



Case Report

Behçet's disease with HIV infection: Response to antiretroviral therapy

Vikram K. Mahajan, Nand Lal Sharma, Vikas C. Sharma, Ramesh Chander Sharma, Sandip Sarin

Department of Dermatology, Venereology and Leprosy, Indira Gandhi Medical College, Shimla, India

Address for Correspondence: Dr. N . L . Sharma , Department of Dermatology, Venereology & Leprosy, Indira Gandhi Medical College Shimla 171001 (H.P.) India. E-Mail: nandlals@hotmail.com

ABSTRACT

The differential diagnosis of oral ulcerations in a patient with AIDS/HIV infection is often challenging to the clinician. While old diseases have appeared in a new garb, many new ones are also being recognized. The association of Behçet's disease and AIDS/HIV infection has been recently recognized. We present an HIV-positive patient having oro-genital aphthosis conforming to the diagnostic criteria for Behçet's disease. Erythema nodosum, periphlebitis, erythematous papulopustular lesions, half and half nails, ocular congestion, raised ESR and dimorphic anemia were some other features present. He had low CD4+/CD8+ counts. He had no other HIV-related disease. He responded well to triple antiretroviral treatment alone. The possible pathomechanism of the occurrence of both diseases is also discussed.

Key Words: Behçet's disease, HIV-disease

INTRODUCTION

Behçet's disease (BD) is a chronic inflammatory multisystem disorder. It is characterized by recurrent oro-genital ulcerations, cutaneous lesions, uveitis, arthritis, thrombophlebitis, arterial aneurysms, and involvement of the gastrointestinal, pulmonary and central nervous systems. Its exact cause remains elusive, but an interplay of viral, bacterial, autoimmune, genetic or environmental factors has been speculated.^[1]

Many of the clinical features of BD may be seen with HIV infection. Arthritis, painful oral aphthous ulcers, recurrent genital ulcerations due to herpes simplex infection, folliculitis, and acneiform eruptions have all been described in association with HIV infection.^[2] An association between BD and AIDS/HIV infection has been noted only recently. A PubMed search for "HIV and Behçet's disease" gave only 21 hits. The aphthous-like oral ulcerations of patients with HIV infection

represent a challenging differential diagnosis.

We report our experience in treating a patient with HIV infection who had developed BD in the absence of any HIV-related clinical disease.

CASE REPORT

A 38-year-male, a lorry driver, was hospitalized with the complaint of recurrent episodes of painful oro-genital ulcerations since 3 months. He had developed slowly enlarging, multiple, painful mucosal ulcers of the upper lip associated with fever, excessive salivation, painful speech and odynophagia. Subsequently, the soft palate, tongue and buccal mucosa were involved. Over the next 7-10 days, new painful ulcerative lesions had appeared on the penoscrotal area, while a few older lesions healed with or without treatment.

He also complained of multiple, erythematous, painful

How to cite this article: Mahajan VK, Sharma NL, Sharma VC, Sharma RC, Sarin S. Behçet's disease with HIV infection: Response to antiretroviral therapy. *Indian J Dermatol Venereol Leprol* 2005;71:276-8.

Received: November, 2004. **Accepted:** April, 2005. **Source of Support:** Nil.



and tender nodular lesions over the shins associated with pain and swelling of ankles during the last 1-2 months. There was a history of joint pains in the knees, elbows, wrists and ankles that subsided with analgesics. He gave history of unsafe sex. He had been treated for tuberculous pleural effusion 2 years back and had significant weight loss in the last 3 months.

Mucocutaneous examination showed poor orodental hygiene and a white coated tongue. There were multiple, round-to-oval, deep, punched out ulcers and a few scars of variable size involving the lateral borders of the tongue [Figure 1], soft palate and buccolabial mucosa. The ulcers were covered with yellow necrotic slough and had an erythematous halo as in aphthous ulcers. Similar lesions were present on the penile shaft, penoscrotal area and frenum. He also had tender subcutaneous nodules suggestive of erythema nodosum on both shins. A few nodular and plaque lesions of periphlebitis observed over the dorsal aspects of the hands were attributed by him to venipuncture done for parenteral alimentation in another hospital a few days earlier. There were a few erythematous papulopustules on the neck, back and thighs. He had half and half nails. His hair was normal.

Examination of the abdomen, lungs, and cardiovascular and central nervous systems showed no abnormality. He weighed 44 kg. Except for conjunctival congestion, the ophthalmic examination was normal. Laboratory investigations showed a normal blood biochemistry, X-ray chest, ECG, stool and urinalysis. Except for a high ESR (115 mm in the 1st hour) and mild dimorphic anemia (Hb, 8 gm%), the hemogram showed no other abnormality. He had a non-reactive VDRL test and a positive latex agglutination test for C-reactive proteins. He was HIV-positive by Genedia HIV-ELISA, Capillus latex agglutination and Unigold rapid card tests. His CD4 and CD8 counts were 107 and 1642 cells/mm³ respectively and the CD4 to CD8 ratio was 0.07 (normal, 0.6-2.8). Viral load studies could not be done because he could not afford them. Direct impression smears stained with Gram's and Giemsa stains, and KOH mounts from orogenital ulcers and the tongue showed no multinucleated giant cells or organisms. Dark ground illumination study from the genital ulcer was negative.

Histopathology of an ulcer on the frenum showed acanthosis, broadened and elongated rete ridges, and an ulcerated area covered with neutrophils and necrotic debris. The deeper vascular channels had a focal mononuclear infiltrate. Biopsy from a subcutaneous nodule showed histologic features of erythema nodosum. The pathology test was negative.

