

Multiple cardiovascular complications in a patient with Behcet's disease

Ji-Eun Chang, M.D., You-Hyun Lee, M.D. and Jisoo Lee, M.D.

Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Korea

Arterial and cardiac involvement of Behcet's disease is a rare but life threatening complication. The rupture of an arterial aneurysm might result in sudden death. We report a 54-year-old man with an established diagnosis of Behcet's disease who presented with multiple cardiovascular complications that eventually lead to his death. He presented with extensive venous occlusions, and sequentially developed right ventricular thrombosis with multiple pulmonary thromboembolisms, and a pulmonary artery aneurysm. We report this unusual sequence of cardiovascular complications in a patient with Behcet's disease.

Key Words : Behcet disease; Aneurysm; Pulmonary embolism; Thrombosis

INTRODUCTION

Behcet's disease (BD) is often complicated by vascular complications with a clear preponderance for venous involvement¹⁾. Arterial and cardiac complications including aneurysms, arteritis, and thrombosis are rare but life threatening complications^{2, 3)}. We report an unusual case of successive vascular complications including extensive venous thrombosis, huge right ventricular (RV) thrombus, multiple pulmonary thromboembolisms, and a pulmonary artery aneurysm (PAA) rupture in a patient with an established diagnosis of BD.

CASE REPORT

In March, 2003, a 54-year-old man presented with cough, dyspnea and intermittent fever that began two months earlier. Two years previously, he was diagnosed with BD based on the clinical manifestations of recurrent oral and genital ulcers, skin manifestations including erythema nodosum and papulopustular lesions, and a positive pathology test. He had a previous history of recurrent venous occlusions at multiple sites, including the

common femoral vein, great saphenous vein and inferior vena cava. He had been on maintenance coumadin therapy until eight months earlier when he stopped treatment and was lost to follow up.

On examination, his body temperature, heart rate and blood pressure were 38.1°C, 110/min and 120/80 mmHg, respectively. Multiple discrete round ulcers were observed on his lower lip mucosa, tongue and scrotum. The skin examination showed multiple 0.2 cm sized papules and pustules on both palms. The chest examinations showed no abnormal findings. The auscultation of the heart revealed a rapid beat without a murmur.

The initial complete blood count revealed a hemoglobin count of 12.6 g/dL, a platelet count of $368 \times 10^9/L$, and a white cell count of $10.6 \times 10^9/L$. The ESR was elevated to 73 mm/hr and the C-reactive protein was positive at 4.7 mg/dL. The anticardiolipin antibodies were negative but the lupus anticoagulant was positive (92.7 sec). The plasma homocysteine concentration was 19.9 mol/L (normal, 4.5-12.4 mol/L). The HLA B51 test was negative. The antithrombin III, protein C and S levels were within the normal range. The chest X-ray revealed haziness in the right middle and left upper lobes. The chest CT

•Received : November 3, 2006

•Accepted : February 15, 2007

•Correspondence to : Jisoo Lee, M.D., Ph.D., Department of Internal Medicine, Ewha Womans University College of Medicine, 911-1 Mok-dong, Yangcheon-gu, Seoul 158-710, Korea Tel : 82-2-2650-6164, Fax : 82-2-2655-2076, E-mail : leejisoo@ewha.ac.kr

