Case report

Resolution of intracardiac and pulmonary thrombi without anticoagulation in a patient with Behçet's disease: a case report

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ABSTRACT

Intracardiac and pulmonary thrombi are rare but serious manifestations of Behçet's disease, the treatment of such cases is a challenge to the treating physician and use of anticoagulants can hold a great risk to some patients. We report a patient who was found to have multiple right intraventricular and bilateral pulmonary artery thrombi and was clinically diagnosed with Behçet's disease. Early in the course of his treatment, the patient developed massive haemoptysis which precluded the further use of anticoagulants. The patient was treated with immunosuppressants alone and had complete resolution of his symptoms and documented resolution of the thrombi. In a review of the literature, only 3 out of around 50 patients reported to have intracardiac thrombi complicating Behçet's disease were treated without anticoagulants (1, 2) *even though there is no clear evidence to support the benefit of anticoagulation to treat arterial or thrombotic lesions* (3). *We conclude that intracardiac thrombi in patients with Behçet's disease may resolve with immunosuppressants without anticoagulation, which is especially important in patients with contraindication to anticoagulation.*

Introduction

Behçet's disease (BD) is a rare multisystem vasculitis disorder. It is known to have a geographic predilection to the Mediterranean, Middle and Far Eastern regions along the ancient Silk Road. It was first described in 1937 by Hulusi Behçet as a triad of orogenital aphthae and recurrent uveitis. Since then, involvement of other organ systems, including a wide range of arterial and cardiac complications have been reported (4-6). The exact prevalence of these complications is not known. Cardiac complications have been estimated in one cohort of patients to reach around 6% (5) and arterial lesions in another cohort around 13.3% (6). Treating physicians are frequently faced with a therapeutic dilemma as no consensus for treatment of these or other complications has been developed. We report a case of BD with bilateral pulmonary and right intraventricular thrombi in which there was complete resolution with immunosuppressant therapy without concomitant use of anticoagulation.

Case report

A 31-year-old male presented complaining of cough, occasional scanty haemoptysis, night sweats, fever, weight loss and progressive dyspnea. He had a history of sagittal sinus thrombosis 3 years ago and recurrent oral ulcers over the past 10 years. He denied any history of genital ulcers, joint pains, skin rash or visual complaints. Family history was non-contributory. Physical examination was unremarkable except for a 2/6 systolic murmur heard over the right parasternal area with no radiation. Initial lab work-up showed haemoglobin: 12.2 gm/dL, platelets: 432,000/mm3, and WBC's: 10.61 x 103/mm^3. PT, INR, PTT and biochemistry values were within normal. ESR was 61 mm in the first hour and CRP was positive.

Transthoracic echocardiogram (TTE), done for evaluation of the patient's dyspnea and murmur, showed right intraventricular lesions. Trans-esophageal echocardiogram (TEE) was done for further evaluation and showed 3 well-defined, non-calcified, hyper-echoic, pedunculated, mobile masses, the largest measuring around 18 x 18 mm (Fig. 1). The appearance was suggestive of

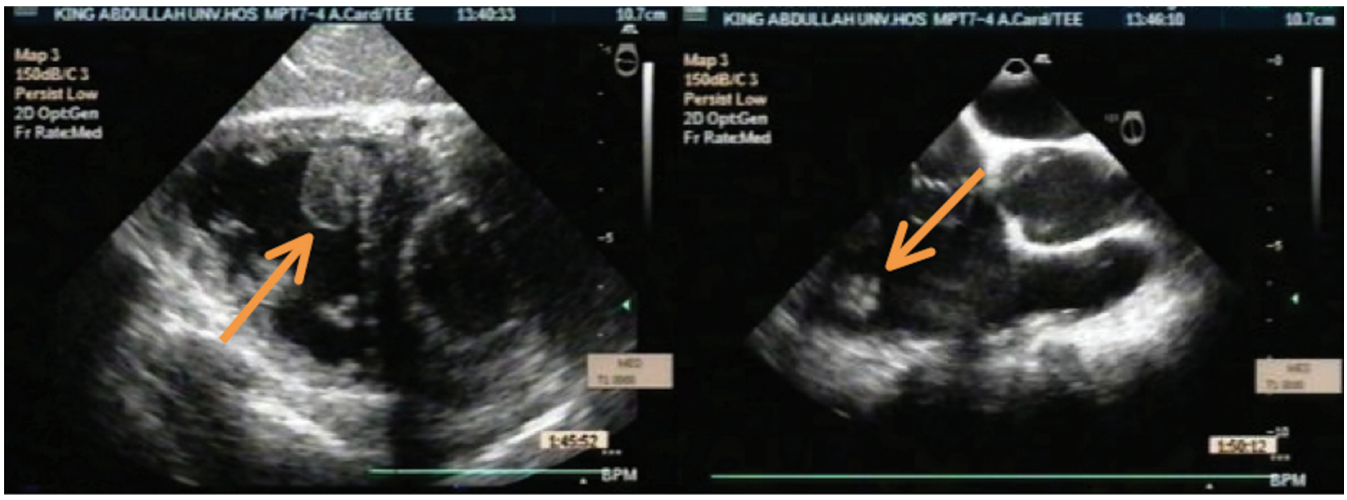

Fig. 1. Echocardiogram showing right intraventricular thrombi.

right intraventricular thrombi and the study was otherwise unremarkable. The patient was offered biopsy for confirmation but refused.

