Behcet syndrome: A rare cause of recurrent genital ulceration

Sanya Kamal Narang, Hiral A. Shah
Department of Dermatology, Venereology and Leprosy, Government Medical College and S.S.G. Hospital, Vadodara, Gujarat, India

Address for correspondence:
Dr. Sanya Kamal Narang, OPD-1, SSG Hospital, Vadodara - 390 001, Gujarat, India.
E-mail: narangsanya14@gmail.com

Abstract

Behcet syndrome (BS) is a chronic relapsing multisystem vasculitis with skin findings with an important contribution of genetics. Here, we present a case of a 16-year-old male with a complaint of recurrent genital, and oral ulceration with skin lesions and a history of recurrent thrombophlebitis at the sites of venepuncture. There were no systemic manifestations. Pathergy test and HLA-B51 were negative. The diagnosis was confirmed based on the International Criteria for Behcet disease (ICBD) for BS. Tapering doses of systemic corticosteroid and colchicine showed promising response and regression of lesions.

Key words: Aphthous ulcers, Behcet, colchicine, genital ulcers

Introduction

Behcet syndrome (BS) is a vasculitic multisystem inflammatory disorder characterized by relapsing bipolar aphthosis and inflammatory eye changes known as triple symptom complex first described in 1937 by the Turkish dermatologist Hulusi Behcet.[1] Associated features include thrombophlebitis, erythema nodosum, arthritis, and involvement of the gastrointestinal tract and central nervous system. It was a leading cause of blindness, most often among young men in Japan.[2] Prominent regional differences exist in the expression of BS around the globe.[3] BS is more prevalent in the Mediterranean and eastern rim of Asia, where the prevalence of HLA-B5 (51) is high.[1] Environmental factors like the microbiome, such as streptococcal strain (*Streptococcus sanguis*) and herpes simplex viruses, are thought to play a role in its pathogenesis.[4] Type 1 helper T-cell (Th1) response, MI-type differentiation of monocytes/macrophages, and hyperactivity of neutrophils have been observed in BS. Endothelial activation, production of neutrophil extracellular traps, and thrombotic tendency are secondary to inflammatory changes in BS.[1] There is no confirmatory laboratory test for BS. As there is no marker for the syndrome, diagnostic criteria have been suggested to define the complex of symptoms and signs. To diagnose BS, different sets of criteria have been developed like Japanese criteria, International Study Group Criteria (ISG), and International Criteria for Behcet Disease (ICBD), but all have limitations at bedside diagnosis.[1]

Case Report

A 16-year-old sexually inactive male presented with recurrent painful oral and genital ulceration for 10 months, increased over the last 15 days. The patient had skin lesions over the legs. On examination, multiple round or oval-shaped superficial lesions with rolled borders, covered with white or grayish pseudo membrane, and surrounded by an erythematous halo over the inner aspect of the labial mucosa and tongue. Similar large ulcers were present over the scrotum, penoscrotal junction, and penile shaft with the scar of healed previous lesions [Figures 1 and 2a]. The patient had high grade fever at the time of presentation. No joint pain or gastrointestinal symptoms were present. Erythema-nodosum (EN)-like lesions were present over the sides of both feet [Figure 3]. The patient had no history of drug intake prior to the appearance of lesions. The rest of the systemic examination was insignificant. All routine investigations, including complete blood count, and liver and renal function tests, were within normal range. Serum HIV antibody test, Venereal Disease Research Laboratory (VDRL) test, and serum Herpes Simplex Virus 1 and 2 IgG, IgM were nonreactive. Chest X-ray was normal. Pathergy test and serum HLA-B51 were negative. Inflammatory markers such as CRP and ESR were elevated. Eye examination was normal. Anti-nuclear antibody was +2 with a coarse speckled pattern, but profile was negative. 2D echocardiogram was suggestive of left ventricular hypertrophy and medicine reference was sought for the same. Recurrent superficial thrombophlebitis was noted in veins where cannulas were inserted. A 4 mm punch biopsy was done from the edge of the genital ulcer. Hematoxylin- and eosin-stained sections showed mixed inflammatory infiltrate. Medium vessels in the dermis were showing necrotizing vasculitis and thrombus formation. Diagnosis of Behcet was considered based on history, clinical, and histopathology findings. The diagnosis was confirmed following ICBD criteria [Table 1].

