INTERNAL MEDICINE

□ CASE REPORT □

Development of Pulmonary Artery Aneurysms Due to Behçet's Disease and Resolution after Treatment

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Abstract

We herein describe a patient with Behçet's disease in whom we followed the development and resolution of pulmonary artery aneurysms. He presented with intermittent hemoptysis, pulmonary thromboembolism was initially diagnosed, and anticoagulant therapy was started. Over the next several months, the expansion of pulmonary arteries was noted. Five months after his initial admission, he was readmitted for massive hemoptysis, and further examinations revealed that he had Behçet's disease. Corticosteroids and intravenous cyclophosphamide were started. Over the next five months, the pulmonary artery aneurysms and thrombosis resolved. The development of pulmonary artery aneurysms led to the diagnosis of Behçet's disease, and they resolved after immunosuppressive therapy.

Key words: pulmonary artery aneurysm, Behçet's disease, vasculitis, thrombosis, deep venous thrombosis

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Introduction

Pulmonary artery aneurysms are localized expansions of the pulmonary arteries. More than half are caused by congenital heart disease (1). Acquired causes are diverse and include infection, such as tuberculosis and syphilis, pulmonary arterial hypertension, chronic pulmonary embolism, lung cancer, and medical procedures (2). Behçet's disease and Hughes-Stovin syndrome can cause inflammation of the pulmonary arteries that results in aneurysms. Among 5,970 patients with Behçet's disease, vascular involvement was identified in 882 (15%), and involved pulmonary arteries, peripheral and central veins, and peripheral and large arteries (3). Deep venous thrombosis (DVT) was the most common manifestation (87% of all vascular involvement), and pulmonary arteries were involved in 90 patients (10%). Large vessel involvement is also the most common cause of death among patients with Behçet's disease (4). We herein describe a patient who initially presented with DVT and pulmonary artery thrombosis and was diagnosed with Behçet's disease after pulmonary artery aneurysms developed. Corticosteroids and cyclophosphamide treatment resolved the pulmonary artery aneurysms and thrombosis.

Case Report

A 42-year-old man presented with intermittent hemoptysis. Chest computed tomography (CT) showed pulmonary embolism and thickening of the pulmonary artery walls (Fig. 1a). DVT was not noted on lower extremity CT but was confirmed by lower extremity ultrasound. The laboratory findings were as follows: white blood cells (WBC) 8,500/μL with no eosinophilia, hemoglobin (Hb) 10.3 g/dL, C-reactive protein (CRP) 8.7 mg/dL, negative anti-nuclear antibodies, negative anti-cardiolipin IgG antibody, myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) <0.5 IU/mL, proteinase 3 (PR3)-ANCA <0.5 IU/mL, and D-dimer 2.4 μg/mL. Pulmonary thromboembolism was diagnosed, and anti-coagulant therapy was started. During follow-up, the patient continued to have bloody sputum, CRP remained elevated at 3 to 6 mg/dL, and gradual expan-

