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HLA typing in retinitis pigmentosa

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SUMMARY HLA serological typing was performed on 173 patients with retinitis pigmentosa (RP) of all hereditary types. No significant difference was found in the frequency of any HLA (A, B, C) antigen, when comparing autosomal dominant and recessive RP patients with a control population.

HLA is the major histocompatibility system in man used for tissue typing and has been used as a research procedure for evaluating various disease states. The loci for HLA are located next to each other on chromosome 6 and have 3 serologically defined loci (HLA A, B, C) and 2 main lymphocyte defined loci (HLA D, DR).[1]

Associations between HLA antigens and systemic diseases are well documented.[2] Ophthalmological diseases reported to be associated with increased frequencies of specific HLA antigens include adult iridocyclitis and anterior uveitis (HLA B27),[3,4] Behçet's syndrome (HLA B5),[5] and presumed ocular histoplasmosis syndrome (HLA B7).[6]

A past HLA study of serologically defined loci in 18 patients with autosomal recessive retinitis pigmentosa (RP) was negative.[7] The present HLA study of serologically defined loci included 173 RP patients of all hereditary types.

Subjects and methods

Volunteer RP patients were recruited on a random basis from the University of California at Los Angeles RP Registry at the Jules Stein Eye Institute. All hereditary types were included (143 autosomal recessive, 24 autosomal dominant, and 6 sex linked). Cases with no family history of RP were classified as autosomal recessive. Diagnoses were made by a combination of clinical history, ophthalmological examination, visual fields, and electrophysiological testing. A detailed family history was obtained from each patient.

HLA typing was performed in the Tissue Typing Laboratory, Department of Surgery, University of California, Los Angeles, by the microcytotoxicity test.[8] Controls (462) were selected by the Tissue Typing Laboratory.

Results

The results of the study appear in Table 1. The chi-square test with Yates's continuity correction for the number of comparisons was used for statistical analysis of the results. P values were calculated by using Fisher's exact probabilities from the distribution of the chi-square. Significance was predefined at $p=0{\cdot}05$.

No significant difference was found in the frequency of any antigen on the serologically defined loci when autosomal dominant or autosomal recessive RP patients were compared with a control population. The frequency of HLA loci was also evaluated between male and female patients and between each sex and normal controls; no significant differences were found. The size of the sex-linked group of RP patients (6) precluded meaningful statistical analysis. However, when the total group of RP patients was compared with a control population, there was a significantly low (p corrected $=0{\cdot}04$) incidence of HLA CW3 in the RP group.

Discussion

The results of this study substantiate the results of the negative HLA study on autosomal recessive RP. In addition we find no significant difference in the frequency of any antigens on the A, B, or C loci

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Table 1 *Frequencies of HLA A, B, and C in Caucasian retinitis pigmentosa patients*

	Controls *n=462*	*Autosomal dominant* *n=24*	*Autosomal recessive* *n=143*	*Total (incl. sex-linked)* *n=173*
A1	29	29	22	23
A2	44	29	43	43
A3	27	33	20	22
A11	11	8	10	10
A25	5	4	3	3
A26	9	13	10	10
A28	9	13	8	9
A29	8	13	13	13
Aw23	5	4	6	6
Aw24	16	21	21	21
Aw30	5	13	8	8
Aw31	4	0	6	5
Aw32	8	0	6	5
Aw33	3	4	6	6
Aw34	0	0	1	1
B5	9	8	12	11
B7	25	33	21	23
B8	21	17	13	14
B12	25	29	27	27
B13	4	4	7	6
B14	8	13	12	12
B15	11	4	4	5
B17	8	4	13	11
B18	8	17	7	8
B27	9	0	5	4
B37	3	4	1	1
B40	11	4	6	6
Bw21	4	13	6	6
Bw22	5	0	4	3
Bw35	21	17	26	24
Bw38	7	8	13	13
Bw39	5	4	4	4
Cw1	4	0	1	1
Cw2	4		1	1
Cw3	18	0	7*	7†
Cw4	19	13	17	17

Cw3: *χ^2=9·89, p corrected =0·07. †χ^2=11·01, p corrected =0·04. All other frequency differenced between control group and patient categories are not statistically significant.

when comparing autosomal dominant RP with a control population. Surprisingly, when comparing the total RP group with a normal control population, we found a significantly lower number of RP patients to have the HLA CW3 antigen. At a significance level of p=0·04 there is a probability of 0·04 that this occurred by chance. Negative associations within the HLA system are not at present understood.

The current belief is that retinitis pigmentosa has multiple causes which share a final common pathway of pigmentary degeneration. If we are dealing with multiple disease, then it would not be expected that any significant HLA antigen association would be found. Our findings support the concept that within hereditary subgroups we may be dealing with multiple diseases. It is possible, however, that when RP is classified according to aetiology a positive HLA association may occur.

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