

Pulmonary Manifestations In Behçet's Disease

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✓ Behçet's disease is a chronic multisystem vasculitis of unknown aetiology, affecting many organs including skin, joint, eyes, central nervous system, gastrointestinal tract, kidneys, epididymis, heart, lung, large arteries and veins. Pulmonary involvement is rare in Behçet's disease, approaching 1-5% in different series. The main features of lung involvement consist of vasculitis forming multilocular aneurysms and thrombosis of the pulmonary artery. Hemoptysis is the dominant clinical feature of Behçet's pulmonary arteritis.

Chest x-ray, computed tomography, angiography, pulmonary perfusion scan and bronchoscopy are useful for evaluating vascular change. It is suggested that corticosteroid treatment alone or in combination with an immunosuppressive agent such as azathioprine, cyclosporin or cyclophosphamide should be considered as a first-line treatment. Anticoagulant treatment in the presence of hemoptysis may be hazardous and should be avoided. If there is no response to medical treatment, surgical excision of pulmonary artery aneurysms or local resection of the involved lung should be considered. Pulmonary involvement in BD is one of the severe and worst prognostic manifestations of the disease.

Key words: Behçet's disease, pulmonary manifestations.

Behçet's disease (BD) was initially described by the Turkish professor of dermatology, Hulusi Behçet in 1937. Although it was originally described as the clinical triad of oral and genital ulceration with iridocyclitis, now is known as a systemic disease affecting many other organs as well⁽¹⁻⁶⁾. Involvement of the pulmonary vascular tree is also reported, and in some studies the prevalence of lung involvement approaches 5 percent^(2,5,6,7,8,9).

BD is most often observed in Mediterranean countries, Japan, and the Middle East^(1-4,10-14). In Japan, its prevalence is reported to be 10 to 80 per 100.000 in different regions, in Turkey two clinical surveys indicate similar prevalences of 10/100.000-40/100.000^(3,4,5,11). BD patients are mainly young adults between 20 and 40 years of age, and it is twice as frequent in men^(2,3,4,7,10,13).

The International study group for BD was formed in 1985 during the 3rd International conference on BD, and, set itself the task of reviewing and revising diagnostic criteria for BD in current use with the aim of developing an internationally agreed set

(15,16). New international diagnostic criteria are shown in Table-I.

Aetiology is unknown, viral and bacterial agents, various environmental chemicals and genetic predisposition have been implicated^(2,3,5,10,14,17,18). An association between HLA B5 and BD implies that HLA linked genes are indeed involved in increased susceptibility^(3-5,10,17-19). Various immunological aberrations have been observed in patients with BD, ranging from autoantibodies to oral mucosa and a decrease in T4 cells especially before exacerbation of this disease, to an increased level of soluble interleukin 2 receptors⁽¹⁰⁾. The immunologic studies of B and T cell function do not yet explain the pathogenesis in this disease^(3,10).

The underlying histologic lesion observed in all organs involved in BD is a non-specific vasculitis, especially affecting veins, venules and capillaries and characterised by infiltration of the vessel wall by mononuclear cells and later by polymorphonuclear leukocytes, with increased permeability^(3,5,6,11-14,20,21). large artery aneurysms and occlusions have been described

Table-I : International criteria for classification of Behçet's disease**Recurrent oral ulcerations**

Minor aphthous, major aphthous or herpetiform ulceration observed by a physician or reported reliably by patient. Recurrent at least three times in one year period Plus 2 of

Recurrent genital ulceration

Recurrent genital aphthous ulceration or scarring, especially males, observed by physician or reliably reported by patient.

Eye lesions

Anterior uveitis

Posterior uveitis

Cells in vitreous on slit lamp examination or retinal vasculitis observed by ophthalmologist

Skin lesions

Erythema nodosum-like lesions observed by physician or reliably reported by patient

Pseudo folliculitis

Papulopustular lesions

or acneiform nodules consistent with Behçet's disease-observed by a physician and in post-adolescent patients not receiving corticosteroids

Positive pathergy test

To be read by physician at 24-48 h

*Findings are applicable if no other explanations is present

in 1.5-2.2 percent of the patients^(14,19).

The pulmonary arteries affected range from the lobar and segmental branches down to the arterioles; these arteries display focal thrombosis and inflammatory lesions with focal, transmural necrosis. Pulmonary artery aneurysms have also been reported⁽¹³⁾.

