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Behçet's disease in Iraqi patients

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SUMMARY The clinical features of 60 patients (45 male, 15 female) with Behçet's disease (BD) are reported in this prospective study. Ninety seven per cent had mouth ulceration, 83% genital ulceration, 75% skin lesions, 48% ocular involvement, 48% synovitis, 17% thrombophlebitis, and 22% of the male patients had epidiymitis, while constitutional symptoms were reported by 63%. The arthritis was intermittent, self limiting, and non-destructive, involving large joints, mainly the knees and ankles. The pathergy test was positive in 37 of 52 patients with BD, and negative in all 120 healthy controls and in 20 healthy volunteers who possessed the HLA-B51 antigen. HLA-B51 was present in 32 of 52 (62%) patients with BD compared with 51 of 175 (29%) unrelated normal controls. Both the pathergy and HLA-B51 tests were negative in four of 52 patients with BD. Behçet's disease is not uncommon in Iraq. Practising physicians, dermatologists, and ophthalmologists must be more aware of its existence.

Key words: pathergy test, HLA-B51.

Since the Turkish dermatologist Hulusi Behçet described a triple syndrome of aphthous ulceration, genital ulceration, and iritis in 1937[1] other systemic and cutaneous manifestations have been reported.

The prevalence of the disease varies widely from country to country and probably from race to race, being reported as 1/10 000 population in Hokkaido, Japan,[2] 0·064/10 000 in Yorkshire, England,[3] and 1/300 000 in Minnesota, USA.[4] The disease is more common in the Middle and Far East than in Europe and the USA.[3 4]

Although the disease was originally reported from the eastern Mediterranean, not much attention has been paid to Behçet's disease (BD) in Arab populations.[5–7] In the last decade we have become more aware of the existence of BD in our country and have studied the clinical manifestations, histocompatibility typing, and pathergy tests in patients who attended the rheumatology, dermatology, and ophthalmology units at the Medical City Hospital, Baghdad.

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Patients and methods

All patients attending during 1981–4 who fulfilled Mason and Barnes' criteria for diagnosis of BD[8] were included in a prospective study. Patients with 'incomplete' disease were excluded.

Full clinical examinations were performed by ZSA and SJK, dermatological lesions were evaluated by KES, and ophthalmological tests were performed by FMA.

The following tests were carried out on all patients by standard methods: complete blood picture; erythrocyte sedimentation rate (ESR-Westergren); urine analysis; LE cell test; antinuclear factor test; rheumatoid factor test; serum uric acid; C reactive protein; serum proteins and electrophoresis; antistreptolysin O (ASO) titre determination; *x* rays of the chest, hands, feet, pelvis, and any other affected joint.

The leucocyte count and the ESR (Westergren) were regarded as raised if they were above 10×10^9 cells/l and 20 mm/1st h, respectively. The upper limit for gammaglobulin was 17 g/l and the lower limit for albumin was 36 g/l. C reactive protein readings were recorded as either positive or negative.

The pathergy test was performed by intradermal needle prick without the intradermal injection of

saline[9] and read after 48 hours on 52 patients with BD, on 120 healthy controls, and on 20 healthy volunteers who possessed the HLA-B51 antigen.

Tissue typing was performed (by JJM) on 52 patients with BD and 175 unrelated normal controls by the standard NIH microcytotoxicity technique[10] using antisera for A, B, and C locus antigen. DR typing was not performed.

Arthritis was defined as joint tenderness, swelling, and/or pain on motion.

Results

Sixty patients (45 male, 15 female) were included in the study. Their ages ranged from 14 to 48 years (six patients 10–19 years; 17 patients 20–29; 25 patients 30–39, and 12 patients >40 years) (Table 1a). Mean duration of the disease was 2·1 years (Table 1b). The main reason for the delay of presentation of patients at our hospital was that patients in Iraq move freely from one physician to another and from one hospital to another.

The overall frequency of clinical features is shown in Table 2. Definite arthritis was observed in 48% of patients, but arthralgia was reported more commonly. Arthritis was oligo- or polyarticular, intermittent, self limiting, and non-destructive, involving peripheral joints. The frequency of joint involvement is shown in the histogram (Fig. 1), the knee being involved most frequently. Arthralgia alone was reported in an additional six patients.

