INDIAN DERMATOL VENEREOL LEPROL 1987; 53 : 282-285

BEHCET'S DISEASE
(A study of 23 cases from Tripoli, Libya)

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In a study of 23 cases of Behcet's disease, we found male prepondrance (males 82.6%, females 17.4%), with commonest age of onset between 21-30 years in 70% cases. During the course of the disease, recurrent oro-genital ulcers were noticed in all the cases, while skin lesions in 15 (including erythema nodosum in 5 and thrombophlebitis in 4), eye involvement in 10, joint involvement in 6, epididymitis in 2 cases and deep vein thrombosis, CNS involvement and oesophageal ulcers in one case each were also seen. Erythrocyte sedimentation rate was raised between 35 and 120 mm during the active phase of the disease. In 15 cases, treatment with oral prednisolone controlled all the manifestations, while treatment with colchicine relieved oro-genital and skin lesions in 7 patients. One patient with eye involvement and recurrent oesophageal ulcers improved well with a combination of prednisolone and cyclophosphamide. Progressive deterioration of vision was noticed in 2 patients in spite of regular treatment.

Key words : Behcet's disease, Tripoli.

Behcet's disease is a clinical syndrome characterised by recurrent oral and genital ulcerations, iritis and other eye manifestations. In addition, there can be involvement of the skin, joints, cardiovascular, CNS and gastrointestinal tract. Although Hippocrates (460-370 BC) is said to have described patients having oro-genital ulcerations with chronic inflammation of the eyes,[1] the disease bears the name of a Turkish dermatologist, Hulusi Behcet, who reported cases in a series of publications starting in 1937.[1] Later, multisystem nature of the disease was recognised. The diagnosis of the disease is based mainly on clinical grounds as there are no pathognomonic laboratory findings. Most of the cases have been reported from the Mediterranean basin, the Middle East and Japan.[2]

Materials and Methods

Twenty three patients of Behcet's disease attending from January 1982 to December 1986, were included in this study. All the patients were admitted to the wards for initial assessment and treatment. Details of the history, physical findings, laboratory data, treatment and follow up were recorded in a special proforma for this purpose. The diagnosis of Behcet's disease was based on clinical features consisting of major and minor criteria, as recommended by the international conference on Behcet's disease in 1985.[3]

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Results

Twenty one patients were Libyan nationals and 2 were Egyptians. The age of onset ranged from 16 to 43 years and the commonest age group was 21 to 25 years. Nineteen cases were males and 4 were females. The first manifestation was oral and/or genital ulcers in 20 (87%) cases, eye involvement, erythema nodosum and furuncles, and epididymitis and erythema nodosum in 1 case each.

All our cases had recurrent aphthous ulcers affecting the mouth (buccal mucosa, 20 cases; lip mucosa, 14 cases; palate, 6 cases and pharynx, 2 cases). Except for one female patient aged 25 years, who had major aphthosis (ulcer 3 cm $\times$3 cm), all other cases had minor aphthosis (ulcers which varied from 1-10 mm in size).

The genital ulcers in males ranged from $\frac{1}{4}$-2 cm in size and were located over the scrotum in 18 patients, penile shaft in 8 patients and the groin in 3 patients. The female patients had ulcers on labia majora (3 patients) and labia minora (2 patients). The size varied from 1-5 cm and the bigger lesions were thick and indurated.

Eye involvement was seen in 10 patients with iritis in all, keratitis in 4, and conjunctivitis in 4 patients. One of the patients had macular atrophy with degenerative changes and one had optic nerve atrophy.

Skin lesions like furuncles and superficial follicular pustules were seen in 15 patients. Erythema nodosum was seen in 5 patients. One patient had a combination of erythema nodosum and erythema multiforme. One of these patients (aged 22 years) came initially with erythema nodosum and a small ulcer in the groin with a few pustular lesions on the face. He developed oral lesions while he was hospitalized. Thrombophlebitis of leg vein was found in 4 patients, while one patient aged 56 years had deep vein thrombosis of the leg.

Two patients had arthritis affecting the ankle joints. Four patients had arthralgia which was affecting the ankles in 2 cases, knees in one case while another patient had generalized arthralgia. None of the patients had small joint involvement.

Two patients had epididymitis. One of them had recurrent attacks and at times this was the only manifestation of the disease. In this case the possibility of other causes of epididymitis were ruled out.

One patient had recurrent oesophageal ulcers. One female patient had incontinence of urine and peripheral neuropathy as one of the manifestations of the disease.

Routine laboratory investigations including complete blood picture, ESR, urine, stool, liver function tests, blood sugar, VDRL, rheumatoid factor, serum proteins, X-ray chest and ECG were performed in all the patients. All the patients had raised ESR ranging from 35 to 120 mm during the active phase of the disease. Five patients showed mild leucocytosis (12000 to 15000/c mm). The differential counts were normal in all cases. Rheumatoid factor was positive in one of the patients who had arthralgia. All the other investigations were within normal limits.

