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Behçet's Disease: An Account of Three Cases

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ABSTRACT

Behçet's disease is a chronic relapsing inflammatory condition affecting multiple organ-systems of the body. Patient's with this disease present to different specialists with wide spectrum of clinical features of varying severity. Worldwide, this disease is clustered around certain parts of Asia, previously known as 'Silk route'. Here we present three cases of Behçet's disease who presented to our clinic with ocular, dermatological, and articular manifestations.

Keywords: arthritis; Behçet's disease; genital ulcers; ocular inflammation; oral ulcers.

INTRODUCTION

Behçet's Disease (BD) is characterized by the presence of recurrent aphthous stomatitis, genital ulcerations and uveitis. The cause is unknown. This entity was first reported by Turkish Dermatologist Hulsi Behçet as a triple symptom complex of hypopyon, iritis, and orogenital aphthosis in 1937. However, subsequent observations showed that the syndrome also includes articular, gastrointestinal, central nervous system and peripheral vascular manifestations.[1]

This disease has been most commonly encountered around the Mediterranean, Middle East, and Far East regions (the old 'silk trade route') but it is rare in the other parts of the world including Indian subcontinent.[2] The prevalence of this disease in Nepal is unknown. In this case series we have attempted to give brief synopsis of this unique disease from Nepal.

CASE 1

A 16 year old boy from eastern Nepal presented with 1 week history of painful swelling of left knee. He had similar episodes of joint pain and swelling in both ankles and knees 5 years and 3 months previously respectively; and both of these episodes had subsided with painkillers. He lost vision in left eye 3 years ago following an illness causing eye pain, redness, and photophobia. From the same time, he was also suffering from intermittent painful red eye in the right side. He gave history of having a genital ulcer 2 years ago. He also reported that for the last 5 years, he had been having frequent oral ulcers, almost continuously; sometimes very large in size.

He denied any constitutional symptoms over the course of the illness. He had periumbilical abdominal pain with occasional vomiting; however there was no haematemesis or bloody stool.

He looked pale and appeared small for age. The examination of oral cavity was normal. Ophthalmic consultation revealed chronic nongranumomatous panuveitis with pale optic disc, occluded retinal blood vessel and vitreous hemorrhage in the right eye; the left eye had already developed phthisis bulbi (Figure 1). The examination of the chest, cardiovascular system, and abdomen was unremarkable.

There was no ulcer or scar in the genitalia. The left knee was tender with gross effusion and the range of motion was decreased in both the ankles.

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Figure 1. Phthisis bulbi in left eye (with ocular inflammation in the right side)

The investigations revealed white blood cell (WBC) count 12200/µL (Polymorphs 86%, Lymphocytes 14%), haemoglobin (Hb) 7%, normal platelet count, and erythrocyte sedimentation rate (ESR) 48mm in Ist hour. The routine urine microscopy and creatinine were normal The Rheumatoid Factor (RF) and Antinuclear Antibody (ANA) were negative. A chest x-ray was normal. A pathergy test was negative.

On the basis of history and examination findings, a diagnosis of BD was established and started on weekly methotrexate and tapering dose of prednisolone starting at 40mg daily. His condition gradually improved, with resolution of symptoms in the right eye and disappearance of synovitis in the knee. One year after the diagnosis, he is still on methotrexate with good control of his disease.

CASE 2

A 44 year old gentleman from western Nepal was referred to our Rheumatic Disease Clinic with bilateral retinal vasculitis and optic neuropathy for suspected BD. He was already on antitubercular treatment (ATT) for 1 month for possible ocular tuberculosis from another hospital, but without any improvement.

On systemic review, he reported that he used to have frequent episodes of pruritic blistering skin lesions in different body parts for last 3 years. Each episode used to last 2 to 3 months at a time. He also gave history of frequent oral ulcers lasting a few days at a time. On examination, he had multiple hyperpigmented scars in different part of the body representing the sequel of previous skin rashes. The remaining systemic examination was normal.

Investigations revealed normal complete blood count, ESR 23 mm in Ist hour, and normal liver and renal function tests. Human immunodeficiency virus (HIV), Hepatitis B surface Antigen (HBsAg), Hepatitis C virus (HCV), and toxoplasma serology (IgG) were negative. Routine urine examination and a chest x-ray were unremarkable. Pathergy test showed induration of more than 2 mm and hence was positive.