Gastrointestinal complaints were reported by 10%, these being vomiting, abdominal pain, flatulence, diarrhoea, or constipation. No pulmonary or renal involvement was detected.

Table 1a *Number and ages of patients at onset and presentation*

	Age (years)				*Mean age (years)*
	10–19	*20–29*	*30–39*	*>40*	
No of patients:					
at onset	8	22	21	9	29·4
at presentation	6	17	25	12	31·5

Table 1b *Duration of disease*

No of patients	*Duration*	*Mean duration*
24	<12 months	2·1 years
13	12–23 months	
19	2–5 years	
4	5 years	

There was a family history of mouth ulcers in six patients, and the brother of one of our patients also had BD.

Table 2 *Clinical features in 60 patients with BD*

	Presenting feature		*Incidence*	
	No	*%*	*No*	*%*
Mouth ulcers	21	35	58	97
Genital ulcers	6	10	50	83
Skin lesions	7	12	45	75
Erythema nodosum			33	55
Acneiform skin lesions			29	48
Eye lesions	8	13	29	48
Uveitis			20	33
Hypopyon			7	12
Retinal lesions			2	3
Corneal ulceration			1	2
Episcleritis			1	2
Mouth ulcers + other features	7	12		
Epididymitis (45 men)	1	2	10	22
CNS (grand mal epilepsy)	1	2	1	2
Thrombophlebitis	1	2	10	17
Synovitis	8	13	29	48
Psychoneurosis/depression			6	10
Gastrointestinal			6	10
Constitutional features			38	63
Fever			34	57
Malaise			38	63
Weight loss			21	35

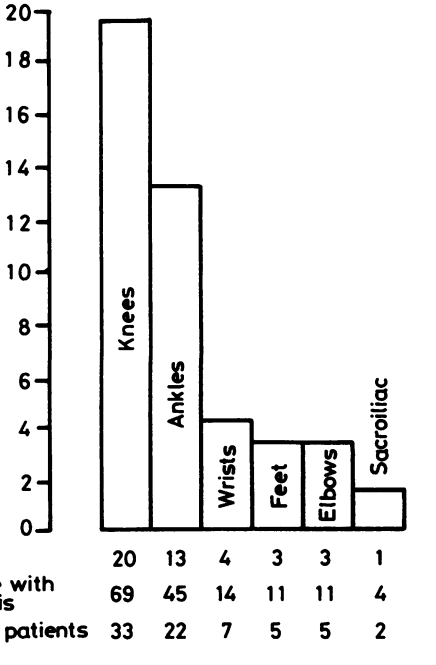

Fig. 1 *Frequency of joint involvement in 29 patients with Behçet's disease and definite arthritis.*

Table 3 *Investigations in 60 patients with BD, and in controls*

	No tested	*Positive/abnormal*	
		No	*%*
Raised ESR	53	41	77
Leucocytosis	60	24	40
C reactive protein	60	22	37
Hypoalbuminaemia	51	13	25
Hypergammaglobulinaemia	51	15	29
Pathergy test			
Patients with BD	52	37	71
Healthy controls	120	0	0
Healthy controls possessing the HLA-B51 antigen	20	0	0
HLA-B51			
Patients with BD	52	32	62
Controls	175	51	29

The results of investigations are shown in Table 3. There was no positive association between eye involvement, arthritis, HLA-B51 tissue typing, and positive pathergy test. The pathergy test and HLA-B51 were both positive in 23 and both negative in four of 52 patients with BD. Urine analysis, antinuclear antibodies, LE cell and rheumatoid factor tests were negative in all patients. The ASO titre was above 200 Todd units in four of 55 patients, but similar results have been reported among normal Iraqi subjects.[11] *x* Rays of the chest and joints were normal in all, except for one patient who had bilateral sacroiliitis but who did not possess the HLA-B27 antigen.