A number of mechanisms have been implicated to account for the high incidence of thrombosis and include impaired fibrinolysis, increased clotting factors and abnormal platelet function. Several studies have reported increased platelet aggregation in patients with BD. Both decreased vessel wall production and reduced plasma concentration of prostacyclin, a potent platelet anti-aggregatory agent have been suggested in the development of high risk thrombosis^(22,23).

The major manifestation of lung involvement is hemoptysis^(2,5-8,20). Massive and often fatal hemoptysis in BD is more likely to be secondary to a ruptured aneurysm than pulmonary infarction^(5,13,25). Other symptoms are dyspnea, pleuritic chest pain,

fever and cough⁽⁵⁻⁸⁾. Lung involvement is characterised by aneurysms, thromboses, infarction, haemorrhages, pleural effusions and vena cava syndrome, and co-existence of pulmonary arterial aneurysms with thromboses should suggest BD^(2,5-8,11,13,24,25). Despite this unique presentation the diagnosis is frequently missed. Indeed, the Hughes-Stovin syndrome, described in 1959, as pulmonary "thromboses", veno-occlusive disease and intracranial venous hypertension, seems today more like a missed diagnosis of BD with pulmonary arteritis^(5,19,20,26).

Rarely pulmonary tuberculosis itself has been reported in association with BD. There are a number of possible factors which might increase the risk of developing tuberculosis in patients with BD. One possibility is that the disease itself may produce a defect in cell mediated immunity which increases the individual susceptibility to tuberculosis. Ethnic factors, genetic predisposition and immunosuppressive drugs might also be important^(2,9).

Thrombotic occlusion of the superior

vena cava is a relatively frequent complication in BD. There are four cases with chylothorax complicated by BD, the condition was caused by a superior vena cava syndrome secondary to superior vena cava thrombophlebitis extending to and obliterating the thoracic duct⁽²⁷⁾.

Chest x-ray findings are often non-specific and may be completely normal. The most commonly described findings are transient alveolar infiltrates, which may represent haemorrhage or infarction; less frequently, nodules and larger central opacities are found and these represent lobar and segmental pulmonary artery aneurysms. Pleural effusions usually relate to pulmonary infarction or vena cava superior syndrome (VCSS). VCSS may also cause mediastinal enlargement^(2,5-7,13,25).

The diagnosis can be made with the observation of defective perfusion on the pulmonary perfusion scan even though chest x-rays are normal⁽⁷⁾.

The vascular pathology can be demonstrated by dynamic CT scans^(5,8). Although pulmonary angiography is a very valuable diagnostic tool, one should know that angiography may aggravate the vasculitis^(5,7,13). Bronoscopic study is also important and reveals the bleeding site but it has been argued that it carries a similar risk with angiography⁽⁵⁾. Nuclear magnetic resonance (NMR) and Digital subtraction angiography (DSA) have also proved to be useful in the diagnosis of vascular lesions^(8,26).

Various treatments are considered to be effective in this disease, including corticosteroids, colchicine, azathioprine, chlorambucil, cyclophosphamide, cyclosporin A, fibrinolytic therapy, interferon and blood transfusions^(2-6,10-12). There is no agreement on how to treat major venous and arterial disease. It seems reasonable to avoid anticoagulants, especially heparin and warfarin, when pulmonary arteritis is present. Anticoagulant therapy may be potentially hazardous to patients suffering from aneurysmatic dilatation of the pulmonary blood vessels^(5,7,11,20). Corticosteroid treatment supplemented by immunosuppressive thera-

py is indicated when active large vessel arteritis is present^(5,6,8,20). Simultaneous use of 300mg acetyl salicylic acid seems prudent in order to prevent secondary thromboses⁽⁵⁾. Immunosuppressive treatment can be tapered over one year⁽²⁰⁾.

Pulmonary involvement in BD carries an extremely poor prognosis. Mortality rate is estimated to be around 50%⁽²⁰⁾. Being a systemic disease, the most severe presentation in pulmonary involvement of Behçet's is aneurysm. Although development of aneurysm can be prevented by the early initiation of medical therapy, surgical aneurysmectomy should be considered especially in a singular lesion^(6,19,20). If hemoptysis continues despite combination of corticosteroid and immunosuppressive therapy, then underlying lesion should be histologically confirmed and, then surgical excision of the involved lobe or even the whole of the lung can be life-saving^(6,20).

It should be kept in mind that unexplained hemoptysis and recurrent pulmonary thromboembolism may be due to Behçet's disease.

Geliş Tarihi: 07.02.1994

Yayına Kabul Tarihi: 28.02.1994

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