Association of juvenile disciform maculopathy with HLA B15

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SUMMARY Twenty patients with juvenile disciform maculopathy (JDM), which clinically cannot be differentiated from presumed ocular histoplasmosis, are presented. Histocompatibility antigen typing showed an increase in HLA B15, but this increase was not significant with respect to the corrected P-value. We are reporting our results in the hope of encouraging those who have cases of JDM in Europe to consider histocompatibility antigens and in particular HLA B15.

The HLA antigen distribution in 20 patients with juvenile disciform maculopathy (JDM) is presented and compared with the HLA typing of a very similar disease, namely, presumed ocular histoplasmosis. Juvenile disciform maculopathy is a clinical entity and patients with JDM show the following characteristics: haemorrhagic disciform detachment of the macular or perimacular region; small well-defined choroidal or pigment epithelial lesions of the posterior pole or at the papillary margin; no involvement of the anterior segment; clear vitreous; prevalence mainly in the age group of 20 to 40 years; negative histoplasmin skin test.

The disease has many names—for example, haemorrhagic exudative retinitis (Hausschild, 1974), ocular histoplasmosis syndrome (Braunstein *et al.*, 1974), multifocal choroiditis (presumed histoplasmosis) (Notting *et al.*, 1975), focal haemorrhagic choroiditis (Schildberg and Wessing, 1975), juvenile haemorrhagic maculopathy (Oosterhuis *et al.*, 1976), and juvenile haemorrhagic macular degeneration or 'histoplasmosis-like choroiditis' (de Laey, 1978).

In effect all these are cases of JDM and cannot be differentiated from presumed ocular histoplasmosis on the clinical picture alone. Since *Histoplasma capsulatum* is rarely seen in Europe (Ellis and Schlaegel, 1973), and since patients with JDM have negative histoplasma skin tests, the relationship with histoplasma must be questioned.

Materials and methods

On the basis of the characteristics listed above 20 patients with JDM were selected, all being con-

firmed by fluorescein angiography. The patients were otherwise healthy, young (average age 35, range 14 to 42 years), and had been observed for an average of 3.9 years (range 0.25 to 8 years). From each of the 20 patients 20 ml of freshly drawn blood was heparinised (2 drops of Thromboliquine) and sent within hours to the HLA typing laboratory of the Department of Immunohaematology at Leiden University.

HLA typing was performed according to the National Institutes of Health lymphocyte micro-cytotoxicity technique (Ray *et al.*, 1976) with a set of 120 typing sera. A group of 4000 healthy Dutch blood donors served as a control population for the HLA A and B specificities. Out of this group 1824 were also typed for HLA C locus groups Cw1 to 5.

Results

Among the 20 cases of JDM 29 HLA A, B, and C locus specificities could be defined (Table 1). An increase in HLA B15 was observed in 8 patients (40%) as compared to 15.7% in the control group. These patients, 3 males and 5 females, with an average age of 35 years (range 15 to 42 years) were observed for an average duration of 3.2 years (range 0.25 to 5 years). All patients had reached the inactive scar stage with the exception of 1 male, who after 3 months' observation still showed an active subretinal neovascularisation. The increase in HLA B15 when compared with the control population gave $\chi^2=7.76$, $P=0.00534$, $RR=3.6$, and corrected $P=0.14$ (Woolf, 1955; Edwards, 1974). The uncorrected P value is just significant, whereas the corrected P value is not.

In presumed ocular histoplasmosis the frequency of the HLA B7 antigen was shown to be statistically

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Table 1 HLA antigen distribution in patients with juvenile disciform maculopathy and in controls

	Patients n = 20		Controls n = 4000	
	Number	Per cent	Number	Per cent
HLA A1	5	25	1254	31.3
A2	11	55	2141	53.5
A3	8	40	1222	30.5
A9	3	15	806	20.2
A10	2	10	275	6.9
A11	0	0	409	10.2
A28	1	5	375	9.4
Aw19	4	20	811	20.2
B5	5	25	410	10.2
B7	7	35	1175	29.4
B8	4	20	932	23.3
B12	3	15	1014	25.3
B13	0	0	196	4.9
B14	0	0	143	3.6
B15	8	40	627	15.7*
Bw16	1	5	256	6.4
B17	1	5	323	8.1
B18	2	10	258	6.4
Bw21	0	0	102	2.6
Bw22	0	0	210	5.3
B27	1	5	312	7.8
Bw35	5	25	698	17.4
B37	0	0	151	3.8
B40	1	5	705	17.6
			n = 1824	
Cw1	0	0	131	7.2
Cw2	1	5	318	17.5
Cw3	9	45	680	37.3
Cw4	6	30	501	27.3
Cw5	1	5	135	7.4

* $\chi^2 = 7.76$ (Woolf, 1955)

significant (Godfrey *et al.*, 1978; Braley *et al.*, 1978). In our cases the HLA B7 antigen occurred in 7 cases, 3 males, and 4 females, average age 37 years (range 24 to 46 years) and were observed during 4.6 years (range 3 to 7 years). All 7 cases have arrived in the inactive scar stage and have shown no activity during the last year.

The frequency of HLA B7 in JDM was 35% as compared to 29.4% in the control group and falls within normal limits.

Discussion

The clinical features of JDM have been recognised

in Europe for at least 10 years. Even in the USA 11% of the patients with presumed ocular histoplasmosis have negative skin tests (Ellis and Schlaegel, 1973). These may be cases of JDM.

Recent publications have shown a statistically significant increase in the frequency of HLA B7 antigen in cases with the presumed ocular histoplasmosis syndrome (Godfrey *et al.*, 1978; Braley *et al.*, 1978). The HLA B7 frequency was not significantly increased in our cases of JDM.

Flaage *et al.* (1977) found no specific HLA antigen frequencies in their 9 cases of juvenile haemorrhagic maculopathy. In our 20 cases of JDM an increase in HLA B15 is not significant with respect to the corrected P value, but it is certainly worthwhile continuing to determine the histocompatibility antigens in cases of JDM.

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