Behçet's disease: case reports

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Behcet diseases is not only orogenital ulcerations but also it can have many systemic manifestations. In this article we presented 3 cases of Behcet disease associated with pulmonary artery aneurysms affecting the large branches. Pulmonary artery aneurysms are common and serious vascular complication of Behcet disease.These are usully large and accompanied with intramural thrombi and multiple pulmonary infarctions with a common presentation of haemoptysis. A detailed discussion of pulmonary manifesttions of Behcet disease was demonstrated.

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Case 1

A male patient 45 years of age presented with haemoptysis. He received complete regular course of antituberculous treatment on radiological basis with remission and recurrence of haemoptysis. A chest radiography was requested.

The patient was referred to Chest Department, Assiut University Hospital. History taking revealed recurrence of orogenital ulceration. Ophthalmological examination demonstrated iritis. A provisional diagnosis of Behçet's disease was established. A computed tomography (CT) chest with pulmonary angiography was performed.

It illustrated large pulmonary artery aneurysm in the proximal part of lower lobe branch of the right pulmonary artery with intramural filling defect reflecting intramural thrombus.

Pulmonary angiography confirmed a fusiform aneurysm in proximal part of the right lower lobe branch of pulmonary artery. Hence, the recurrent haemoptysis can be explained by recurrent pulmonary infarction caused by detachment of emboli from intramural thrombus, and other cuts of CT pulmonary angiography confirmed this.

Case 2

A blind male patient presented with recurrent haemoptysis and recurrent orogenital ulcerations. He seeked dermatological advice, and diagnosis of Behçet's disease was recognized. He was referred to Chest Department, Assiut University Hospital. A Chest radiograph and CT chest with pulmonary angiography were accomplished.

CT angiography showed bilateral pulmonary artery aneurysms with large intramural filling defect in the right one reflecting bulky intramural thrombus with multiple infarcts in the right lung.

Pulmonary angiography of the right pulmonary artery confirmed a large aneurysm in the three branches of pulmonary artery.

Case 3

A patient presented with his chest radiograph.

He consulted a cardiothoracic specialist and a diagnosis of multiple hydatid cysts was made. During thoracotomy, pulsating lesions were noticed, and hence operation was ended, and the patient was referred to Chest Department, Assiut University Hospital. History taking was compatible with Behçet's disease.

CT angiography verified bilateral pulmonary artery aneurysms with large intramural filling defect in the left one reflecting huge intramural thrombus.

Discussion

History

Behçet's disease is a chronic inflammatory disorder of unknown aetiology characterized by recurrent attacks. Although the triple symptom complex of oral and genital ulcerations with uveitis was reported by Hippocrates and other authors who attributed the symptom triad to major infections, Hulusi Behçet, a Turkish dermatologist, discarded the association with other illnesses and was the first to delineate the disease that now bears his name. Clinical manifestations additional to this triad were described later including involvement of the skin,

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joints, large vessels, lung, brain, gastrointestinal and genitourinary tracts. It is now recognized as a multisystem disease with vasculitis as the main pathological finding.

Pulmonary manifestations of Behçet's disease

Tables 1 and 2.

Epidemiology

Although Behçet's disease has a worldwide distribution, most cases cluster along the ancient Silk Road, which extends from far eastern Asia to the Mediterranean basin. The highest prevalence rate was reported from Turkey as 80–370 per 100 000. The prevalence ranges from two to 30 cases per 100 000 in other Asian countries, with lower figures in Europe and the USA. The age of disease onset is usually the second or third decade of life, and the male-to-female ratio is reported to be almost equal. However, the disease runs a more severe course in men and in those with an onset before 25 years of age.