Discussion

BD has been seen more frequently in the last decade among hospital patients in Iraq. The initial manifestations of the disease and the major clinical features are similar to descriptions of the disease from other parts of the world.[3 8 12]

The arthritis was intermittent, oligo- or polyarticular, self limiting, and non-destructive, involving peripheral joints in an asymmetrical pattern. These findings are similar to those of other studies.[3 8 13 14] Only one of our patients had bilateral sacroiliitis compared with 0·5–1·0% of Japanese patients[15] and one of 25 British patients.[8 16] In contrast, the incidence of radiological sacroiliitis in a large series from Turkey was 65%[17] and 50% in another report from Britain.[18]

Gastrointestinal symptoms were less frequently reported during this study, in only 10% of patients compared with 50% in other studies.[19–21] Epididymitis, however, was reported in 22% of our male patients compared with 4·5% and 8% in other series.[19 22]

The pathergy test was positive in 71% of patients in this study compared with 82% in Turkish patients.[23] The test is similarly reported as a common feature of BD in Japan.[24 25] In contrast, a minority of British patients have a positive pathergy test.[26–28] The pathergy test was negative in all 120 healthy controls and in 20 healthy volunteers possessing the HLA-B51 antigen, which is in agreement with other reports.[9 27 28]

The histocompatibility antigen HLA-B51 was present in 62% of our patients compared with 29% of controls.[29]

These results are therefore similar to those reported from Turkey (84% of patients: 27% of controls)[23] and Japan (62% of patients: 21% of controls)[30], while the frequency of the HLA-B51 antigen in two British studies was 17·8%[3] and 29%[26] which is not significantly different from our control group.

There was no positive association between HLA-B27 and BD in this study, which thus differs from other reports which showed a modest increase in British patients, including an incidence of 25% of HLA-B27 positivity in BD independent of the clinical type of presentation.[3 26] Yazici *et al* proposed the combination of a positive pathergy test and the presence of the HLA-B5 antigen as a diagnostic marker of BD,[23] their dual negativity virtually excluding the diagnosis. Both tests were positive in 65% of the Turkish patients. A report from Britain has questioned this proposal, concluding that the positivity of the pathergy tests, and hence its diagnostic usefulness, differs between Britain and Turkey and that this difference is not related to the possession of the HLA-B5 antigen.[27] In the present study both tests (the pathergy test and HLA-B51) were positive in 44% and negative in 7·7% of patients with BD.

We also conclude that the positivity of the pathergy test and the possession of the HLA-B51 antigen differ from country to country and that positivity of the pathergy test is not related to the presence of the HLA-B51 antigen.

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References

1 Behçet, H. Uber rezidivierende aphthöse, durch ein Virus verursachte Geschwüre am Mund, am Auge und an den Genitalien. *Dermatol Wochenschr* 1937; **105:** 1152–7.

2 Aoki K, Katsumata H. Epidemiological studies on Behçet's disease in the Hokkaido district of Japan. *J Clin Ophthalmol* 1971; **25:** 2239–43.

3 Chamberlain M A. Behçet's syndrome in 32 patients in Yorkshire. *Ann Rheum Dis* 1977; **36:** 491–9.

4 O'Duffy J D. Summary of international symposium on Behçet's disease. Istanbul, Turkey, September 1977. *J Rheumatol* 1978; **5:** 229–33.

5 Madkour M, Kudwah A. Behçet's disease. *Br Med J* 1978; **ii:** 1786.

6 Ben Ayed H, Hamza M. *La maladie de Behçet.* Tunis: Imprimerie Officielle, 1976.

7 Hamza H, Ben Ayed H. Clinical and histological study of 55 cases of Behçet's disease. In: Dilşen N, Konice M, Ovul C, eds. *Behçet's disease.* Amsterdam: Excerpta Medica, 1979: 107. (International Congress Series No 467.)

8 Mason R M, Barnes C G. Behçet's syndrome with arthritis. *Ann Rheum Dis* 1969; **28:** 95–103.

9 Tuzun Y, Yazici H, Pazarli H, Yalkin B, Yurdakul S, Muftuoglu A. The usefulness of the non-specific skin hypersensitivity (the pathergy test) in Behçet's disease in Turkey. *Acta Derm Venereol (Stockh)* 1979; **59:** 77–9.

10 Department of Health, Education and Welfare. *Manual of tissue typing techniques.* London: NIH, 1976–7. (NIH No 77-545.)

