Senile cataracts and the HLA system

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SUMMARY HLA A, B, and C typing was performed on a group of 309 southern Spanish people, namely, 207 controls and 102 patients who underwent a senile cataract extraction. Comparison of the results in the 2 groups (chi-square test) showed in the senile cataract group a significant increase in the association with HLA A9 ($p<0.01$), HLA A blank ($p<0.005$), HLA B5 ($p<0.005$), HLA B13 ($p<0.03$), and HLA B blank ($p<0.01$) and a significant decrease in the association with HLA A2 ($p<0.05$), HLA Aw24 ($p<0.001$), HLA B27 ($p<0.025$), HLA Cw2 ($p<0.001$), and HLA Cw5 ($p<0.01$). The factors underlying these increased and decreased associations are conjectural.

The major histocompatibility system of man (the HLA system) consists of many closely linked genes on the short arm of chromosome 6. Several loci can be distinguished. Some of them are responsible for graft rejection and are serologically defined (loci A, B, C, and DR), and another controls the mixed lymphocyte reaction (locus D).¹

The association between the HLA system and several diseases has been reported by different authors.² In ophthalmology it has been reported in the cases of glaucoma,³ anterior uveitis,⁴ Behçet's disease,^{5,6} retinitis pigmentosa,⁷ and myasthenia gravis.⁸

Senile cataracts and the HLA system have been studied recently⁹ without significant differences being found apart from a slight increase in the frequency of association with HLA A blank in relation to a control group.

Material and methods

A group of 309 southern Spanish people, 207 controls and 102 patients with senile cataracts, were studied. For an appropriate selection of the control group all those people suspected of suffering from a disease supposed to be related to the HLA system were rejected. The results were compared with those of other series in order to ascertain their significance value, the comparison being by the genetic identity

index. The criteria for selection of patients with senile cataracts were: age 45 or over, family history negative, and the recorded character of the primary cataract.

HLA typing was performed by the Sección de Inmunología, Servicio de Análisis Clínicos de la Ciudad Sanitaria 'Virgen de las Nieves' de Granada, Spain, by the standard lymphocyte microcytotoxic test.

Results

The results are shown in Table 1. The chi-square test was used for a statistical analysis of the results. Values of p were calculated from the distribution of the chi-square¹⁰ and by Fisher's exact test¹¹ (antigen B13). The significance level was predefined at $p=0.05$.

Comparison between the 2 groups showed a significant increase in the association with HLA A9 ($p<0.01$; $\chi^2=7.425$), HLA A blank ($p<0.005$; $\chi^2=8.971$), HLA B5 ($p<0.005$; $\chi^2=10.210$), HLA B13 ($p<0.03$; $\chi^2=4.794$), and HLA B blank ($p<0.01$; $\chi^2=7.825$) and a significant decrease in the association with HLA A2 ($p<0.05$; $\chi^2=4.071$), HLA Aw24 ($p<0.001$; $\chi^2=16.302$), HLA B27 ($p<0.025$; $\chi^2=5.620$), HLA Cw2 ($p<0.001$; $\chi^2=17.962$), and HLA Cw5 ($p<0.01$; $\chi^2=7.587$). The relative risks appear in Table 1.

Discussion

The clinical interest of the HLA-associated diseases in ophthalmology has been reduced to the above-

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Table 1 Phenotypic frequencies (PF) of the HLA antigens of loci A, B, and C in senile cataracts patients

HLA antigen	PF (%)		Relative risk	χ^2	p
	Controls	Patients			
	(n=207)	(n=102)			
A1	23.18	22.54	0.96	0.016	
A2	46.37	34.31	0.60	4.071	<0.05
A3	17.39	9.80	0.51	3.104	
A9	6.76	16.66	2.75	7.425	<0.01
A10	8.21	8.82	1.08	0.033	
A11	14.97	15.68	1.05	0.027	
Aw19	1.44	1.96	1.36	0.112	
Aw23	0.48	0.00	0.0	—	
Aw24	18.35	1.96	0.08	16.302	<0.001
A25	5.31	4.90	1.07	0.024	
A26	0.96	2.94	3.12	1.674	
A28	3.86	2.94	0.75	0.170	
A29	14.97	17.64	1.21	0.365	
Aw30	8.69	14.70	1.81	2.588	
Aw31	1.93	1.96	1.01	0.0002	
Aw33	4.34	5.88	1.37	0.348	
A blank	21.25	37.25	2.19	8.971	<0.005
B5	10.62	24.50	2.73	10.210	<0.005
B7	15.94	13.72	0.83	0.260	
B8	10.14	14.70	1.92	1.381	
B12	2.89	3.92	1.37	0.228	
B13	1.44	5.88	4.27	4.749	<0.03
B14	15.45	9.80	0.59	1.861	
B15	8.69	7.84	0.89	0.064	
Bw16	3.38	7.84	2.43	2.945	
B17	4.83	1.96	0.39	1.508	
B18	15.45	13.72	0.87	0.162	
Bw21	8.69	6.86	0.77	0.309	
Bw22	5.31	2.94	0.54	0.889	
B27	9.17	1.96	0.19	5.620	<0.025
Bw35	20.77	17.64	0.81	0.421	
B37	0.48	0.00	0.0	—	
Bw38	0.48	0.00	0.0	—	
B40	8.21	6.86	0.82	0.174	
Bw42	0.00	0.98	0.0	—	
Bw44	17.05	20.58	0.69	1.526	
Bw45	1.44	1.96	1.36	0.112	
Bw47	0.97	0.00	0.0	—	
Bw48	0.48	0.00	0.0	—	
Bw49	0.48	0.98	2.05	0.263	
Bw50	5.31	4.90	0.91	0.024	
Bw51	6.76	0.00	0.0	—	
Bw52	0.96	0.00	0.0	—	
Bw62	0.00	0.98	0.0	—	
B blank	13.52	26.47	2.30	7.825	<0.01
Cw2	31.88	9.80	0.23	17.962	<0.001
Cw3	10.44	13.72	1.36	0.872	
Cw4	21.25	18.62	0.84	2.291	
Cw5	9.17	0.98	0.09	7.587	<0.01