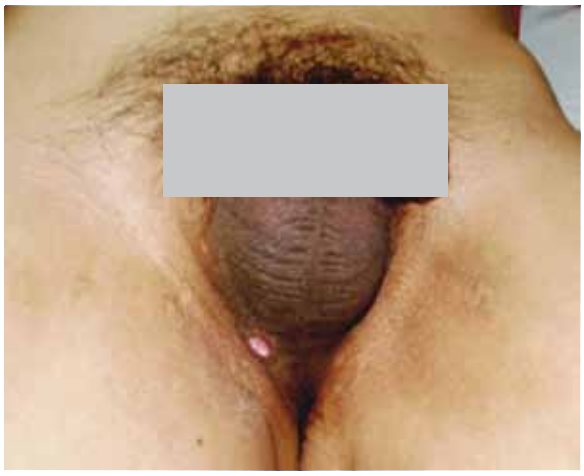

Figure 2. Genital ulcer in scrotum

In view of bilateral retinal vasculitis, frequent skin rashes and oral ulcers, genital ulcer, and positive pathergy test a diagnosis of BD was made. Immunosuppressive treatment in the form of azathioprine and tapering dose prednisolone was started and ATT stopped. However the patient discontinued these medicines after few weeks and again presented with increasing ocular pain and decreasing vision along with a recently developed ulcer in the genitalia. He also complained of gradual memory loss, forgetfulness, and occasional headache. However, a neurological assessment was normal. A 2x2cm ulcer was present in the lower part of the scrotum (Figure 2). Remaining physical examination was unremarkable.

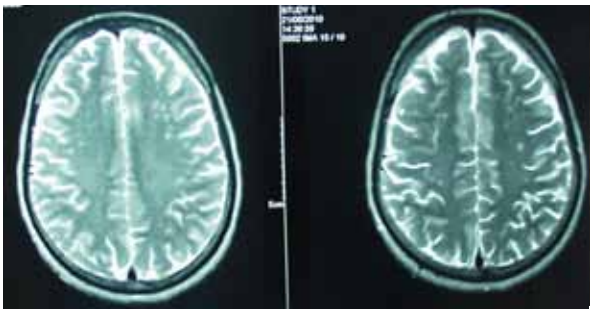

Figure 3. Foci of demyelination on MR images

The routine laboratory work up was normal as in the previous visit. The examination of the cerebrospinal fluid was also unremarkable. However, an MRI of head showed multiple white matter hyperintensities in different parts probably representing foci of demyelination (Figure 3). A diagnosis of BD with central nervous system involvement was made and azathioprine and prednisolone restarted. When seen last on his regular follow up, there were no more oral, genital, and skin ulcers and the eyes were stable.

CASE 3

A 30 year old lady from central Nepal presented with longstanding oral and genital ulcers and recent onset of bilateral ankle pain and swelling. Oral ulcers were frequent, sometimes very large occurring for last 5 years. She was treated for a genital ulcer at local clinic 5 years ago. About 2 years ago, she suffered from acute bilateral non-granulomatous panuveitis. Investigations at that time showed ESR 40 mm in 1st hour, negative mantoux test, non-reactive venereal disease research laboratory (VDRL) & treponema pallidum haemagglutination assay (TPHA) tests. With the suspicion of BD, she was treated with oral steroids and methotrexate for two years until the remission of uveitis. Systemic review this time was unremarkable for constitutional as well as system-specific complaints.

Examination revealed normal eyes. There were a few small ulcers in the dorsal surface of the tongue. An erythema nodosum was present in the left shin. Both the ankles were swollen and tender. The examination of the respiratory, cardiovascular, gastrointestinal, and central nervous system was unremarkable.

Investigations revealed WBC 10600/µL (Neutrophils 71%, Lymphocytes 27%), Hb 13.1, platelets 340000/ µL, ESR 38mm in Ist hour, and negative RF and ANA. Urine showed microscopic haematuria without RBC casts. The renal function and the chest x-ray were normal. Pathergy test was negative.

BD was diagnosed on the basis of presence of uveitis, frequent oral ulcers, genital ulcer, arthritis, and erythema nodosum. She was started on methotrexate 10mg/week along with low dose prednisolone. The patient improved in few weeks with the disappearance of all of active features of disease. Prednisolone was stopped after few weeks. Now 1 year after the treatment, she enjoys disease-free state on methotrexate therapy.

DISCUSSION

Each of the three cases presented above are from different parts of Nepal, implying that cases of BD are potentially scattered, though the exact prevalence is not known. Internationally, this disease has the highest incidence in the Middle East, the Mediterranean basin and the Far East regions; it is rare in most developed countries.[1] There are only a few reports from India.[2]

BD usually begins at 30 to 40 years of age; though childhood cases have also been reported. This is true in our series too; the first case had onset of disease as early as age 11 years of age.

