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The possible role of *Staphylococcus epidermidis* in the development of pulmonary artery aneurysm in Behçet's disease

Behçet hastalığında pulmoner arter anevrizması oluşumunda Staphylococcus epidermidis'in olası rolü

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Pulmonary artery aneurysm (PAA) has dreadful consequences and is one of the leading causes of death in Behçet's disease (BD). A 35-year-old male patient with a five-year history of BD had symptoms of hemoptysis, dyspnea, intermittent fever, and chest pain. He received immunosuppressive therapy for three months by peripheral venous catheterization because of general vasculitis involving the eyes, pulmonary vasculature, and neurological system. A chest X-ray showed a circular opacity obliterating the right hilum. Computed tomography of the thorax revealed a PAA, 74 mm in diameter, originating from the right upper lobe artery. Another PAA, 2-3 mm in size, was identified at the upper branch of the left pulmonary artery. White blood cell count was $12x10^6$/ml, erythrocyte sedimentation rate was 67 mm/hr, and bacteriological analyses were all negative for bacteria. The PAA was removed by a right upper lobectomy. Bacteriological examination of fluid samples taken from the aneurysm pouch showed coagulase-negative staphylococcus *(Staphylococcus epidermidis)*. Vancomycin was initiated according to the antibiotic sensitivity tests. After three weeks of antibiotherapy, leukocyte count was $7x10^6$/ml, and erythrocyte sedimentation rate was 25 mm/hr. It was thought that peripheral venous catheterization might be responsible for the access of infectious agent, which then gave rise to the development of PAA.

Key words: Aneurysm/surgery; Behcet Syndrome/complications; pulmonary artery/pathology; Staphylococcus epidermidis.

Pulmoner arter anevrizmasının (PAA) çok kötü sonuçları vardır ve Behçet hastalığında önde gelen ölüm nedenlerinden biridir. Beş yıldır Behçet hastalığı olan 35 yaşında erkek hasta hemoptizi, dispne, intermitan ateş ve göğüs ağrısı yakınmalarıyla başvurdu. Hastanın üç aydır, gözleri, pulmoner damarları ve nörolojik sistemi tutan genel vaskülit nedeniyle, periferik ven yoluyla immünsupresif tedavi gördüğü öğrenildi. Akciğer grafisinde sağ hilusu oblitere eden sirküler opasite saptandı. Toraks bilgisayarlı tomografisinde sağ üst lob arterinden kaynaklanan, 74 mm çapında PAA görüldü. Ayrıca, sol pulmoner arterin üst dalında, 2-3 mm çapında başka bir PAA görüldü. Laboratuvar incelemelerinde, lökosit $12x10^6$/ml, sedimantasyon hızı 67 mm/sa olarak saptandı. Bakteriyolojik incelemeler bakteri varlığı açısından negatif idi. Sağ üst lobektomi ile PAA başarılı bir şekilde çıkarıldı. Anevrizma kesesinden alınan sıvı örneğinin bakteriyolojik takibinde koagülaz-negatif stafilokok (*Staphylococcus epidermidis*) üredi. Antibiyotik duyarlılık testi sonuçlarına göre vankomisin tedavisine başlandı. Antibiyotik tedavisinden üç hafta sonra lökosit sayısı $7x10^6$/ml'ye, sedimantasyon hızı 25 mm/saat'e düştü. Enfeksiyöz ajanın girişinden, periferik venöz kateterizasyonun, PAA'nın gelişiminden de *S. epidermidis*'in sorumlu olabileceği düşünüldü.

Anahtar sözcükler: Anevrizma/cerrahi; Behçet sendromu/komplikasyon; pulmoner arter/patoloji; Staphylococcus epidermidis.

Behçet's disease (BD) is a multisystemic inflammatory disorder classified among vasculitides, affecting all types of blood vessels.[1] When it is associated with lesions in the large vessels, it is referred to as "vasculo-Behcet's disease" and includes venous or arterial occlusions and aneurysm formation. Systemic arterial manifestations of BD are less frequent compared with venous involvement, accounting for only 12% of vascular complications.[1] The pulmonary arteries are the second most common site of arterial involvement, preceded by the aorta. Pulmonary artery aneurysm (PAA) is the best-defined type of pulmonary disease in BD, leading to significant morbidity and mortality.[2] While extravascular infections including tuberculosis, syphilis, and fungal cavitary lesions appear to be more commonly associated with PAAs in older series,

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endovascular infections due to bacterial emboli predominate in the more recent series.[3]

CASE REPORT

A 35-year-old male patient with a five-year history of BD had symptoms of hemoptysis, dyspnea, intermittent fever, and chest pain. He had received pulsed immunosuppressive therapy (cyclophosphamide and methylprednisolone) for three months by the peripheral venous access because of general vasculitis involving the eyes, pulmonary vasculature, and neurological system.

On physical examination, uveitis was determined in both eyes, leading to severe visual deficiency. Inspiratory crackles were auscultated on the right hemithorax. Chest X-ray showed a circular opacity obliterating the right hilum (Fig. 1a). A computed tomographic scan of the thorax revealed a PAA originating from the right upper lobe artery, 74 mm in diameter. Another PAA, 2-3 mm in size, was identified at the upper branch of the left pulmonary artery (Fig. 1b). Laboratory findings were as follows: white blood cell count was over $12x10^6$/ml, erythrocyte sedimentation rate was more than 67 mm/hr, and bacteriological analyses were all negative for bacteria. In spite of the immunosuppressive therapy, the size of the aneurysm did not regress. The patient was prepared for surgery to terminate the risk for rupture of the aneurysm. The PAA was successfully removed by a right upper lobectomy. Intraoperatively, a fluid sample was taken from the aneurysm pouch for bacteriological examination. The result of the culture was reported to be coagulase-negative staphylococcus identified as *Staphylococcus epidermidis*. Vancomycin therapy was initiated according to the antibiotic sensitivity assay. After three weeks of antibiotherapy, leukocyte count fell below $7x10^6$/ml, and erythrocyte sedimentation rate declined to a level less than 25 mm/hr.