11 Al-Rawi Z S, Al-Khateeb N. Clinical features of first attack of rheumatic fever in adults. *Rheumatol Rehabil* 1982; **21:** 195–200.

12 Oshima Y, Shimizu T, Yokohari R, *et al.* Clinical studies on Behçet's syndrome. *Ann Rheum Dis* 1963; **22:** 36–45.

13 Ehrlich G E. Intermittent and periodic arthritic syndromes. In: McCarty D J, ed. *Arthritis.* Philadelphia: Lea and Febiger, 1979: 663–80.

14 Strachan R W, Wigzell F W. Polyarthritis in Behçet's multiple symptom complex. *Ann Rheum Dis* 1963; **22:** 26–33.

15 Shimizu T, Ehrlich G E, Inaba G, Hayashi K. Behçet's disease. *Semin Arthritis Rheum* 1979; **8:** 223–60.

16 Barnes C G. Behçet's syndrome—joint manifestations and synovial pathology. In: Lehner T, Barnes C G, eds. *Behçet's syndrome — clinical and immunological features.* London: Academic Press, 1979: 199–212.

17 Dilşen N, Konice M, Ovul C. Arthritic patterns in Behçet's disease. In: Dilşen N, Konice M, Ovul C, eds. *Behçet's disease.* Amsterdam: Excerpta Medica, 1979; 145–9. (International Congress Series No 467.)

18 Caporn N, Higgs E R, Dieppe P A, Watt L. Arthritis in Behçet's syndrome. *Br J Radiol* 1983; **56:** 87–91.

19 Beittie G B, Bruna R. An ophthalmic report on Behçet's disease. In: Monacelli M, Nazzaro P, eds. *Behçet's disease.* Basel: Karger, 1966: 77–110.

20 Shimizu T, Saito Y. Behçet's syndrome. *Clin Sci* 1971; **7:** 451.

21 Shimizu T, Ogino T. Clinico-pathological studies on the intestinal lesions in Behçet's disease with special reference to entero-Behçet's syndrome. *Stomach Intestine* 1975; **10:** 1593.

22 Shimizu T, Matsumura M. Clinical features and etiology of Behçet's syndrome. *Jap J Clin Med* 1968; **26:** 2–17.

23 Yazici H, Tuzun Y, Pazarli H, Yalcin B, Yurdakul S, Muftuoglu A. The combined use of HLA-B5 and the pathergy test as diagnostic markers of Behçet's disease in Turkey. *J Rheumatol* 1980; **7:** 206–10.

24 Nazzaro P. Cutaneous manifestations of Behçet's disease—clinical and histological findings. In: Monacelli M, Nazzaro P, eds. *Behçet's disease.* Basel: Karger, 1966: 15–41.

25 Suzuki K, Mizuno N. Intracutaneous test with physiological saline in Behçet's disease. In: Inaba G, ed. *Behçet's disease—pathogenetic mechanism and clinical future.* Tokyo: University of Tokyo Press, 1982: 333–42. (Japan Medical Research Foundation Publication No 18.)

26 Lehner T, Batchelor J R. Classification and an immunogenetic basis of Behçet's syndrome. In: Lehner T, Barnes C G, eds. *Behçet's syndrome—clinical and immunological features.* London: Academic Press, 1979: 13–32.

27 Davies P G, Fordham J N, Kirwan J R, Barnes C G, Dinning W J. The pathergy test and Behçet's syndrome in Britain. *Ann Rheum Dis* 1984; **43:** 70–3.

28 Yazici H, Chamberlain M A, Tuzun Y, Yurdakul S, Muftuoglu A. A comparative study of the pathergy reaction among Turkish and British patients with Behçet's disease. *Ann Rheum Dis* 1984; **43:** 74–5.

29 Munir J J. Immunity center and tissue typing in Iraq. *As-saidali* 1980; **2:** 37–42.

30 Ohno S, Ohguchi M, Matsuda H, *et al.* Close association of HLA-Bw51, Mt2, and Behçet's disease. Summary of the third international conference on Behçet's disease. Tokyo, Japan, 1981. *J Rheumatol* 1983; **10:** 154–8.