The definite cause of BD is unclear and may be multifactorial. There is some degree of genetic risk as certain HLA alleles, particularly HLA-B*5101 and -B*5108 has been found to be associated with this disease.[3] As oral aphthae typically precede the onset of systemic disease by months to years, and frequently herald the relapse of the disease, microbiological trigger could have important role in the pathogenesis of this disease.[4] Pathologically, this disease is characterized by systemic perivasculitis; however, this is distinct from other causes of vasculitis, particularly autoimmune diseases.[5]

BD is essentially a clinical diagnosis as there are no laboratory tests for its confirmation. An International Study Group has proposed diagnostic criteria for research purpose and this is also used in clinical practice (Table 1).[6]

Table 1. International Study Group criteria for BD

Criteria present	Description
Recurrent oral ulcerations:	Minor aphthous, major aphthous, or herpetiform ulcerations observed by physicians or patient, which recurred at least 3 times in one 12 month period
Plus two of: Recurrent genital ulcerations:	Aphthous ulceration or scarring, observed by physician or patient
Eye lesions:	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination, or retinal vasculitis observed by ophthalmologist
Skin lesions:	Erythema nodosum observed by physician or patient, pseudofolliculitis, or papulopustular lesions; or acneiform nodules observed by physician in post-adolescent patients not on corticosteroids
Positive pathergy test:	Read by physician at 24 to 48 hours

BD causes chronic inflammation in multiple organ-systems. The clinical course and degree of organ involvement is often similar in successive relapses for a given patient.[7] Mucocutaneous findings i.e., recurrent oral and genital ulcerations with papulopustular and nodular skin lesions are the hallmark findings of BD. Minor ulcers (<10 mm size) are far more common than major and herpetiform apthous ulcers. Genital ulcers are usually found in scrotum in males and labia majora in females [1] which was also true in our case. BD patients exhibit a positive reaction to pathergy test, meaning development of a papule or pustule, 24 to 48 hour after a needle prick. However, there is great variation in this skin reaction as two thirds of patients with this syndrome in Turkey and Japan have a positive response as compared to its relative rarity in Europe and North America. Only

one of our patients had positive pathergy test. Eye disease occurs in approximately 70% of patients and is mostly biocular. It typically occurs after the onset of oral aphthosis, though in 10% patients eye disease could be the initial presentation of BD. Ocular inflammation can be variable and include anterior uveitis, hypopyon, inflammatory retinal vein occlusion, macular oedema, retinal vasculitis, and scleritis.[7] It is most frequent and severe among the males and the young. All of our patients had some form of ocular inflammation; however, both the male patients had severe eye disease with the development of phthisis bulbi in one patient and panuveitis in another.

Musculoskeletal involvement is present in half of the patients with BD and usually includes a transient arthralgia to nonerosive peripheral arthritis. The knees are the most frequently affected joints.[1] Approximately 1 in 20 patients develop neurological involvement, and this can either be parenchymal (80%), or dural sinus thromboses (20% of cases).[7] One of our patients had severe parenchymal neurological disease as evidenced in the MRI.

Patients of BD are at an increased risk of developing systemic venous thrombosis, and male patients develop this far more common than females.[8] Common thromboses include superficial and deep vein thrombophlebitis, and recurrent retinal vascular occlusion, though major vessel involvement is less frequent. Arterial aneurysms though rare, can be a cause of death if haemoptysis occurs due to rupture of pulmonary arterial aneurysms.[1] Fortunately none of our patients developed vascular complications until their last follow up.

Treatment of BD depends upon the nature and severity of disease and includes steroids, immunosuppressives, and in some conditions cytotoxic drugs. Majority of patients with BD go into complete remission with appropriate therapy.[1] Until few decades ago, three-quarters of patients with BD with eye involvement would eventually lose their vision; this is now rare with early therapy, though this is still not uncommon in areas where medical care is limited.[7] In our own series one patient had already developed phthisis bulbi and another had severe visual impairment. Mortality which is mostly due to rupture of pulmonary arterial aneurysms and neurological involvement is rare, though can be significantly increased among males and the young especially if diagnosis and treatment is delayed.

REFERENCES

1. Yazici H, Fresko I and Yurdakul S. Behçet's syndrome: disease manifestations, management, and advances in treatment. Nature. 2007;3:148-55
2. Sachdev N, Kapali N, Singh R, Gupta V, Gupta A. Spectrum of Behçet's disease in the Indian population. Int Ophthalmol. 2009 Dec;29(6):495-501. doi: 10.1007/s10792-008-9273-8.
3. Ohno S, Ohguchi M, Hirose S, et al. Close association of HLA-Bw51 with Behçet's disease. Arch Ophthalmol. 1982;100:1455-8.
4. Demirkesen C, Tuzuner N, Mat C, et al. Clinicopathologic evaluation of nodular cutaneous lesions of Behçet's syndrome. Am J Clin Pathol. 2001;116:341-6.
5. Bang D, Yoon KH, Chung HG, et al. Epidemiolgical and clinical features of Behçet's disease in Korea. Yonsei Med J. 1997;38:428–36.
6. International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's disease. Lancet. 1990;335:1078–80.
7. Verity DH, Wallace GR, Vaughan RW, Stanford MR. Behçet's disease: from Hippocrates to the third Millennium. Br J Ophthalmol. 2003;87:1175–83.
8. Ames PR, Steuer A, Pap A, et al. Thrombosis in Behçet's disease: a retrospective survey from a single UK centre. Rheumatology 2001;40:652–5.