Table 1 Frequency of clinical manifestations in Behçet's disease

Lesions	Frequency
Oral ulcers	96–100
Skin lesions	
Folliculitis	40–50
Erythema nodosum	25–80
Positive pathergy test	10–50
Genital ulcers	65–90
Eye lesions	35–70
Arthritis	30–80
Neurological involvement	10–50
Gastrointestinal involvement	5–60
Vascular involvement	5–30
Pulmonary involvement	1–8

Pulmonary involvement

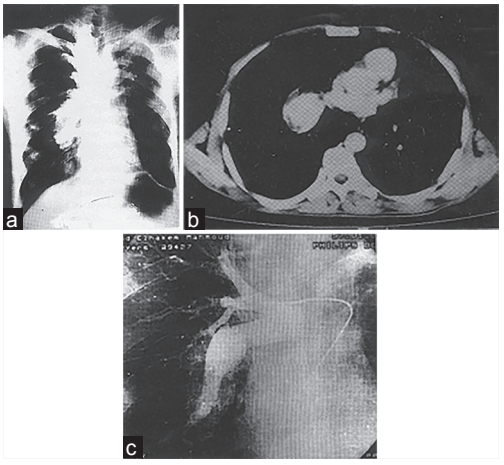
More than 200 cases of Behçet's disease with pulmonary involvement have been reported in the literature. The pulmonary arteries are the second most common site of arterial involvement, preceded by the aorta. Aneurysms are more common than thrombosis.

Pulmonary artery aneurysms, arterial and venous thrombosis, pulmonary infarction, recurrent pneumonia, bronchiolitis obliterans organizing pneumonia and pleurisy are the main features of pulmonary involvement in Behçet's disease. The true prevalence of the pulmonary manifestations in Behçet's disease is unknown because no prospective study has evaluated all pulmonary symptoms in an unselected group of patients. The reported prevalence has ranged from 1 to 7.7%.

Pulmonary artery aneurysms

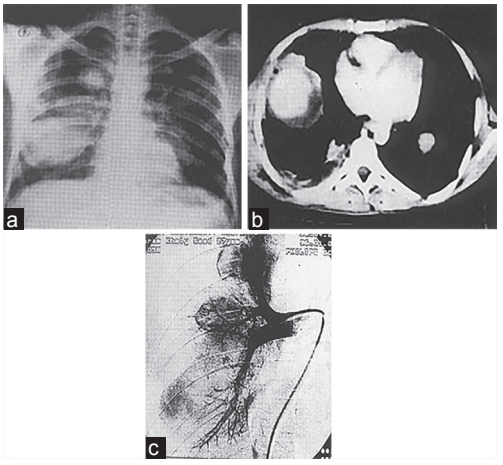
Pulmonary artery aneurysms affect mainly young men. Haemoptysis of varying degrees (up to 500 ml) is the most common and predominant symptom. Rupture of an aneurysm with erosion into a bronchus and the development of in-situ thrombosis from active vasculitis have been suggested as explanations for haemoptysis. Sudden hilar enlargement or the appearance of polylobular and round opacities on the chest radiograph can represent pulmonary artery aneurysms When associated with an acute episode of haemoptysis, they appear poorly marginated; otherwise, they have a distinct outline. Helical CT is currently the method of choice for the diagnosis because it provides excellent vascular images with only a small quantity of contrast material. Aneurysms are seen as saccular or fusiform dilatations that show homogeneous contrast filling simultaneously with the pulmonary artery. Pulmonary artery aneurysms are located most frequently in the right lower lobar arteries, followed

Fig. 1



Radiology of case 1

Fig. 2

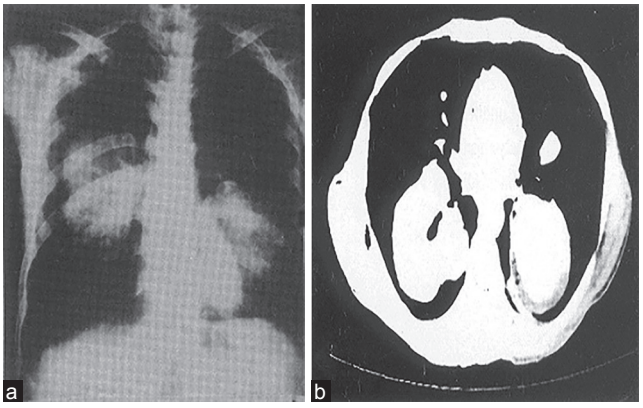


Radiology of case 2

Table 2 The International Study Group criteria for the diagnosis of Behçet's disease