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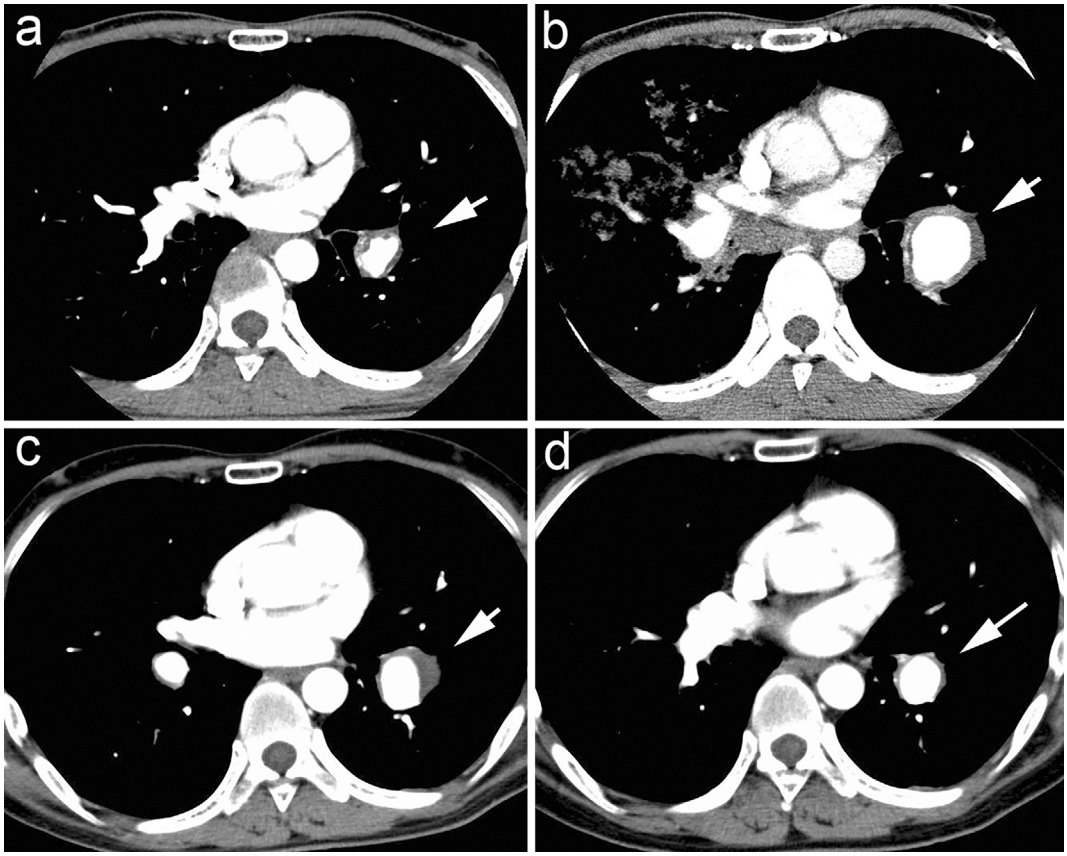

Figure 1. **Chest CT at first admission (a), second admission (b), three months after the second admission (c), and five months after the second admission (d). The arrows indicate the left pulmonary artery.**

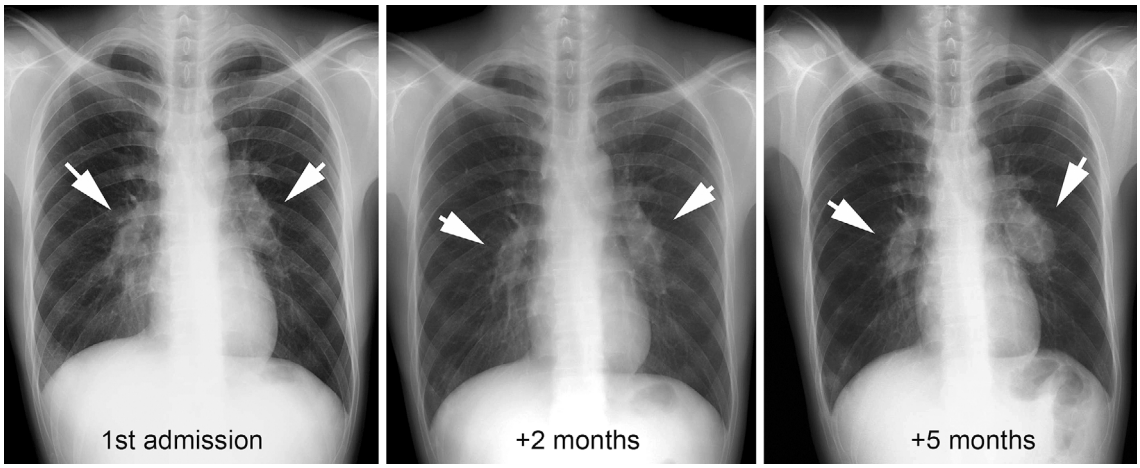

Figure 2. **Expansion of the pulmonary arteries. The right and left pulmonary arteries (arrows) had slightly expanded two months after first admission and clearly expanded five months after first admission (one week before second admission).**

sion of the pulmonary arteries was noted on chest X-ray (Fig. 2).

