



**Case Report**

**Extensive Thrombophlebitis in a patient with Behçet's disease**

**Vaibhav C Chewoolkar<sup>\*¶</sup> MD, Raminder K Singh<sup>†</sup> MD and Shailesh H Bamborde<sup>‡</sup> MBBS**

**\*Assistant Professor, <sup>†</sup>Professor and Head, <sup>‡</sup>Resident, Department of Medicine, Seth GS Medical College & KEM Hospital, Mumbai, Maharashtra, India**

*(Received 24 May 2010 and accepted 18 July 2010)*

**ABSTRACT:** Behçet's disease (BD) is a systemic vasculitis of unknown origin. It is well established that Behçet's disease predisposes strongly to venous and arterial thrombosis and recurrent superficial and deep thrombophlebitis of the lower extremities. There are different considerations about the pathogenesis of the vascular complications and the tendency for thrombosis in BD. We came across a patient of Behçet's disease in whom extensive thrombophlebitis and erythema nodosum, which was precipitated by a needle prick, responded to corticosteroids. This case highlights the importance of suspicion of this disease in patients presenting with extensive thrombophlebitis.

**KEY WORDS:** *Thrombophlebitis; Behçet's disease; Vasculitis*

**INTRODUCTION**

Behçet's disease is a multisystem disorder with varying clinical presentation. Mucocutaneous involvement in the form of oro-genital ulcers, erythema nodosum, papulo-pustular lesions and superficial thrombophlebitis are frequently found. We came across a case of Behçet's disease in whom massive thrombophlebitis was precipitated during fever in a patient which responded equally rapidly to treatment. This case underscores the need for a very cautious approach in managing such patients.

**CASE REPORT**

A 20-year-old Indian male was admitted to our hospital with complaints of high grade fever and joint pain involving small joints of hands and feet for last five days. The patient reported repeated episodes in the previous two months, with symptomatic relief with analgesics and antipyretics. The joint pain was of symmetrical distribution involving small hand and foot joints and was also accompanied by early morning stiffness lasting

more than an hour. Also, peculiarly, the history was given that every time for about a day after analgesic injection, the pain used to worsen followed by gradual relief. On repeated questioning, the patient revealed the history of recurrent aphthous oral ulcerations (**Figure 1**) with genital ulcers (**Figure 2**). Three painful lesions of erythema nodosum on the legs were noticed during the physical examination over his feet. Maculopapular rash was present all over the body.



**Figure 1: Oral ulcer**

<sup>¶</sup>**Correspondence at:** Department of Medicine, Seth GS Medical College & KEM Hospital, Mumbai 400012, Maharashtra, India; Tele-fax: 022-24172267; Email: [drvaibhavc@yahoo.com](mailto:drvaibhavc@yahoo.com)



**Figure 2: Ulcer under the prepuce**

Hemoglobin, leukocyte count and thrombocyte count were 11.8 g/dl, 12,400/mm<sup>3</sup> and 3,50,000/mm<sup>3</sup>, respectively on presentation. Erythrocyte sedimentation rate was 47 mm/hour. Tests for antinuclear antibodies (ANA), rheumatoid factor (RF), anti dsDNA and anti-neutrophil cytoplasmic antibodies (ANCA) were negative. Patient was started on oral Diclofenac, Paracetamol and intravenous Ceftriaxone. On the second day of his inpatient stay, approximately 24 hours after a needle prick for infusion of normal saline, he developed massive swelling and severe pain of both lower and upper extremities along with pain and swelling at the prick site. Clinical examination revealed severe tenderness of the extremities with prominent superficial veins (**Figure 3**) and palpable tender nodules. All hand and foot joints were swollen and tender with stiffness.



