Graefe's Arch Clin Exp Ophthalmol (1994)
232:589–590

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HLA antigens in a Japanese family with Behçet's disease

Received: 1 December 1993
Revised version received: 18 March 1994
Accepted: 18 March 1994

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Abstract • Background: Familial Behçet's disease is rare. • Methods: HLA antigens in a Japanese family with Behçet's disease were examined. • Results: The affected patients had HLA B51, and unaffected family members also had the same antigen. • Conclusion: It is likely that not only HLA B51 but also other factors may be involved in the pathogenesis of Behçet's disease in Japanese patients.

Introduction

The cause of Behçet's disease is still unclear. Familial occurrence of the disease has rarely been reported [1, 3, 4, 9]. There has been a close association of HLA B51 with Behçet's disease in Japanese patients [8]. We recently examined HLA antigens in a Japanese family in which two sisters had concurrent manifestations of oral and genital ulceration, uveitis, and erythema nodosum-like skin lesions.

Case reports

A pedigree of the family is shown in Fig. 1. The HLA antigens identified in the family are listed in Table 1. Antisera for HLA typing were obtained from One Lambda, Calif., USA.

Patient II-2. In 1987, a 30-year-old woman (the proband) complained of blurred vision in the left eye. Her visual acuity was 1.2 OD and 0.7 OS. Keratic precipitates and intracameral and intravitreal cells were seen in both eyes. No iridial nodules were noted. Small whitish lesions were observed ophthalmoscopically in the inferotemporal periphery of the left fundus. Leakage of dye from the peripheral retinal vessels in the left eye was found by fluorescein angiography. Oral and genital ulceration and erythema nodosum-like skin lesions were also observed. Test results of blood cell counts, blood chemistry analyses, urinalysis, chest X-ray, *Treponema pallidum* hemagglutinin, serum titers to human T-cell lymphotropic virus type 1, serum titers to *Toxoplasma gondii*, angiotensin-converting enzyme level, antinuclear antibody, and anti-DNA antibody were negative or within normal range. The patient was treated with topical instillation of steroid and atropine and oral administration of colchicine. The inflammatory signs diminished 4–5 days later. Thereafter, similar attacks occurred twice a year. In 1993, at the age of 36 years, she had good visual acuity (1.2) OU. The identified HLA types were A24, A26, B51, B62, CW3, BW4, BW6, DRW52, DRW53, and DQ7.

Patient II-3. The 34-year-old sister of the proband complained of blurred vision in the left eye in early July 1993. Her visual acuity was 1.5 OD and 0.8 OS. Intracameral and intravitreal cells were found in both eyes. No iridial nodules were noted. A small whitish lesion was observed ophthalmoscopically in the inferior region of the left macula. Leakage of dye from the inferotemporal vein in the left fundus was found by fluorescein angiography. Oral and genital ulceration and erythema nodosum-like skin lesions were also observed. Test results of blood cell counts, blood chemistry analyses, urinalysis, chest X-ray, *Treponema pallidum* hemagglu-

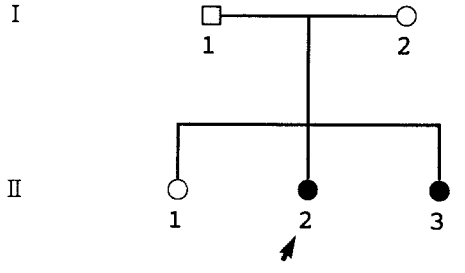

Fig. 1 A pedigree of the family (□ symptom-free man, ○ symptom-free woman, ● woman with Behçet's disease, ↙ proband)

Table 1 HLA Antigens in Family Subjects

HLA antigens	Subjects				
	I-1	I-2	II-1	II-2	II-3
A locus	24	24	24	24	24
	26	31	26	26	Blank
B locus	52	51	51	51	51
	62	52	62	62	52
C locus	W3	W1	W3	W3	Blank
	Blank	W2	Blank	Blank	Blank
BW 4, 6	+, +	+, −	+, +	+, +	+, −
DR locus	9	9	9	9	9
	Blank	Blank	Blank	Blank	Blank
DRW 52, 53	+, +	− , +	+, +	+, +	− , +
DQ locus[a]	7	7	7	7	3
	Blank	Blank	Blank	Blank	Blank

[a] DQ7 is a subtype of DQ3

tinin, angiotensin-converting enzyme level, antinuclear antibody, and anti-DNA antibody were negative or within normal range. The patient was treated with topical instillation of steroid and atropine and oral administration of colchicine. The clinical inflammatory signs were reduced 1 week later. A similar attack recurred in late September 1993. However, the patient had good visual acuity (1.5) OU. The identified HLA types were A24, B51, B52, BW4, DR9, DRW53, and DQ3.

Subject I-1. The 69-year-old father of the proband had no ocular complaints. His visual acuity was 1.0 OU. Cortical opacities in the lenses and posterior hyaloid detachment were seen in both eyes. His eyes appeared otherwise normal. No oral or genital ulceration or skin lesions had been noted. The identified HLA types were A24, A26, B52, B62, CW3, BW4, BW6, DR9, DRW52, DRW53, and DQ7.

Subject I-2. The 60-year-old mother of the proband had no ocular complaints. Her visual acuity was 1.0 with correction (+1.5 D) OU. Multiple drusen weren observed in both fundi. Her eyes appeared otherwise normal. No oral or genital ulceration or skin lesions had been noted. The identified HLA types were A24, A31, B51, B52, CW1, CW2, BW4, DR9, DRW53, and DQ7.

Subject II-1. The 37-year-old sister of the proband had no ocular complaints. Her visual acuity was 1.0 OU. Her eyes appeared normal. No oral or genital ulceration or skin lesions had been noted. The identified HLA types were A24, A26, B51, B62, CW3, BW4, BW6, DR9, DRW52, DRW53, and DQ7.

Discussion

In our present study, two family members fulfilled the criteria for the diagnosis of Behçet's disease [2, 5].

Familial occurrence of Behçet's disease, as found here, has rarely been reported [1, 3, 4, 9]. A close association of HLA B51 with Behçet's disease has been described in Japanese patients [8]. In our present study, both the affected patients (II-2 and II-3) and two unaffected family members (I-2 and II-1) had HLA B51. The HLA B51 antigen has recently been found to comprise three alleles, HLA B5101, HLA B5102, and HLA B5103 [7]. Mizuki and associates [7] have reported that all patients with Behçet's disease and HLA B51 carry HLA B5101. In our present study, HLA B5101 could not be examined. Lehner and associates [6] have reported a significant correlation between HLA DR2 and DR7 in Caucasian patients with Behcçet's disease. HLA DR2 and DR7, however, were not found in our affected family members.

Our data support the hypothesis proposed by Ohno and associates [8] that HLA B51 is closely associated with Behçet's disease in Japanese patients. We suggest that factors other than HLA B51 may be involved in the pathogenesis of the disease.

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