mentioned conditions.³⁻⁶ But the disorders of the lens and, above all, senile cataracts have been reported without conclusive results only once.⁹ In that study an investigation of the HLA system in 60 patients suffering from senile cataract did not prove that they were associated and showed only an increase in the relation

with HLA A blank against a control group. This may imply that HLA A homozygotes are more susceptible to this disease.

It was therefore thought we could work in an almost unexplored field because of the high frequency of disturbances in the transparency of the lens and the difficulty of their treatment and prophylaxis (apart from symptomatic cataracts).

Although nuclear sclerosis of the lens is a physiological process, not everybody develops an actual opacity; neither nuclear senile cataracts nor cortical opacities are universal. It follows that there is a difference between people suffering from senile cataract and the rest of the population. Without underrating the role of the phenotypic factors, environmental or not, we cannot exclude the possibility of a genetic factor, at least causing a predisposition. That is why the comparative study of HLA antigens in healthy people and in patients with senile cataract from the same geographic area was performed.

Our results may suggest that the antigens whose frequencies are significantly increased (in patients with senile cataract) point to a predisposing factor, whereas the antigens whose frequencies are significantly decreased point to a resistance or protective factor.

It can be assumed that the relationship between HLA and senile cataract is not very strong, and we cannot rely too much on an apparent association with different antigens. Nevertheless, as happens in other HLA-related diseases, the presence or absence of a specific antigen serves only as a predisposing or protective factor, but never involves a determinant character. Ankylosing spondylitis is a clear example of how only a low percentage of people who are HLA B27 positive suffer from the disease, though more than 90% of the patients possess the HLA B27 antigen.

References

- 1 Bodmer WF. The HLA system: introduction. *Br Med Bull* 1978; **34**: 213-6.
- 2 Dick HM. HLA and disease: introductory review. *Br Med Bull* 1978; **34**: 271-4.
- 3 Ritch R, Podos SM, Henley W, Moss A, Southren AL, Fotino M. Lack of association of histocompatibility antigens with primary open-angle glaucoma. *Arch Ophthalmol* 1978; **96**: 2204-6.
- 4 Ohno S, Kimura SJ, O'Connor GR, Char DH. HLA antigens and uveitis. *Br J Ophthalmol* 1977; **61**: 62-4.
- 5 Ohno S, Sugiura S, Itakura K, Aizawa M. Further studies on HLA antigens in Behçet's disease. *Jpn J Ophthalmol* 1978; **22**: 62-7.
- 6 Gálvez Torres-Puchol J, Gimenez-Padilla L-F, Sanchez Ortega S, Pareja Tello E. Enfermedad de Behçet: consideraciones clínicas e inmunológicas. *Arch Soc Esp Ofal* 1981; **41**: 845-55.
- 7 Heckenlively JR, Bastek JV, Pearlman JT, Gladden J, Terasaki

- P. HLA typing in retinitis pigmentosa. *Br J Ophthalmol* 1981; **65**: 131–2.
- 8 Kaakinen A, Pirskanen R, Tiilikainen A. LD antigens associated with HL-A8 and myasthenia gravis. *Tissue Antigens* 1975; **6**: 175–82.
- 9 Hida M, Kuwahara K. Cataract and HLA antigen. *Nippon Ganka Gakkai Zasshi* 1978; **82**: 751–4.
- 10 Remington RD, Schork MA. *Estadística Biométrica y Sanitaria. Prentice internacional*. 1978.
- 11 Greym F, Salmon D. *Bases Statistiques*. Paris: Dunod. 1969.