Against Rheumatism (EULAR) recommendations for the management of acute deep venous thrombosis in BD include immunosuppressive agents (6). The primary pathology leading to venous thrombosis in BD is inflammation of the vascular wall. Systemic immunosuppressive treatments are used to reduce this inflammation. There is no evidence of the beneficial effects of anticoagulation in the management of venous thrombosis, and controlled clinical trials are warranted (7).

In general, evolution to CTEPH may occur in 3.8% of cases of acute PE (8). PEA is the treatment of choice in CTEPH when the central pulmonary arteries are affected (9, 10). Long-term survival after PEA is excellent and cardiopulmonary function may be almost normalised in most patients (11).

We describe a patient with BD with recurrent PE who developed severe CTEPH, a previously unreported complication in BD. However, it is important to keep in mind that the nature of the present case in exceptional. Although thrombotic tendency is a well-known feature of BD, venous thrombosis is infrequently associated with pulmonary thromboembolism in this entity. Moreover, the histological study of pulmonary artery of this patient did not find inflammatory changes. Finally, CTEPH has not been described at present in larger series of patients with BD with *in situ* pulmonary thrombosis or pulmonary vasculitis. In any case, the patient was successfully managed with PEA, showing normalisation of pulmonary haemodynamics despite persistence of some defects in segmental-subsegmental branches. At fourteen months of follow-up, no further thromboses were detected after immunosuppressive and anticoagulant treatment.

In BD, surgical manipulation of vessels may promote further thrombosis and, for this reason, some surgeons are reluctant to treat patients with BD (12). The decision to operate on our patient was based on the severe clinical status, the poor prognosis, the young age and the accessibility of the thrombotic lesions. We decided not to insert a vena cava filter due to the high risk of local thrombosis. The surgical procedure did not differ from other cases of CTEPH. There were no difficulties in vascular suturing.

To our knowledge, this is the first case of BD with CTEPH successfully treated with PEA. Based on the high prevalence of venous thrombosis in BD, it is likely that more cases of chronic pulmonary thrombosis, with a potential risk of PH, may occur. In patients who do not respond to anticoagulation or immunosuppressive therapy, PEA may be a therapeutic option when thrombotic lesions are surgically accessible. Due to the high risk of perioperative mortality, the procedure should be undertaken in centers with experience.

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