An adolescent case of extensive Behçet’s disease successfully treated with Infliximab

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Received: 9th January 2018, Revised: 14th April 2018, 12th May 2018, Accepted: 24th May 2018


Cardiac involvement is an uncommon and life-threatening complication of Behçet’s Disease. We present a 14-year-old boy, admitted to our hospital for recurrent hemoptysis. In his radiologic evaluation, a right ventricular thrombus and pulmonary arterial aneurysm were identified. He was diagnosed with Behçet’s Disease, and then he received prednisone and cyclophosphamide. However, his cardiac thrombus enlarged. After his treatment was replaced with infliximab, the pulmonary aneurysms regressed, and the cardiac thrombus disappeared. In conclusion, infliximab should be considered as a reliable option for vascular Behçet’s Disease resistant to conventional treatment.

Key words: Behçet’s disease, infliximab, intracardiac thrombus, pulmonary embolism.

Behçet’s Disease (BD) is an auto-inflammatory disease, characterized by recurrent oral and genital aphthous ulcers, uveitis, skin lesions and potentially life-threatening conditions such as vascular involvement and thrombotic tendency.

Within systemic vasculitides, BD is a vasculitis that can affect arteries and veins of all sizes.¹⁻⁵ Although corticosteroids, immunosuppressive agents, and immunomodulators have been used to treat vascular involvement of BD, a standard treatment has not yet been established. Here we report a 14-year-old boy with Behçet’s Disease, who was successfully treated with infliximab after being diagnosed due to an intracardiac thrombus and aneurysm in the pulmonary vascular system.

Case Report

A 14-year-old adolescent boy who had been previously evaluated at different local centers with complaints of cough, dyspnea, and hemoptysis was admitted to our clinic for further evaluation with massive thrombus and aneurysms in his cardiopulmonary system. In his medical history, he had oral ulcers, 5-6 times per year, one uveitis attack and weight loss of 8 kg during the last three months. The patient’s physical examination was unremarkable. Complete blood count was normal. Sedimentation rate (38 mm/h) and CRP (16.9 mg/L) were high. The markers of Anti-dsDNA, ANA, antiphospholipid and anticardiolipin antibodies, p-ANCA, c-ANCA were all negative. HLA B51 was positive. Except for deficiency of protein C, protein S and heterozygous MTHRF mutations (C677T/1298C), other thrombophilia tests were negative. Ophthalmological examination was normal as were pathergy and tuberculin tests. Echocardiography showed a 12x14 mm. irregularly organized thrombus adjacent to the right ventricular posterior wall. Chest computed tomography angiogram (CTA) revealed aneurysms of segmental branches of the right and left pulmonary arteries with
thrombotic occlusion of the basal trunk which supplies the lower lobar segments of the right lung (Fig. 1). With the diagnosis of vascular BD, the patient who had not received any treatment before was initiated on oral steroids following intravenous (IV) pulse steroid, IV cyclophosphamide and low-molecular-weight heparin (LMWH). In the first month of treatment, the pulmonary aneurysms and intracardiac thrombus regressed, in the fourth month the intracardiac thrombus disappeared, while there was no significant change in the pulmonary aneurysm and thrombus. After the seventh dose of IV cyclophosphamide, he was readmitted with complaints of swelling and pain in the left leg. Doppler ultrasonography showed thrombi in the main superficial and deep femoral veins. Cardiac thrombus at the size of 2x1 cm reappeared (Fig. 2), new thrombus formations in the right hepatic vein and infrarenal level of inferior vena cava were detected. Cyclophosphamide was discontinued because of extensive thrombotic disease. Azathioprine and infliximab were added to the steroid and LMWH. The infliximab was administered 0, 2nd and 5th weeks and then every four weeks. After the fifth dose of infliximab, the left superficial and deep femoral vein thrombus formations disappeared. Following the tenth dose of infliximab, the intracardiac thrombus disappeared (Fig. 3). Thrombus in the right hepatic vein and inferior vena cava disappeared just after the sixteenth dose of infliximab. After six years of infliximab with azathioprine and low dose steroid treatment, no complaints remained. Moreover, his echocardiography and abdominal and lower extremity Doppler ultrasonography investigation results were normal. Improvements in aneurysms with chronic thrombotic changes were detected in thorax CTA (Fig. 4). Two years after the diagnosis LMWH was replaced with oral anticoagulant since his thrombus regressed, and no more thrombus developed.
Written informed consent for the publication of this case report and any accompanying images were obtained from the patient’s parents.

