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Case Report

Behçet's Disease: Pulmonary Aneurysms Resolution with Immunosuppressive Therapy

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Abstract

The occurrence of pulmonary artery aneurysms (PAAs) in behçet's disease is rare; they are a major complication of the disease, with bad prognosis. We report a case of a 23-year-old patient, who has been diagnosed with behcet's disease on clinical criteria, with PAAs, in whom the evolution was marked by resolution of aneurysms after immunosuppressive therapy. We discus through this clinical case the thoracic angiobehçet, the therapeutic possibilities and the prognosis.

Keywords: Behçt's Disease; Pulmonary Artery Aneurysms; Immunosuppressive Drugs

Introduction

Behçet's disease is a chronic autoimmune, auto-inflammatory disease of unknown etiology, which evolves by relapses. The diagnosis is clinical, associating oral or more often oral and genital aphthous as well as systemic manifestations, the most frequent of which are cutaneous, ocular and articular, more rarely neurological, cardiac and vascular. Thoracic angio-Behçet corresponds to the involvement of the large intrathoracic vessels, it is related to the well-known vascular tropism of the disease, and includes venous or arterial thrombosis, as well as PAAs. They constitute one of the most severe manifestations of the disease. Surgical indications for these patients are now limited, as surgery carries a risk of triggering a relapse of the disease, it is also associated with significant morbidity and mortality, and treatment is medical using immunosuppressive drugs.

Presentation of Case

A 23 years-old man, without any pathological antecedent, consulted for an intermittent dry cough evolving since 3 months, with episodes of haemoptysis of weak to average abundance since 1 month, with feverish feelings. He reported to have recurrences oral and genital Ulcers for four years, three times a years. Physical examinations were normal, SaO2 was 97%, the cutaneous-mucosal examination found an oral aphthous, with white scars on the scrotum, without evidence of pseudo folliculitis. The neurological examination was unremarkable, a detailed ophthalmological examination was normal. The chest X-ray showed a right perihilar opacity suggesting a vascular origin. A thoracic CT scan with contrast injection confirmed the vascular origin of the lesion, with the presence of aneurysms of the right inferior lobar and left inferior lobar arteries (Figure 1). Behçet's disease with vascular involvement was strongly suspected, and the workup was completed: the pathergey test came back positive, Doppler ultrasound exploring the vascular axes showed an inflammatory

thickening of the left superficial femoral artery, and staged deep venous thrombosis of the left lower limb, exploration of the supra-aortic trunks did not show any abnormality. The diagnosis of Behçet's disease was therefore retained. I.V. corticosteroid boluses were given over 3 days, at a dose of 15mg/kg/d, with oral relay at a dose of 1 mg/kg/d, with monthly courses of cyclophosphamides for 6 months, and introduction of azathioprine. Two years later, the patient reported a clear clinical improvement, with disappearance of cough and haemoptysis, no more oral or genital apotheosis, nor skin lesions. The follow-up thoracic angioscan shows the complete disappearance of the aneurysms on the right and left sides (Figure 2).

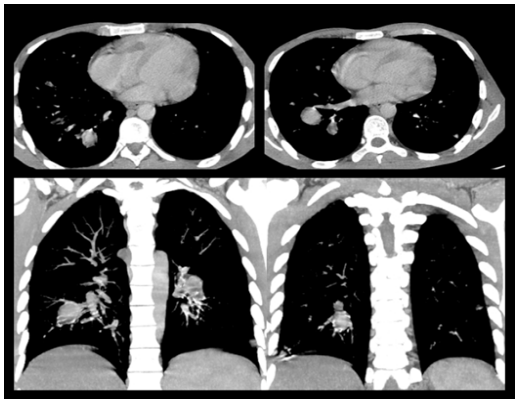

Figure 1: Thoracic CT; axial and coronal sections after injection of PDC at the arteriovenous time objectifying the presence of two addition images emanating from the branches of the right inferior lobar artery, and another one from the LIG, having an enhancement similar to that of the artery in connection with aneurysms

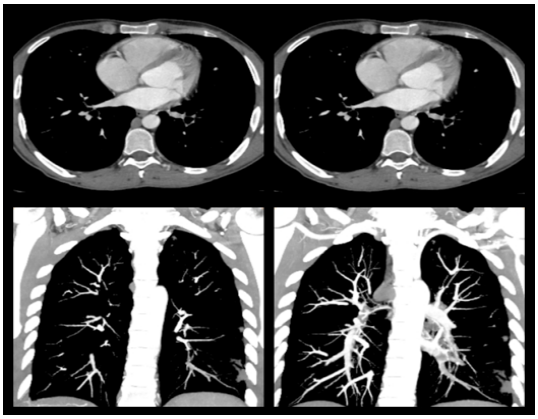

Figure 2: Control thoracic CT: axial and coronal section, after injection of PDC at the arterial time, showing the disappearance of the addition images, previously described, emanating from the branches of the right inferior lobar pulmonary artery, and left inferior lobar.

