Cardiovascular Involvement in Behçet Disease: Clinical Implications

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Abstract

Keywords

- Behçet disease
- cardiovascular involvement
- vasculitis
- pulmonary embolism
- intracardiac thrombus

Behçet disease (BD) is a multisystem disorder, with vasculitis as its underlying pathological process, in contrast to the classic triad of recurrent oral and genital ulcerations, with uveitis. Vascular involvement in BD includes venous thrombosis, arterial occlusion, and pulmonary artery and aortic aneurysm formation. Cardiac involvement is rare and often obscure. It includes intracardiac thrombi formation, and is associated with a poor prognosis. Our objectives are to describe two cases with BD, complicated with vascular and cardiac involvement, and to raise awareness of these rare complications, the needed routine surveillance, and thus to prevent inappropriate interventions, serious outcomes, and mortality. We present two male patients from the Mediterranean Basin with BD. The first was diagnosed early as a BD patient. The second was diagnosed at the time of cardiovascular (CV) involvement. We recommend that patients who are diagnosed, or even suspected of suffering from BD, especially in endemic areas along the Silk Route pathway, should be followed up routinely for CV involvement, even if rare, obscure, or with a bizarre presentation.

Behçet disease (BD) is a multisystem disorder that involves joints, blood vessels, the heart, the central nervous system, and the gastrointestinal tract. The disease is considered more prevalent in the areas surrounding the old Silk Trading Route, in the Middle East, and in Central Asia. A large number of studies have shown a linkage between the disease and HLA-B51 and HLA-B27 antigens.^{1–4}

Vasculitis is the underlying pathological process, in contrast to the classic triad of recurrent urogenital ulcerations, with uveitis.^{5,6}

Vascular involvement in BD includes venous thrombosis, arterial occlusion, pulmonary artery, and aortic aneurysm formation.^{7–12}

Cardiac involvement is rare, often obscure. It is associated with a poor prognosis and involvement of major vascular structures of the heart with coronary artery aneurysm formation; the conduction system; the endocardium with endomyocardial fibrosis; the pericardium; and the cardiac

skeleton with aneurysm of the interatrial septum and patent foramen ovale, ventricular aneurysm, mitral valve prolapse with mitral regurgitation, and aortic aneurysm and sinus of Valsalva aneurysm.^{13–17}

It was mentioned that younger age and cardiac involvement may be specific to our geographic area (the Mediterranean Basin).¹⁸

Our *objectives* are to raise awareness to these rare cardiovascular (CV) complications in BD and to emphasize the importance of routine surveillance for CV involvement and thus to prevent serious outcomes, inappropriate interventions, and mortality.

Method

We present two male patients from the Mediterranean Basin with BD. The first was diagnosed early as a BD patient. The second was diagnosed at the time of CV involvement.

Fig. 1 Angiographic study of the upper thoracic veins, showing significant obstruction with collateral circulation.

Case 1: A 65-year-old man, known to suffer from BD, required permanent pacemaker (PPM) therapy for a complete heart block. Two attempts of implanting an endocardial PPM via the upper thoracic veins failed, due to an old obstruction (► **Fig. 1**).

Case 2: A 22-year-old man with severe clinical (fever and dyspnea) and chest X-ray findings was suspected of having bilateral pneumonia. His chest X-ray demonstrated right side less transparency (Westermarck sign) (► **Fig. 2**). His CT angiogram documented pulmonary embolism (PE) (► **Fig. 3**), and an echocardiogram revealed a large thrombus in the right atrium (► **Fig. 4**).

Fig. 2 Chest X-ray of Case 2, demonstrating right side less transparency (Westermarck sign).

His past history included recurrent epididymitis and aphthous stomatitis, compatible with a BD diagnosis.

Therapy with steroids, immunosuppressive, and anticoagulant therapy was initiated. Two months later, a recurrent PE was diagnosed.

Discussion

BD is an inflammatory disorder, with multisystem manifestations, of unknown cause, characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions. All these common manifestations are self-limiting, except uveitis, that can cause blindness. The disease consists of recurrent attacks of acute inflammation. BD is considered more prevalent in the area surrounding the old Silk Route, in the Middle East, and in Central Asia. Involvement of the gastrointestinal tract, central nervous system, and large vessels is less frequent, although it can be life threatening.¹ It has been documented that there are geographical differences in the expression of the disease, in different areas of the world. In Turkey and the Mediterranean Basin, it is more prevalent in younger males, and the clinical expression is greater CV involvement,^{2,18} whereas in Japan it is more prevalent in women, who suffer from gastrointestinal involvement; thus, the question of genetic polymorphism has been raised.

It has been shown that susceptibility to BD is strongly associated with the presence of HLA-B51 cells,¹ and the frequency within families has been shown to be up to 15%. Environmental factors, such as infectious agents, have also been implicated in this pathogenesis.

It is accepted and concluded according to epidemiologic findings that both environmental and genetic factors contribute to the development of the disease.¹

It has been shown that the common histological lesion of all clinical manifestations appears to be vasculitis.^{4,5} Many studies concerning the vascular involvement and the thrombotic

Fig. 3 CT angiogram of Case 2, demonstrating right pulmonary artery with right pulmonary embolism.

Fig. 4 Transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE), demonstrating a large thrombus in the right atrium.

tendency in BD have documented the importance of the thrombotic tendency associated with T-cell-mediated neutrophilic inflammation as one of the main features of the disease.

Also, the finding of decreased plasminogen fibrinolytic activity in patients with active BD presents a possible disturbance in the blood coagulation mechanism in BD patients.⁶

Notably, the issue of CV involvement in BD, which was thought to be a relatively rare manifestation of the disease, has attracted much attention of cardiologists over the past few decades, owing to the widespread use of highly informative diagnostic techniques, such as echocardiography. As a result, many reports have been published, indicating symptomatic and asymptomatic involvement of different structures of the heart and all types of vessels, with predominantly right-sided heart disease and venous thrombotic pathology, including superior vena cava obstruction, hepatic veins, Budd–Chiari syndrome, and pulmonary artery aneurysms.^{6–18}

Conclusion

We have described two male patients with BD, and with CV involvement.

We recommend that patients who are diagnosed, or even suspected of suffering from BD, especially in endemic areas along the Silk Route pathway, should be followed up routinely for CV involvement, even if rare, obscure, or with a bizarre presentation, so that it can be treated early in time, preventing death and unnecessary or faulty intervention approaches.

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