Fifteen patients were treated with oral prednisolone 30-60 mg/day, according to the severity of the disease. All the manifestations were under control after 2-8 weeks therapy. Two patients needed long maintenance therapy with 10 mg and 20 mg respectively. Oro-genital ulcers, arthralgia and erythema nodosum responded very well to this therapy. In 6 patients, the eye manifestations including iritis improved after corticosteroid therapy. We administered colchicine, 1 mg/day to 7 patients. Oro-genital and skin lesions healed within 4 weeks in all the 7 patients. Two patients who had arthralgia and iritis, did not respond well, hence we supplemented this therapy with systemic prednisolone 40 mg/day which relieved these symptoms. One patient who had recurrent oesophageal ulcers and severe uveitis, did not respond to prednisolone alone and had to be supplemented with cyclophosphamide 100 mg/day. The symptoms were controlled within 3 months. He is now on a maintenance dose (prednisolone, 20 mg and cyclophosphamide 50 mg/day) for the last one year and is presently symptom-free.

Eleven patients are attending for follow up. Three of these have been in remission for about a year, while 6 patients had recurrence after 2-6 months. Two patients are taking maintenance therapy for the last 2 years because even after a week's discontinuation of the treatment, they get recurrence. Two of these patients had progressive deterioration of vision in spite of regular treatment. Five patients came for follow up initially for 3-6 months,

without recurrence of the lesions. Rest of the 7 patients are lost to follow up after the initial treatment in the hospital.

Comments

There is disagreement on the exact definition of Behcet's disease. Recommended criteria for diagnosis have been advanced by Barne, Simizu and O'Duffy. Major criteria for diagnosis include, oral aphthae, genital aphthae, ocular involvement, cutaneous lesions, neurologic or arthritic involvement and other criteria.[3] Lehner[4] has further subdivided the cases into muco-cutaneous (MC), arthritic (MC arthritic), ocular (arthritic-ocular), and neurologic sub-groups.

The world-wide incidence of Behcet's disease is variable. Most of the cases have been recorded in the Mediterranean basin, the Middle East and Japan. It may have some relationship to the historical silk trading routes.[3] Genetic predisposition seems likely. It is worth noting that HLA studies from Japan, Turkey and southern France have shown 3 to 4 fold increased frequency of HLA-B5 in cases of Behcet's disease.[2,5-7] Recent studies from Japan and Britain showed increased frequency of HLA-B51 and HLA-DRw52 as disease susceptibility genes and decreased incidence of HLA-DR1 and HLA-DOwl as probable disease resistant genes.[3] It is believed that the previously reported HLA-B27 association in Behcet's disease may have resulted from inappropriate inclusion of patients with Reiter's disease. So far, no HLA studies in Behcet's disease have been reported from this country.

In our study male to female ratio was around 5 to 1. Similar male preponderance has been recorded before but in North America, Britain and Australia, female cases are in the majority.[26] Age of onset in 70% of our cases was between 21 to 30 years. Similar pattern has been reported in previous studies.[8]

We observed raised ESR during activity of the disease in all the patients. ESR, more than 50 mm was especially observed in patients who had arthropathy, erythema nodosum, epididymitis or thrombophlebitis. Similar association has been reported by Muftuoglu et al.[9] They have also recorded an elevation of C-reactive protein along with elevation of ESR in such cases.

As there is no specific treatment for Behcet's disease, several treatment schedules have been used with varying results. Fifteen of our patients treated with systemic corticosteroids had good response, controlling most of the manifestations of the disease. Corticosteroids have been tried by many workers and similar beneficial effects have been noticed.[6,10,11] O' Duffy[12] has noticed progression in the lesions even while corticosteroids were being used. We did not observe such progression in any of our patients treated with systemic corticosteroids. Seven of our patients treated with colchicine showed good response regarding oro-genital and skin lesions. Similar beneficial results have been reported in previous reports.[13,14] However, a double blind study has cast doubt on the efficacy of this drug.[15] One of our patients who did not respond well to systemic corticosteroids alone, showed good results by supplementing the therapy with cyclophosphamide. Similar results have been observed in a previous study,[16] while another study did not reveal any satisfactory result with cyclophosphamide therapy.[17] Some workers have also noticed encouraging results with a combination of corticosteroids and azathioprine in resistant cases having eye involvement.[18,19] However, other authors prefer chlorambucil as a treatment for cases with significant eye involvement and other neurological manifestations.[17] The various manifestations of the disease have shown good response to this drug and some workers have called this the best available drug in Behcet's

disease but the long-term risk of this treatment limits its use in general.

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