The patient was started on injection dexamethasone 6 mg IV once in the morning and a tablet of colchicine

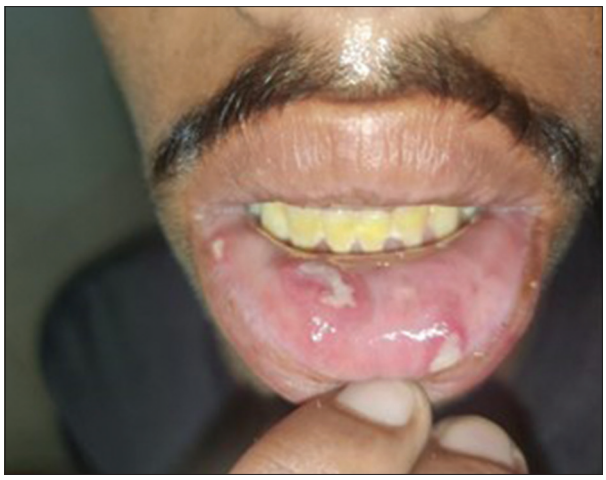

Figure 1: Multiple round or oval-shaped superficial lesions with rolled borders, covered with white or grayish pseudo membrane, and surrounded by an erythematous halo over inner aspect of labial mucosa and tongue

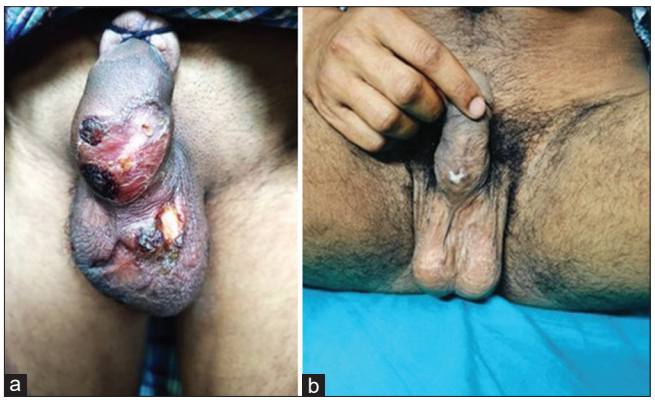

Figure 2: (a) Multiple large ulcers with sloping edges over scrotum, peno-scrotal junction and penile shaft with scar of healed previous lesions. (b) Scar tissue over penile shaft after complete resolution of genital lesions

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0.6 mg three times a day along with the course of antibiotics and supportive treatment. The patient became afebrile within 3 days with the resolution of EN-like lesions. The patient was discharged on tapering doses of systemic steroid and colchicine. Oral lesions were resolved after a week. Complete resolution of genital lesions took 8 weeks [Figure 2b]. The patient responded very well to the treatment, and remission was maintained with colchicine. The patient lost to follow-up and, after 2 months, again presented with multiple shallow ulcers over the scrotum and in the oral mucosa [Figure 4]. Oral colchicine was started after investigations and the patient responded well. The patient was maintained on low-dose colchicine and had no recurrence of lesions till then. The patient is being followed up regularly.

Discussion

Adamantiades-Behcet, also known as Silk road disease is a systemic vasculitis, affecting many organ systems with cardinal features that occur on the mucous membrane and skin and may cause serious morbidities and a fatal outcome. In India, BS is predominantly mucocutaneous and arthritic.[5] The average age of presentation is between 20 and 40 years.[6,7] Younger age of onset (<25 years) is a poor prognostic marker.[1] Our patient was 16 years old at the time of onset of symptoms which was lower as compared to studies done by Singal *et al*. and Pande *et al*. in India (27.4 years and 33.1 years, respectively).[5,7] HLA-B51 has limited diagnostic value in endemic regions. Skin pathergy reaction is the hyper-reactive inflammatory response to various triggers with the specificity of 98.4% when positive.[8] In our case, the pathergy was negative [Figure 5]. Pande *et al*. and Singal *et al*. reported positivity in 8.6% and 31%, respectively.[5,7] Singal *et al*. reported that oral ulcerations were the most common finding seen in 100% of cases, followed by genital lesions in the form of active ulcers or healed scars and cutaneous lesions in 93.1%, of which erythema nodosum was the most common in 62%.[7] All these cutaneous findings were present in our patient. This diagnostically tantalizing syndrome has bits and parts that may be separated by years and this may influence the prognosis. The diagnosis of BS was made according to the ICBD criteria in our case. ICBD 2010 criteria have the highest sensitivity (98.83%) with a specificity of 95.12%, while ISG criteria are the most specific (99.49%).[9]