**Figure 3: Superficial thrombophlebitis with prominent veins**

A color doppler examination done at this time showed incompetent and dilated saphenous, and femoral veins within the entire course with extensive thrombophlebitis of the superficial veins. Deep veins and arteries were normal. Thrombophilia testing was negative which included antithrombin III, protein C, protein S, homocysteine, activated protein C resistance test and antiphospholipid antibodies. Biopsy from a single nodule on the shin showed infiltration by

neutrophils in the vessel walls. A pathergy test was done keeping in mind, the possibility of Behçet's disease which turned out to be positive. A slit lamp examination showed no uveitis. With this clinical picture, a diagnosis of Behçet's disease was made and patient was started on intravenous Dexamethasone 8 mg eight hourly and continued for three days. Triamcinolone buccal paste was started for painful oral ulcers. The patient's high fever present throughout the first two days of his hospitalization subsided after starting steroids. Oral Prednisone (1 mg/kg/day) was started on fourth day. Limb edema, thrombophlebitis and pain also responded to this treatment. Rash gradually faded over one week. The patient was discharged on oral Prednisone.

## DISCUSSION

Behçet's disease is a rare form of vasculitis of obscure etiology characterized by a triad of recurrent oral aphthous ulcers, genital ulcers and uveitis. As there is no specific test for the definite diagnosis of BD, the diagnosis of this disease depends on the clinical criteria.<sup>1</sup> It is now recognized as a multi-system disorder manifesting with attacks of mucocutaneous lesions, arthritis, venous thrombosis, arterial aneurysms, intestinal ulcers, pulmonary lesions and central nervous system lesions.<sup>2</sup>

Characteristic manifestations of Behçet's disease are recurrent, which may last a few days to several weeks. Mucocutaneous findings, including oral and genital ulcers, erythema nodosum-like vasculitic nodular lesions, acneiform lesions, papulopustular lesions and superficial thrombophlebitis, are the most frequently observed features of Behçet's disease.

The pathogenesis of Behçet's disease is unknown. An enhanced and dysregulated immune response has been suggested as the underlying pathology, and this can be triggered by environmental agents, mainly microbes, in genetically susceptible individuals.<sup>3</sup> Behçet's disease has been strongly associated with HLA-B51, and this association has been confirmed in different ethnic groups.<sup>4,5</sup>

The skin pathergy reaction, another skin manifestation, has been recognized as a pathognomonic feature of Behçet's disease, and it demonstrates the hyperreactivity of skin to nonspecific trauma.<sup>6</sup> In a positive pathergy test, pricking the skin with a sterile needle, with or without the injection of a small amount of saline, gives rise to a 1 to 2-mm papule usually surrounded by an erythematous halo. The papule may remain unchanged or transform into pustule which becomes maximum in size after 48 hours, and disappears within 4-5 days. A positive reaction is the development of an erythematous papulopustular skin reaction, similar to those observed

spontaneously in patients, at the needle prick site at 48h. A similar hyperreactivity can be elicited at other body sites, and other Behçet's disease manifestations such as oral and genital ulcers, arthritis, superficial thrombophlebitis and even arterial aneurysms can be induced following trauma. Multiple mechanisms have been implicated in the hyperinflammatory response seen in BD including endothelial activation induced by vessel wall trauma, over expression of a Th1 inflammatory cytokine profile<sup>7</sup> and poly morpho nuclear cell hyperfunction.<sup>8</sup> Vasculitis is an important feature of Behçet's disease. Although any large or small arteries or veins may be involved in Behçet's disease, previous reports have emphasized the high frequency of venous involvement and the rarity of arterial involvement.<sup>9</sup> Deep vein thrombophlebitis was the most frequent venous manifestation, and the most commonly involved site was the lower extremities followed by the superior vena cava, the inferior vena cava and the upper extremities with unpredictable large or small venous involvement<sup>10</sup>.