Discussion

We reported a patient with BD associated with intracardiac thrombus and pulmonary artery aneurysms, that was unresponsive to conventional treatment but responded well to infliximab. Due to recurrent oral ulcers, uveitis, thrombus, and aneurysms, the patient was diagnosed with BD. The diagnosis of BD is made by recognizing the presence of certain clinical findings in a patient since there are no pathognomonic signs, or specific laboratory, radiologic or histologic findings for BD. In 2016 the Pediatric Behçet’s Disease (PEDBD) study group established a new consensus including six categories (Recurrent oral aphthosis, Genital ulceration or aphthosis, Skin involvement, Ocular involvement, Neurological signs and Vascular signs). According to this new consensus, at least three of the aforementioned categories are required to define pediatric BD.

The prevalence of cardiovascular involvement in BD varies between 7.7% to 43% according to different ethnic groups. Intracardiac thrombosis is the most common form of cardiac involvement. It usually involves the right side of the heart (in 78% of cases). Aksu et al. recommended that the diagnosis of BD should also be considered if a mass in the right-sided cardiac chamber is present even in the absence of the other clinical findings. It is strongly associated with pulmonary artery involvement, such that, when detected, it also becomes mandatory to evaluate pulmonary arteries with thorax CT. Seyahi et al. studied pulmonary artery involvement in BD including 25% of them associated with the intracardiac thrombus formation.

The methodology of treatment in BD is directly related to the disease’s severity and organ involvement. It is well known that the prognosis of cardiac and vascular thrombi during BD is poor. However, there is no consensus on the treatment of cardiac, pulmonary and vascular thrombi associated with BD. Treatment aims to resolve the thrombus and prevent recurrences. Initial treatment for intracardiac thrombus and pulmonary aneurysms commonly involve cyclophosphamide and prednisone. However, recurrences of intracardiac thrombus while administering these conventional agents led us to switch the treatment to infliximab with azathioprine. Although there are few studies on azathioprine with vascular manifestations...
of BD, its use is suggested by Hatemi and colleagues for the treatment of cardiac and pulmonary involvement.\textsuperscript{16} Infliximab (TNF-α antagonist) seems to be a practical new treatment option. The pathogenesis of the thrombosis in BD is unknown, and the underlying mechanisms are unclear; however, it is thought that it is mainly due to the endothelial damage and dysfunction of vessels. Prothrombotic factors along with common prothrombotic polymorphisms have been studied. However, the data collected up to now have been conflicting. Infliximab may inhibit the activation of infiltrated mononuclear cells by blockade of TNF and TNF-producing cells, resulting in the prevention of thrombosis.\textsuperscript{16-20} After four years of infliximab, azathioprine, low dose steroid and oral anticoagulant treatment, our patient had no complaint or new thrombus. Anticoagulation treatment together with immunosuppressive therapy is an advised treatment option in Behçet’s cases with intracardiac thrombus formation. However, there is no agreement between rheumatologists in the therapeutic approach to thrombosis in BD.\textsuperscript{12,20}

In conclusion, cardio-pulmonary involvement is a rare and life-threatening condition in BD. Cyclophosphamide and steroid remain the mainstay of initial treatment for such cases. However, infliximab should be kept in mind for vascular BD resistant to conventional treatment.

REFERENCES