Marfatia *et al*. reported a case of a 26-year-old male with mucocutaneous lesions of BS which responded to oral prednisolone and dapsone and remission was maintained on dapsone.[10] Kharkar *et al*. reported a case of a 32-year-old HIV-positive married female with BS mimicking secondary syphilis with biological false-positive VDRL.[11] Our patient responded to systemic corticosteroids in tapering dosage and colchicine. Remission was maintained on low-dose colchicine. Colchicine is considered a first-line agent for muco-cutaneous lesions of BS.[12] It is an antimitotic with anti-inflammatory and anti-neutrophilic properties.[13] Alternative drugs with good responses for muco-cutaneous lesions of BS are apremilast and thalidomide.

Table 1: Diagnostic criteria for Behcet syndrome

International Criteria for Behcet Disease (ICBD) 2010		
Sign or symptom	Points	Present in this patient
Ocular lesion	2	-
Genital aphthosis	2	2
Oral aphthosis	2	2
Skin lesions	1	1
Neurologic manifestations	1	-
Vascular manifestations	1	1
Pathergy test result	1	-

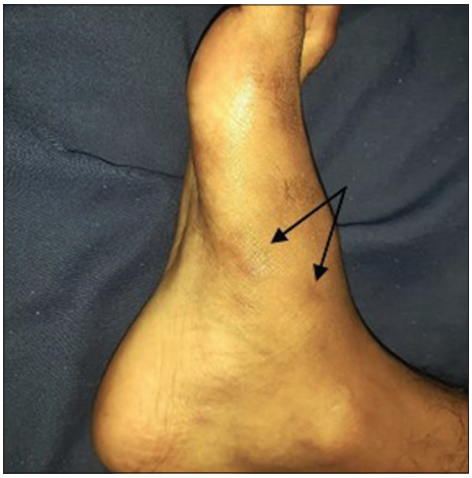

Figure 3: Erythematous to skin colours papulo-nodular lesions over foot

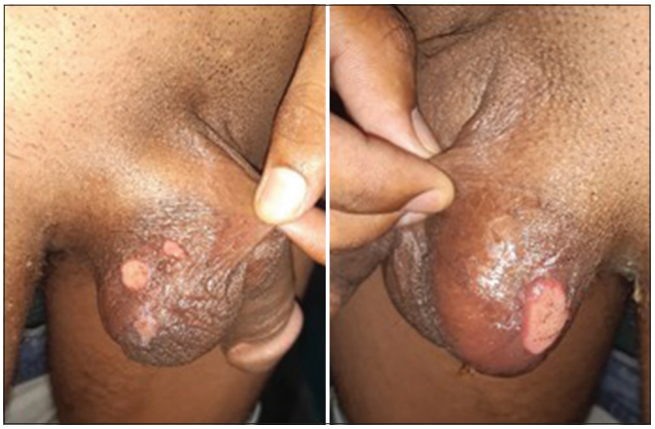

Figure 4: Multiple indurated plaques with yellowish slough over scrotum and penile shaft

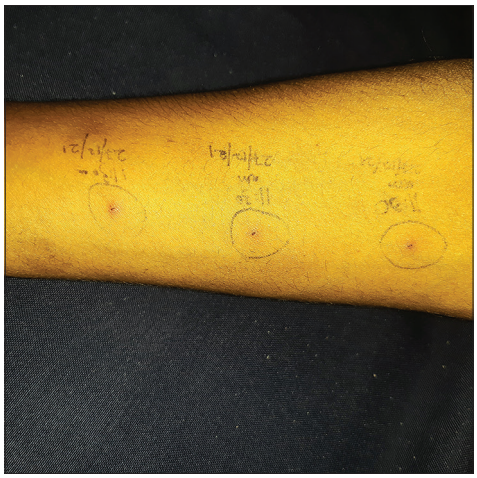

Figure 5: Negative pathergy test done on volar aspect of forearm of the patient

Conclusion

BS is a rare but important cause of recurrent genital ulceration. Younger age of presentation and male gender are poor prognostic factors for BS. HLAB51 and pathergy tests are strongly associated with BS, but are not diagnostic. BS mimics many other dermatological conditions; hence, high index of suspicion is required for diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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