Approximately 5% of patients with Behçet's disease have neurological involvement, out of which, 80 % have parenchymal involvement with pyramidal signs and symptoms and approximately 20% cases can have dural sinus thrombosis.<sup>11</sup> It can occur even in relatively young patients with no vascular risk. Our patient had certain unusual features, such as precipitation of extensive thrombophlebitis with disseminated erythema nodosum after needle prick in addition to the classical symptoms. Behçet's disease itself may explain thrombophlebitis in this case, but an additional risk factor, like venous incompetence, could be a reason for extensive involvement. Probably, the flaring up of pain and swelling after injections which the patient used to get earlier could be episodes of repeated thrombophlebitis.

Treatment is usually multidisciplinary, requiring close collaboration among specialists in rheumatology, dermatology, ophthalmology, and others. The goal of therapy is to suppress inflammation and prevent relapses, especially involving ocular vessels. Systemic corticosteroids are the first line agents. Immunosuppressive agents like Cyclophosphamide and Azathioprine are used in severe and recurrent relapses. Novel therapeutic armamentarium includes use of TNF-alpha inhibitors and Interferon-alpha.

This case reinforces the need for consideration of cautious attitude before even minor surgical procedures or needle pricks in those with BD. Unless intervention is urgently required, it is prudent to postpone invasive approaches in these patients until the inflammatory component of BD has been controlled with medical therapy.<sup>12</sup> Behçet's disease runs a chronic course with unpredictable exacerbations and remissions, the

frequency and severity of which may diminish with time.

## CONCLUSION

Behçet's disease remains an elusive disorder, having variable clinical presentations and unknown etiology. Behçet's disease thus remains a significant challenge to clinicians of many specialties. It should be suspected in any patient presenting with repeated or extensive thrombophlebitis. Caution should be exercised in such patients before any invasive intervention in order to prevent a flare.

## REFERENCES

1. International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's disease. *Lancet*. 1990 May;335(8697):1078-80.
2. Sakane T, Takeno M, Suzuki N, et al. Behçet's Disease. *N Engl J Med*. 1999 Oct;341(17):1284-91.
3. Lehner T, Lavery E, Smith R, et al. Association between the 65-kilodalton heat shock protein, *Streptococcus sanguis*, and the corresponding antibodies in Behçet's syndrome. *Infect Immun*. 1991 Apr;59(4):1434-41.
4. Mizuki N, Inoko H, Ohno S. Molecular genetics (HLA) of Behçet's disease. *Yonsei Med J*. 1997 Dec;38(6):333-49.
5. Mizuki N, Ota M, Yabuki K, et al. Localization of the pathogenic gene of Behçet's disease by microsatellite analysis of three different populations. *Invest Ophthalmol Vis Sci*. 2000 Nov;41(12):3702-8.
6. Ozdemir M, Balevi S, Deniz F, et al. Pathergy reaction in different body areas in Behçet's disease. *Clin Exp Dermatol*. 2007 Jan;32(1):85-7.
7. Ben AM, Houman H, Miled M, et al. Involvement of chemokines and Th1 cytokines in the pathogenesis of mucocutaneous lesions of Behçet's disease. *Arthritis Rheum*. 2004 Jan;50(7):2291-5.
8. Yamashita N. Hyperreactivity of neutrophils and abnormal T cell homeostasis: a new insight for pathogenesis of Behçet's disease. *Int Rev Immunol*. 1997;14(1):11-9.
9. Koc Y, Gullu I, Akpek G, et al. Vascular involvement in Behçet's disease. *J Rheumatol*. 1992 Mar;19(3):402-10.
10. Sagdic K, Ozer ZG, Saba D, et al. Venous lesions in Behçet's disease. *Eur J Vasc Endovasc Surg*. 1996 May;11(4):437-40.
11. Yazici H, Fresko I, Yurdakul S. Behçet's syndrome: disease manifestations, management and advances in treatment. *Nat Clin Pract Rheumatol*. 2007 Mar;3(3):148-55.

12. Park MC, Hong BK, Kwon HM, et al. Surgical outcomes and risk factors for postoperative complications in patients with Behçet's disease. *Clin Rheumatol.* 2007 Sep;26(9):1475-80.