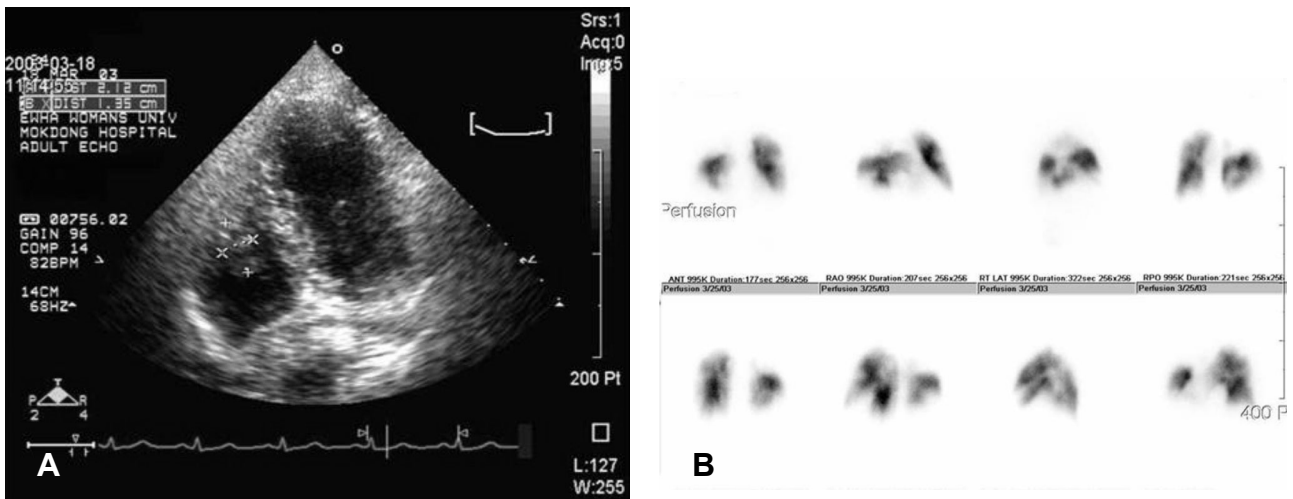


Figure 1. Echocardiographic findings show mobile intracardiac mass (1.3×2.0 cm) in the right ventricle (A). Lung perfusion scan shows multiple perfusion defects on both lung fields (B).



Figure 2. Chest CT finding shows a rupture of the right pulmonary artery aneurysm with a thrombus within the aneurysm.

scan revealed a large mass in the RV. Transthoracic echocardiography showed a mobile ill-defined 2.0×1.3 cm sized mass that was attached to the tip of the papillary muscle of RV but valvular vegetation was not observed (Figure 1A). The ventricular functions were normal. The lung scan revealed multiple perfusion defects on the right upper, right lower, and left lower lung fields (Figure 1B). Doppler ultrasonography of the lower extremities did not show venous thrombosis.

Coumadin and methylprednisolone 24 mg/d were started under a diagnosis of BD complicated by intracardiac thrombosis and multiple pulmonary thromboembolisms. His symptoms improved rapidly. After the coumadin treatment for one year, the right ventricular thrombus was completely resolved.

In October 2004, he suddenly developed a hemoptysis of 700

mL associated with chest pain and dyspnea. The body temperature, heart rate, respiratory rate and blood pressure were 38°C, 140/min, 44/min and 110/70 mmHg, respectively. Coarse crackles were heard over both lung fields. The complete blood count showed a hemoglobin level, a white blood cell count and a platelet count of 11.0 g/dL, $16.4 \times 10^9/L$ and $405 \times 10^9/L$, respectively. The coagulation profile, ESR, CRP, and blood chemistry were within the normal limits. The chest CT scan and pulmonary angiography revealed a pulmonary hemorrhage from a rupture of the right pulmonary artery and a thrombus within the aneurysm (Figure 2).

The patient was diagnosed with a rupture of PAA and was started on high dose glucocorticoid and cyclophosphamide pulse therapy. After the completion of 6 cycles of cyclophosphamide therapy, he was maintained on azathioprine 100 mg/d and methylprednisolone 8 mg/d. His progress was uneventful for 10 months, and the PAA decreased in size. In August 2005, he developed recurrent hemoptysis, which resolved with high dose glucocorticoid therapy. However, he died during a third episode of massive hemoptysis in October 2005, twelve months after the initial presentation.

DISCUSSION

Since the main pathological feature of BD is vasculitis, the condition is often complicated by vascular complications with an incidence of vascular involvement ranging from 7 to 29%⁽²⁾. The venous lesions are mainly venous occlusions, while arterial lesions are either arterial aneurysms or arterial occlusions. Arterial complications, particularly when multiple vessels are involved, have grave consequences often leading to mortality. The

pathogenesis of thrombosis in BD is unclear. Endothelial cell injury by the deposition of immune complexes has been implicated as an important cause of hypercoagulability and thrombosis. Vascular inflammation can lead to the enhancement of platelet aggregation and an impairment of fibrinolysis resulting in a thrombosis^{4, 5)}. Recently, the von Willebrand factor antigen⁶⁾, hyperhomocysteinemia, and antiphospholipid antibodies were reported to play a role in thrombus formation in BD^{7, 8)}. Thrombosis can occur in any type of vein or artery. However, thrombosis within the cardiac chamber is extremely rare⁹⁾ and can only occur in settings where the immune system is extensively activated. This is because the endocardium is less prone to damage from circulating immune complexes and various inflammatory mediators due to high velocity dynamic blood flow within the cardiac chambers. In our patient, the increased lupus anticoagulant and plasma homocysteine concentration was documented during the severe disease flare up resulting in a thrombosis of the pulmonary artery and RV. Our case demonstrates that multiple thrombophilic factors act cumulatively to trigger a fulminant thrombotic phenomenon.