In the absence of other clinical explanations, patients must have:
(1) Recurrent oral ulceration (aphthous or herpetiform) observed by the physician or patient recurring at least three times in one 12-month period
+ two of the following:
(2) Recurrent genital ulceration
(3) Eye lesions:
Anterior uveitis
Posterior uveitis (cells in the vitreous observed by slit-lamp examination) or
Retinal vasculitis observed by an ophthalmologist
(4) Skin lesions:
Erythema nodosum
Pseudofolliculitis
Papulopustular lesions or acneiform nodules in postadolescent patients not on corticosteroids
(5) Positive skin pathergy test read by a physician at 48 h – that is, a 2 mm erythematous papule or pustule at the prick site 48 h after the application of a sterile hypodermic 20–22-G needle, which obliquely penetrated avascular antecubital skin to a depth of 5 mm

Fig. 3



Radiology of case 3

by the right and left main pulmonary arteries. In this study, the diameter of the aneurysms ranged from 1 to 7 cm, and between two and seven aneurysms have been detected in the same patient. MRI is also helpful in the diagnosis of pulmonary artery aneurysms. Although no comparative studies are available, it is considered to be less sensitive than helical CT in demonstrating small aneurysms. Digital subtraction angiography has also been used in the diagnosis but it may be inadequate if aneurysms or vessels are completely thrombosed. Imaging techniques such as aortography, venography and pulmonary angiography are no longer used, as they carry a higher risk for complications. The frequency of such complications with digital subtraction angiography is unknown. In one case report, radionuclide angiography showed alterations in the pulmonary artery blood flow as clearly as did subsequent contrast pulmonary angiography. Normal or aneurysmally dilated pulmonary arteries frequently become obliterated by large thrombi. On chest radiography, this may result in hyperlucent areas of the lung supplied by these vessels. CT scanning can show a mosaic pattern of variable attenuation reflecting nonhomogeneous perfusion. Ventilation–perfusion lung scans show bilateral, well-defined, mismatched areas. Although deep venous thrombosis of the lower extremities frequently accompanies pulmonary artery aneurysms, pulmonary thromboembolism is very rare in Behçet's disease because the thrombi in inflamed veins are strongly adherent.

Pulmonary parenchymal findings

Atelectasis, volume loss, wedge-shaped or linear shadows and ill-defined, nodular or reticular opacities have been described in Behçet's disease, with or without pulmonary artery aneurysms. These findings are generally accepted as foci of pulmonary haemorrhage and/or infarcts. However, the pathological correlation of the parenchymal opacities has only been documented in a few cases. A recent case report reported prominent clinical, radiological and pathological findings of organizing pneumonia associated with pulmonary artery aneurysms. Organizing pneumonia may accompany various collagen vascular diseases including systemic lupus erythematosus and systemic vasculitides such as Wegener's granulomatosis. Patients with secondary organizing pneumonia have a worse prognosis than cryptogenic or primary cases. In another patient with Behçet's disease and peripheral nonsegmental pulmonary infiltrates, eosinophilic pneumonia was found on transbronchial biopsy.

Other thoracic manifestations of Behçet's disease

Involvement of major veins including occlusion of the superior vena cava is a more prevalent finding than arteritis. Thrombosis of the innominate and subclavian veins may accompany superior vena caval occlusion. MRI is the suggested diagnostic method. Pseudoaneurysms of the aortic arch as well as the subclavian and coronary arteries have been described in Behçet's disease. Mediastinal mass, mediastinitis, chyloptysis and pleurisy are other associated conditions. Pleural effusion may result from vasculitis of the pleura or thrombosis of the superior vena cava.