DISCUSSION

Pulmonary manifestations in patients with BD are mainly associated with vasculitis involving pulmonary arteries and veins. Pulmonary vascular involvement can lead to aneurysm formation.[1,2]

About 40% to 50% of PAAs are seen in patients with structural heart lesions. Besides, inflammatory lesions such as giant cell arteritis and BD are rare causes of PAA. In addition, endovascular infections due to bacterial emboli outweigh in the development of PAA.[3]

Endarteritis is the inflammation of the arterial wall. Arterial infections may result from several mechanisms such as microembolization, hematogenous seeding, and direct bacterial contamination. Besides, intravascular catheters provide a direct route through the skin and into the bloodstream, contributing to potential dissemination of pathogens to distant foci. As might be expected from infections related to a cutaneous focus, the causative pathogens are frequently *S. aureus* or *S. epidermidis*. This might play a role in the pathogenesis of endarteritis and mycotic aneurysms.[4]

The severity of hemoptysis and the number of aneurysms are key factors in choosing therapy. Immunosuppressive drugs alone or in combination with steroids (a combination of cyclophosphamide and methylprednisolone) are most beneficial when given in early stages before irreversible damage to the arterial wall develops.[5]

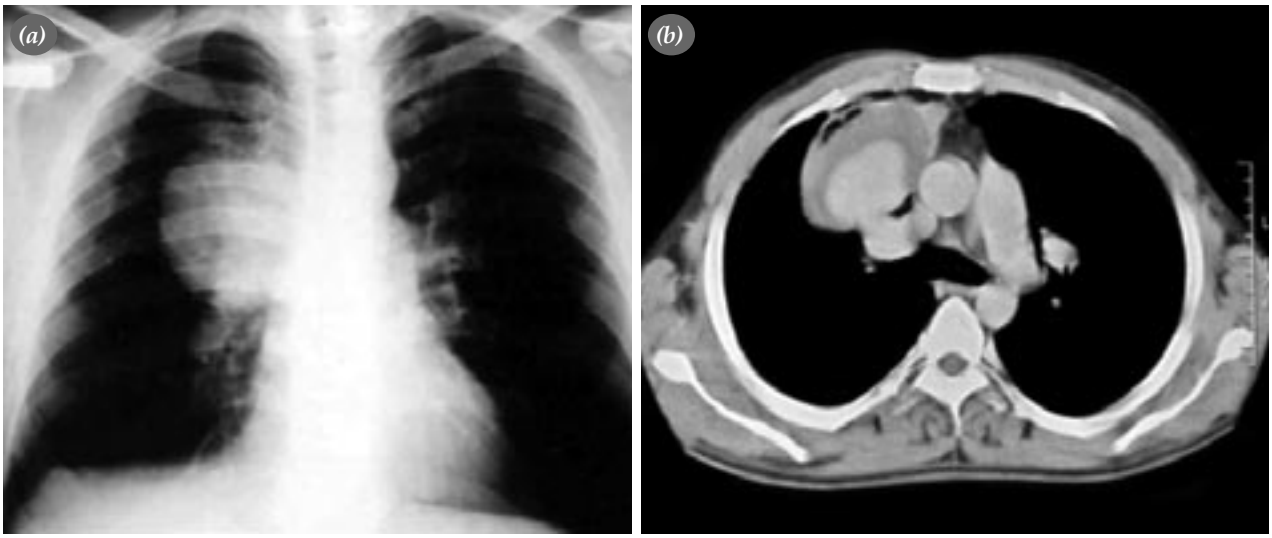

Fig. 1. (a) A preoperative chest X-ray showing a giant mass lesion obliterating the right hilum. **(b)** Preoperative computed tomographic scan of the thorax showing a pulmonary artery aneurysm originating from the right upper lobe artery division (70x74 mm in size). Another aneurysm, 2-3 mm in size, is identified in the upper branch of the left pulmonary artery.

Embolization is the first line of treatment for massive hemoptysis in patients with Behçet's disease. On the other hand, the size and number of aneurysms, the presence of superior or inferior vena cava occlusion, and the potential complication of severe bleeding are the main limitations for the use of embolization in Behçet's disease.[6] From the point of surgical intervention for BD, lobectomy and pneumonectomy or embolization of the aneurysm may be considered together with the remedial therapy for selected cases only because of a high perioperative mortality, chiefly in patients with multiple and bilateral aneurysms.[7] Although the risks of operation in patients with Behçet's syndrome are high, it could be a life-saving procedure.

In our case, PAA was a giant one for which right upper lobectomy was performed avoiding the serious complication, rupture of the aneurysm. We contemplated potential mechanisms for the formation of PAA and reached a conclusion that it might well be related to coagulase-negative staphylococcus that was isolated from the aneurysm pouch. He had intermittent fever, though no bacteria were cultivated in blood samples. The possible route for the entry of the bacteria was suggested to be the venous catheters that were used several times during immunosuppressive therapy. Hence, *S. epidermidis* infection coinciding with vasculitis due to BD might be responsible for the development of PAA.

In conclusion, every effort should be made to isolate bacteria in any potential source. It should be kept in mind that if appropriate antibiotherapy can be administered to BD patients as well as other drugs, then it will be most likely to be effective to prevent the development of any PAA or at least to reduce the threat of rupture of the aneurysm.

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