Aneurysms occupy approximately 60% of reported arterial lesions associated with BD¹⁰⁾. The aorta is the most commonly affected artery followed by the pulmonary artery¹¹⁾. PAA is known to occur as a result of immune-mediated vasculitis¹⁾. The consequent neovascularization and degeneration of arterial wall result in the formation of an aneurysm¹²⁾. Hemoptysis is the main presenting symptom but thrombi within PAA can cause secondary ischemia in the lung parenchyma. Medical treatment with immunosuppressive agents is preferred over surgery because a recurrent aneurysm or fistula at the anastomotic site is a common complication after a surgical resection¹³⁾. There are reports of the regression of PAA associated with BD after a treatment with high dose glucocorticoid and cyclophosphamide combination^{14, 15)}. However, the successful control of the symptoms with these therapeutic regimens is not always enough to prevent a recurrence or rupture. Once an aneurysm develops, it carries the risk of rupture at any time. Approximately 30% of BD patients with PAA die within 2 years¹⁵⁾.

When a BD patient with thrombophilic tendency experiences a major flare in the disease activity, a search for other vascular complications is recommended because multiple catastrophic vascular events can be triggered by the inflammation.

REFERENCES

- 1) Calamia KT, Schirmer M, Melikoglu M. *Major vessel involvement in Behcet disease*. *Curr Opin Rheumatol* 17:1-8, 2005
- 2) Kuzu MA, Özaslan C, Köksoy C, Gürler A, Tüzünler A. *Vascular involvement in Behcet's disease: 8-year audit*. *World J Surg* 18:948-953, 1994
- 3) Koc Y, Gullu I, Akpek G, Akpolat T, Kansu E, Kiraz S, Batman F, Kansu T, Balkanci F, Akkaya S, Telatar H, Zileli T. *Vascular involvement in Behcet's disease*. *J Rheumatol* 19:402-410, 1992
- 4) Schmitz-Huebner U, Knop J. *Evidence for an endothelial cell dysfunction in association with Behcet's disease*. *Thromb Res* 34:277-285, 1984
- 5) Chajek T, Aronowski E, Izak G. *Decreased fibrinolysis in Behcet's disease*. *Thromb Diath Haemorrh* 29:610-618, 1973
- 6) Direskeneli H, Keser G, Cruz D, Khamashta MA, Akoglu T, Yazici H, Yurdakul S, Hamuryudan V, Ozgun S, Goral AJ, Hughes GR. *Anti-endothelial cell antibodies, endothelial proliferation and von Willebrand factor antigen in Behcet's disease*. *Clin Rheumatol* 14:55-61, 1995
- 7) Hull RG, Harris EN, Gharavi AE, Tincani A, Asherson RA, Valesini G, Denman AM, Froude G, Hughes GR. *Anticardiolipin antibodies: occurrence in Behcet's syndrome*. *Ann Rheum Dis* 43:746-748, 1984
- 8) Aksu K, Turgan N, Oksel F, Keser G, Özman D, Kitapcioğlu G, Gümtüşdiş G, Bayindir O, Doğanavşargil E. *Hyperhomocysteinemia in Behcet's disease*. *Rheumatology* 40:687-690, 2001
- 9) Mogulkoc N, Burgess MI, Bishop PW. *Intracardiac thrombus in Behcet's disease: a systematic review*. *Chest* 118:479-487, 2000
- 10) Park JH, Han MC, Bettmann MA. *Arterial manifestations of Behcet's disease*. *AJR Am J Roentgenol* 143:821-825, 1984
- 11) Uzun O, Akpolat T, Erkan L. *Pulmonary vasculitis in Behcet disease: a cumulative analysis*. *Chest* 127:2243-2253, 2005
- 12) Hamuryudan V, Oz B, Tuzun H, Yazici H. *The menacing pulmonary artery aneurysms of Behcet's syndrome*. *Clin Exp Rheumatol* 22(Suppl 34):S1-S3, 2004
- 13) Tüzün H, Beşirli K, Sayin A, Vural FS, Hamuryudan V, Hizli N, Yurdakul S, Yazici H. *Management of aneurysms in Behcet's syndrome: an analysis of 24 patients*. *Surgery* 121:150-156, 1997
- 14) Tunaci M, Özkokmaz B, Tunaci A, Gül A, Engin G, Acunas B. *CT findings of pulmonary artery aneurysms during treatment of Behcet's disease*. *AJR Am J Roentgenol* 172:729-733, 1999
- 15) Hamuryudan V, Yurdakul S, Moral F, Numan F, Tuzun H, Tuzuner N, Mat C, Tuzun Y, Ozyazgan Y, Yazici H. *Pulmonary arterial aneurysms in Behcet's syndrome: a report of 24 cases*. *Br J Rheumatol* 33:48-51, 1994