Five months after starting anti-coagulant therapy, he was readmitted for massive hemoptysis. On arrival, his oxygen saturation was 76% breathing ambient air and 94% on 10 L/min of oxygen. The findings on his physical examination were normal, including lung sounds and lower extremity evaluation. Chest X-ray showed consolidation in the right lower lung field (Fig. 3, left). The laboratory findings were as follows: WBC 13,000/μL, Hb 8.4 g/dL, CRP 6.3 mg/dL, erythrocyte sedimentation rate (ESR) 107 mm/hr, and D-dimer 7.9 μg/mL. Chest CT showed prominent aneurysms and thickening of the pulmonary artery walls (Fig. 1b) with consolidation predominantly located in the right middle

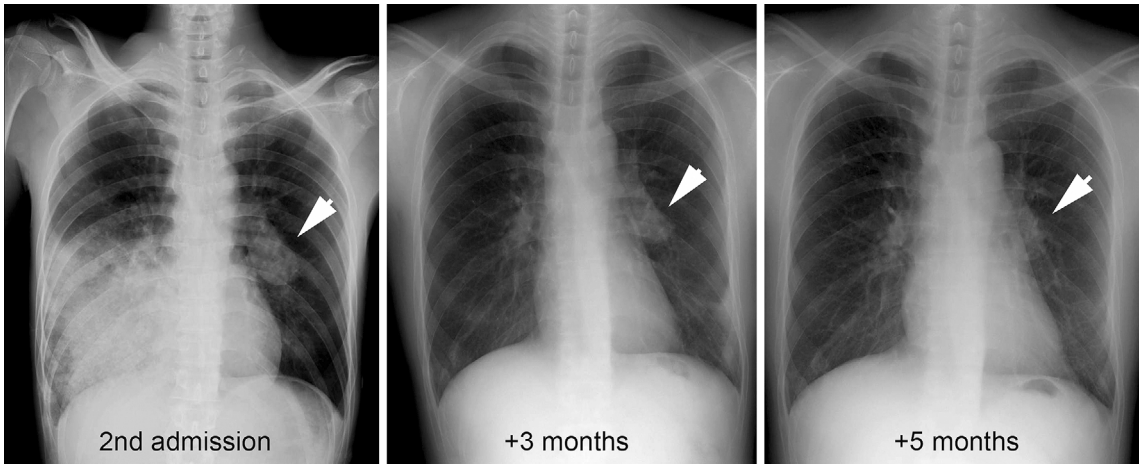

Figure 3. **Resolution of the pulmonary artery aneurysms. At second admission, chest X-ray showed consolidation in the right lower lung field (left). The left pulmonary artery aneurysm (arrows) had shrunk in size at 3 months after beginning therapy with corticosteroids and cyclophosphamide. The aneurysm appeared to be resolved at the end of the cyclophosphamide pulse therapy regimen, which was five months after starting treatment.**

lobe, findings which were all suggestive of hemorrhage. The results of echocardiography were normal with an estimated right ventricular systolic pressure of 27 mmHg, and right heart catheterization was not performed due to the risk associated with the procedure. Anti-coagulant therapy was immediately discontinued.