Natural history and prognosis

The natural history of Behçet's disease is one of exacerbations and remissions. Male sex and young age of onset are markers of a more severe prognosis. Pulmonary artery aneurysm formation has a very poor prognosis and is one of the leading causes of death in Behçet's disease; 30% of patients with this condition die within 2 years. Mean survival after the onset of haemoptysis was reported to be about 10 months in one study of patients with Behçet's disease and pulmonary artery aneurysms. A more recent follow-up study of CT findings in 13 patients receiving immunosuppressant treatment showed complete disappearance or regression of pulmonary artery aneurysms during 3–42 (mean 21) months of treatment. Disappearance and regression of the aneurysm were preceded by thrombus formation. After treatment, the thrombi regressed and pulmonary artery aneurysms disappeared. Massive bleeding has been reported in patients receiving immunosuppressant treatment, although a partial remission was achieved.

Management

Immunosuppressant treatment

Empirical anti-inflammatory and/or immunosuppressive drugs tailored to the severity of the disease remain the mainstay of treatment. A combination of cyclophosphamide and methylprednisolone is used most frequently for patients with pulmonary artery aneurysms, although no controlled trial has assessed the efficacy of this combination. For patients with pulmonary artery aneurysms, we give cyclophosphamide 1000 mg monthly as intravenous pulses or 2 mg/kg/day orally with oral methylprednisolone 1 mg/kg. For patients with severe haemoptysis, we start with intravenous pulses of methylprednisolone 500–1000 mg for 3 days together with pulsed cyclophosphamide. The prednisolone dose is then tapered depending on the clinical response, whereas the cyclophosphamide regimen is continued for at least 1 year after complete remission when it is frequently switched to azathioprine. Cyclosporine combined with coumarin was reported to be successful in a patient with a single pulmonary artery aneurysm, and FK506 was used with good results in a patient with pulmonary infiltrates. Double-blind controlled trials are needed to assess the efficacy and long-term effects of currently used and new immunosuppressant drugs for eye lesions and/or life-threatening complications in Behçet's disease.

Thrombolytic and anticoagulant treatment

Haemoptysis in Behçet's disease frequently leads to the misdiagnosis of pulmonary thromboembolism due to the frequent presence of a peripheral deep vein thrombosis and an abnormal ventilation–perfusion scan. Anticoagulation carries significant risks for patients with pulmonary artery aneurysms and must be used cautiously and only after systemic immunosuppressant treatment has been given. If thrombi are not extensive, antiplatelet treatment with, for example, low-dose aspirin is probably sufficient. Thrombolytic treatment with urokinase was tried in one patient with a thrombosed pulmonary artery aneurysm and streptokinase was given to a patient with superior vena cava syndrome. There was no evidence of new thrombotic episodes over the subsequent 2-year follow-up period. Both patients were also receiving immunosuppressive treatment; hence, the risks and efficacy of thrombolytic treatment are difficult to assess. There are no controlled studies on anticoagulants or antiplatelet aggregation therapy, and there is a lack of consensus on their use.

Clinical trials are needed to address the place of these drugs in the management of thrombotic disease in these patients.

Embolization

Embolization of a pulmonary artery aneurysm was attempted in one patient with massive bleeding. The size and number of aneurysms, the presence of superior or inferior vena caval occlusion and the potential complication of severe bleeding are the main limitations to the use of embolization in Behçet's disease.

Surgery

In cases of massive haemoptysis, urgent surgical resection may be necessary. The main problem faced by the vascular surgeon is the 25% incidence of recurrent anastomotic aneurysms after both inlay graft repair and patching. False aneurysms and arteriovenous fistulae are also common at sites of previous iatrogenic trauma. Perioperative steroid cover has been suggested to reduce the risk for complications.

Conclusion

Therefore, the mainstay of treatment in Behçet's disease is immunosuppressant therapy as in other severe vasculitides. Other treatment modalities should be used only in combination with this therapy and as palliative measures for specific complications [1].

Acknowledgements

Conflicts of interest

None declared.

Reference

1 Erkan F, Gül A, Tasali E. Pulmonary manifestations of Behçet's disease. *Thorax* 2001; **56**:572–578.