Discussion

Behçet's disease is a systemic vasculitis affecting young people, generally between 20 and 30 years of age, with a male predominance [1]. It was the Turkish dermatologist Hulusi Behçet who first described the classic triad of uveitis, oral apotheosis and genital apotheosis in 1937, which is suggestive of the disease that bears his name. BD is rare, and is seen along the Silk Road, from 20 to 420/100,000 in Turkey and 80/100,000 in Iran, to 0.64/100,000 in the UK [1]. This disease is characterized by a multi-systemic involvement, its pathogenesis is still very much debated, and it involves several genetic, infectious, environmental and immunological factors. The anatomical substrate of this disease is a vasculitis, affecting vessels of all sizes, veins and arteries. The vasa vasorum are the initial site of inflammatory infiltration leading to their obstruction and the development of neovascularization. This disease is characterized by a perivascular infiltrate of CD4 T lymphocytes, B-lymphocytes neutrophils, with production of TNF α, IL1 and IL6 cytokines; the latter are at the origin of the alteration of endothelial cells. The activation of the endothelium leads to the destruction of the 3 tunics with structural disorganization through the production of nitric oxide (NO), free radicals and matrix metalloproteinase (MMP). These parietal changes lead to localized vascular distension forming aneurysms. The chromogenic tendency of MB is thought to be due to an inhibition of the fibrinolytic power of serum and an increase in platelet agreeability, which is explained by an increase in the level of von, will brand factor and a decrease in prostacyclin due to the dysfunction of vascular endothelial cells [2, 3]. PAAs in Behçet's disease are very rare. It should be noted that Behçet disease is the most frequent cause of PAA [4]. They predominantly affect the right lower lobar artery, followed by the right and left main pulmonary arteries [5]. Clinically, the most frequent symptom is recurrent haemoptysis of low abundance due to erosion into a bronchus, as in our patient's case, with a risk of massive haemoptysis caused by aneurysm rupture. The best imaging method to confirm the diagnosis of PAA is computed tomography pulmonary angiography, it allows studying the aneurysms, to distinguish the thrombosed part of the circulating channel, shows the vascular parietal thickening by the inflammatory phenomena and the thrombosis. It will also show frosted glass witnessing an active haemorrhage or thrombosis phenomena. The spontaneous evolution of these aneurysms is towards an increase in their size and their fissuring in the bronchi with haemoptysis, as well as the occurrence of other aneurysms.

The treatment of the different manifestations of Behçet's disease remains controversial due to the scarcity of controlled therapeutic trials and the absence of standardized criteria for measuring the evolution of the disease.

Management of PAAs can be done by endovascular treatment such as embolization, but often the evolution is dominated by recurrence of haemoptysis. Surgical indications are now limited and patients are ideally operated outside of inflammatory flare-ups. The surgical options are ligation, resection with graft interposition, or stenting. Postoperative mortality and morbidity are high: thrombosis, loosening of anastomotic sutures, rapid increase in size of aneurysms left in place and rapid recurrence at the lesion site or in other vessels. Any surgery in patients with Behçet's disease carries a risk of triggering a disease flare [6]. In case of emergency, the immediate combination of immunosuppressive and anticoagulant therapy improves the postoperative prognosis, but with the potential risk of poor healing and infectious complications. Surgical treatment is required whenever the risk of aneurysm rupture is significant. Thus, the treatment of deep vein thrombosis in Behçet's disease remains controversial; venous thrombosis adheres to the vessel wall and therefore does not lead to emboli. Pulmonary embolism is rare despite the high frequency of venous thrombosis. Therefore, anticoagulants, antiplatelet agents and anti-fibrinolytic are not recommended. Another reason to avoid these agents is the possibility of coexisting pulmonary arterial aneurysms that may result in a fulminant haemoptysis. Thus, it appears that anticoagulants do not reduce the risk of recurrence of thrombosis [7]; randomized controlled trials are needed. Although there are no large-scale prospective clinical trials, in view of the series and clinical cases published, immunosuppressant is combined with, corticosteroids are essential for the treatment of vascular disorders: azathioprine for peripheral venous thrombosis, and bolus cyclophosphamide for thrombosis of the large veins and arterial aneurysms. There is therefore no consensus and treatment is most often discussed on a case-by-case basis. The protocol recommended by the European League Against Rheumatism (EULAR) for pulmonary arterial disease combines monthly bolus intravenous cyclophosphamide with bolus corticosteroids, followed by oral corticosteroids at 1 mg/kg/d. Immunosuppressive therapy is prolonged for up to 2 years in PAAs, cyclophosphamide sometimes being followed by azathioprine [7]. This was our therapeutic attitude, with good clinical evolution and total disappearance of the aneurysms. The EULAR 2018 recommendations strongly suggest the use of high-dose steroids in association with cyclophosphamide in PPAs, while the use of anti-TNF-α should be considered for refractory cases [8]; A significant increases in the level of several Th1-type cytokines, including interleukin (IL)-2, Tumour Necrosis Factor (TNF)-α, interferon (IFN)-γ, IL-12 and IL-18 has been found in serum and in some lesions of the disease [9]. These findings provide a rational basis for the development of new forms of immunomodulatory treatments. The use of biological therapies has been studied more in ocular and cutaneous involvement, but the data concerning the use of these therapies in the vascular disorders of Behçet's disease are limited. They come from a few anecdotal cases or small series, and the evaluation of their effect was biased by the concomitant administration of other treatments.

Conclusion

The treatment of PAAs in Behçet's disease remains a controversial issue, given the complications that arise from this treatment. Surgery is associated with high morbidity and mortality. Immunosuppressive drugs may be an alternative treatment, with the possibility of complete remission and disappearance of these aneurysms.

Conflicts of interest: The authors declare no conflict of interest

Authors' contributions: All authors participated in the development of this article. They also read and approved the final version of the manuscript.

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