Further examinations revealed that the patient had had recurrent oral ulcers since his early 30s and a history of uveitis two years prior and erythema nodosum one year prior. The uveitis and erythema nodosum had been successfully treated with topical steroids. The patient was diagnosed with Behçet's disease. Human leukocyte antigen testing was positive for B51, and findings from an interferon gamma release assay for tuberculosis and serologic tests for syphilis were negative. Intravenous methylprednisolone (1 g/day) for 3 days was followed by oral prednisone 50 mg/day (1 mg/kg/day), which was subsequently tapered. Intravenous cyclophosphamide at a dose of 750 mg (15 mg/kg) was also given every 3 weeks for a total of 6 cycles, followed by oral azathioprine. Within two weeks, hemoptysis disappeared, his CRP values normalized, and his ESR decreased to 15 mm/hr. The pulmonary artery aneurysm and thrombosis gradually resolved, and nearly returned to normal state at the end of cyclophosphamide pulse therapy, which was five months after starting treatment (Fig. 1c and d, 3).

Discussion

This patient initially presented with DVT and pulmonary artery thrombosis and was given anticoagulant therapy. He was diagnosed with Behçet's disease after pulmonary artery aneurysms developed, and subsequent corticosteroids and cyclophosphamide treatment resolved the pulmonary artery aneurysms and thrombosis.

Pulmonary artery aneurysms have several different causes (1, 2). In our case, congenital heart disease and pulmonary arterial hypertension were ruled out by echocardiography, the patient was serologically negative for tuberculosis and syphilis, chest CT ruled out tuberculosis and lung cancer, and he had no history of medical procedures. Chronic thromboembolism was considered an unlikely cause for three reasons: the pulmonary artery aneurysms and mural thrombosis worsened with anticoagulation but resolved with immunosuppression, the pulmonary artery aneurysms developed and resolved over a matter of months rather than years, and the estimated right ventricular systolic pressure was normal on echocardiography. Behçet's disease was diagnosed based on the presence of recurrent oral ulcers, uveitis, and erythema nodosum.

Pulmonary arteritis can be caused by different diseases. Behçet's disease can involve arteries and veins, both small and large. ANCA-associated vasculitides (i.e., microscopic polyangitis, granulomatosis with polyangitis, and eosinophilic granulomatosis with polyangitis) affect small pulmonary arteries and can cause alveolar hemorrhage. Although the CT findings in the present case suggested hemorrhage from smaller pulmonary arteries, ANCA-associated vasculitides were considered unlikely, as there were no other symptoms or signs suggestive of ANCA-associated vasculitis, such as fever, arthritis, airway disease, lung disease, or kidney disease, and tests for both MPO-ANCA and PR3-ANCA were negative. Takayasu's arteritis affects larger vessels. However, most patients are female, DVT is a rare complication, and in rare cases where only pulmonary arteries are involved and not large systemic arteries, it usually leads to vascular stenosis (5). Our patient not only met the diagnostic criteria for Behçet's disease, but other diseases were also considered unlikely.

No optimal treatment for pulmonary artery aneurysms caused by Behçet's disease has yet been developed. Hamu-

ryudan et al. reported in a case series of 26 patients that intravenous pulses of corticosteroids and cyclophosphamide followed by long-term oral corticosteroids with oral cyclophosphamide or azathioprine improved 5-year survival, from approximately 40% to 80% (6). As such, the European League Against Rheumatism currently recommends the use of immunosuppressive agents such as corticosteroids, cyclophosphamide, and azathioprine for treating major vessel diseases. Anti-coagulant therapy is not recommended for treatment of DVT and/or pulmonary artery thrombosis due to the increased risk of fatal hemoptysis in these cases. Surgery is also discouraged unless performed in an emergency setting, due to the high risk of complications and recurrence (7). We decided to administer intravenous pulses of corticosteroids and cyclophosphamide followed by oral corticosteroids and azathioprine, which resulted in resolution of the pulmonary artery aneurysms.

The development of pulmonary artery aneurysms in the present case led to a diagnosis of Behçet's disease, and the aneurysms were successfully resolved with immunosuppressive therapy.

The authors state that they have no Conflict of Interest (COI).

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