CT angiogram (CTA) of the chest was done and revealed multiple filling defects in the descending branches of both pulmonary arteries consistent with pulmonary thrombi. There were also bilateral infiltrates and peripheral sub-pleural opacities suggestive of pulmonary infarcts. Venous Doppler ultrasound of bilateral lower limbs was normal and thrombophilia and connective tissue screening were negative. The patient was started on therapeutic LMWH followed a day later by warfarin. Two days into anticoagulation, he developed massive haemoptysis leading to respiratory compromise which required endotracheal intubation and mechanical ventilator support. Anticoagulation was reversed and the patient was successfully extubated uneventfully 2 days later.

On further direct questioning, the patient admitted to having recurrent scrotal ulcers over the past 4 years, which he denied on presentation due to social reasons. A Pathergy test was done and was positive. Ophthalmology evaluation showed no evidence of current or past inflammatory process. The patient fulfilled the criteria for the diagnosis of BD and immunosuppressive therapy was started accordingly.

The patient was treated with IV methylprednisolone 1 gm daily, colchicine 1 mg daily and azathioprine 50 mg daily without anticoagulation, given the catastrophic bleeding he previously developed. He was counselled about the use of more potent immunosuppression but refused cyclophosphamide due to side effect profile, and refused infliximab due to cost. Three days later, steroids were changed to 60 mg oral prednisolone with a plan to slowly tapper. He was discharged 5 days post extubation in stable condition with marked improvement in presenting complaints, to be followed as outpatient. CTA of the chest done at one month follow-up showed complete resolution of pulmonary artery filling defects and disappearance of pulmonary nodules and infiltrates. Follow-up TTE showed marked decrease in size of intraventricular thrombi at 4 months and complete resolution at 6 months. The patient remained asymptomatic with no relapses for the 2 years he remained at follow-up at our centre.

Discussion

BD is a rare disorder with highly variable prevalence depending on geographic area. The highest reported prevalence is in Turkey where it is estimated to range from 80 to 370 per 100,000 (7). Diagnosis requires presence of recurrent oral ulcers plus at least 2 of: genital ulcers, eye involvement, skin lesions and a positive Pathergy reaction (8). Cardiovascular involvement, although well documented as part of the syndrome, is not a diagnostic criterion. It has been reported to affect around 6% of patients with BD, with intracardiac thrombosis being even less common and estimated to affect only around 19.2% of these patients (5). In most cases, there is obvious predilection to the right heart, but the reason is still unknown (1).

Due to rarity of intracardiac thrombosis as a complication of BD, there is no evidence-based consensus regarding best treatment. In their literature review, Mogulkoc *et al*. (1) suggested that medical management with anticoagulants and immunosuppressants might be associated with better outcome than surgical intervention. The role and safety of anticoagulants is still controversial, however, and one study found a significant difference in therapeutic approach among treating rheumatologist regarding use of anticoagulants in patients with thrombosis (9). The use of anticoagulation can prove to be a therapeutic dilemma in some patients as in our patient, who developed massive hemoptysis. Also, there is a well reported association between intracardiac thrombi and pulmonary aneurysms which have high risk of rupture and can lead to fatal bleeding (1). The EULAR recommendations for treatment of BD published in 2008 concluded there is no evidence of benefit for use of anticoagulation for arterial lesions of BD (3). Two of the 25 patients with intracardiac thrombi reviewed by Mogulkoc *et al*. (1) were treated with immunosuppression without anticoagulants and were reported to have had resolution of symptoms

but outcome was not radiologically documented. Huong *et al*. (2) reported a patient with intracardiac thrombosis and bilateral pulmonary aneurysms who had complete resolution by treatment with immunosuppressants and low-dose aspirin, also without anticoagulants.

The use of immunosuppressants has been shown to significantly improve survival and prognosis in patient with thrombotic and arterial lesions (6). Regarding the choice of immunosuppressant, there are no strong recommendations to support superiority of one regimen over another. Azathioprine has long been used and efficacy was repeatedly reported (10). Cyclophosphamide has been used to induce remission along with steroids. Anti-TNF agents are also more frequently being used in patient with major system involvement and show promising results (11, 12).

Our patient had a lengthy history suggestive of BD but was never formally diagnosed. He had an obvious prothrombotic tendency as evident by his past history of sagittal sinus thrombosis and the later pulmonary and intracardiac thrombi. The massive haemoptysis he developed post anticoagulation was possibly precipitated by active inflammation in pulmonary vasculature or undetected microaneurysms. The further use of anticoagulants was precluded by risk of recurrent bleeding and so he was treated by immunosuppressants alone which proved to be effective.

We hereby report a patient diagnosed with BD complicated by right intraventricular and bilateral pulmonary thrombi in which anticoagulation was contraindicated due to pulmonary hemorrhage, and we conclude that in BD patients with anticoagulants contraindication, the use of immunosuppressants alone may allow the resolution of intracardiac thrombi.

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