The patient was given ampicillin 500 mg qid and fluconazole 100 mg/day empirically for 10 days. With the diagnosis of Behçet's disease and HIV infection, he was started on anti-retroviral treatment (ART), a combination of stavudine (300 mg) lamivudine (150 mg) and nevirapine (200 mg) twice daily along with supportive treatment such as liquid/semisolid nutritional supplements and antiseptic oral swishes.

After 4 weeks of ART, while most of his orogenital ulcers healed with scarring, a few new ones kept appearing. Other cutaneous lesions subsided and his general condition improved. He was discharged with the advice to continue ART. Oral colchicine 0.5 mg twice daily was added on a subsequent visit as new lesions were still appearing. He is under follow up.

DISCUSSION

The diagnosis of BD in our patient was based on clinical criteria established by an International Study Group.^[1] In addition to extremely painful orogenital aphthosis, he had erythema nodosum, polyarthritis, periphlebitis and conjunctival congestion. He also had serological evidence of HIV infection.

Most HIV related oral ulcers are candidal, viral or bacterial in origin, and in a few cases, are neoplastic or just idiopathic. In HIV infected patients, recurrent aphthous ulcers (RAU) are more severe and prolonged, in contrast to oral herpes simplex, and occur on the non-keratinized mucosa of the buccolabial areas and the lateral margins of the tongue.^[3] Major RAU have larger lesions (> 1 cm) associated with severe pain, and difficulty in swallowing and speech.^[3] However, the simultaneous occurrence of oral and genital aphthae, as in our patient, suggests the coexistence of BD with HIV infection.

BD is characterized by vasculitis and thrombosis histologically.^[4] Immune complex mediated vasculitis of small as well as large vessels is common and accounts for most of the pathologic process in BD.^[5] The pathology of BD, however, is not diagnostic and varies with the type and duration of the lesion sampled. Peripheral neutrophils from patients with BD show increased expression of the adhesive molecule integrin Mac-1 (CD 11b/CD 18), as well as a greater degree of migration and adhesiveness to lesional endothelial cells.^[6] Studies also implicate immune dysregulation due to decreased T-cells, abnormal B-cell function and decreased natural killer cell activity in BD.^[4] The number of IL-2- and interferon- γ -producing CD4 and CD8 cells was found to be significantly higher in untreated patients with active Behçet's disease and significantly lower in patients treated with immunosuppressive drugs,^[7] suggesting their importance in the immunopathogenesis of BD. However, whether autoimmunity is a primary or a secondary event in the development of BD is not known.^[8] In our patient, the overall immunosuppression induced by HIV infection may be responsible for the low CD4+/CD8+ counts.

The occurrence of both Behçet's disease and HIV infection may be coincidental, a Behçet's-like presentation of the complications of HIV disease, or HIV infection causing or predisposing to a Behçet's-like illness.^[2] The disturbances in the immune system due to HIV infection may result in clinical or immunological findings usually associated with autoimmune diseases as also increased susceptibility to certain viral infections.^[2] These, in turn, possibly have a direct effect on the vessel wall through an immune complex mechanism or an indirect effect. Considering the number of reported cases, an association between BD and HIV infection seems plausible irrespective of the stage of HIV disease.

The frequency and spectrum of HIV associated mucocutaneous manifestations increase with clinical and immunologic deterioration due to HIV infection. There may be an increased risk of autoimmune disease

secondary to immune dysregulation.^[9] Interestingly, our patient did not show any clinical signs of HIV infection in spite of low CD4 counts. Weight loss appears to be due to poor oral intake because of painful oral ulcers and we do not know his HIV status at the time that he had a pleural effusion.

In immunocompetent individuals, oral aphthae heal in 3 to 4 weeks. After the institution of ART, our patient, who had severe persistent BD lesions for more than 3 months, had symptomatic improvement, a decrease in the severity, size and number of lesions, and fewer recurrences. With the progression of HIV disease, autoimmune diseases tend to improve.^[9] However, the improvement of Behçet's disease with zidovudine,^[10] and in our patient with triple drug ART suggests otherwise and also favors the association of BD with HIV infection.

REFERENCES

1. MacCormack M, Phillips T. A clinical review. Behçet's disease: Wounds 2002;14:275-83.
2. Stein CM, Thomas JE. Behçet's disease associated with HIV infection. J Rheumatol 1991;18:1427-8.
3. Greenspan D, Greenspan JS. HIV-related oral disease. Lancet 1996;348:729-33.
4. Gbate JV, Jorizzo JL. Behçet's disease and complex aphthosis. J Am Acad Dermatol 1999;40:1-18.
5. Rizzi R, Bruno S, Dammacco R. Behçet's disease: an immune-mediated vasculitis involving vessels of all sizes. Int J Clin Lab Res 1997;27:225-32.
6. Kanekura T, Gushi A, Iwata M, Fukumaru S, Sakamoto R, Kawahara K, et al. Treatment of Behçet's disease with granulocyte and monocyte adsorption apheresis. J Am Acad Dermatol 2004;51:S83-7.
7. Sugi-Ikai N, Nakazawa S, Nakamura S, Ohno S, Minami M. Increased frequencies of interleukin-2 and interferon- γ producing T-cells in patients with active Behçet's disease. Invest Ophthalmol Vis Sci 1998;39:996-1004.
8. Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. New Eng J Med 1999;341:1284-91.
9. Hodgson TA, Fidler SJ, Speeght PM, Weber JN, Poter SR. Oral pemphigus vulgaris associated HIV infection. J Am Acad Dermatol 2003;49:313-5.
10. Buskila D, Gladman DD, Gilmore J, Salit IE. Behçet's disease in a patient with human immunodeficiency virus infection. Ann Rheum Dis 1991;50:115-6.