British Journal of Ophthalmology, 1977, **61**, 62–64

HLA antigens and uveitis

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SUMMARY We have studied the antigen frequencies in a group of adult patients with acute and chronic iridocyclitis and chronic cyclitis. In patients with iridocyclitis a statistically significant increased incidence of HLA-B27 was noted, even in those patients without joint or systemic disease. Patients with chronic iridocyclitis also were noted to have an increased incidence of B27; however, those patients with chronic cyclitis did not. On the basis of HLA-B27 studies there appears to be a fundamental difference between adult and juvenile iridocyclitis.

A number of investigators have noted an association between HLA-B27 and acute anterior uveitis (Brewerton *et al.*, 1973; Ehlers *et al.*, 1974; Mapstone and Woodrow, 1974; Brewerton and James, 1975; Woodrow *et al.*, 1975). Both ankylosing spondylitis and Reiter's syndrome are associated with iridocyclitis, and there is a statistically significant increased incidence of HLA-B27 in these systemic diseases (Caffrey and James, 1973; Brewerton *et al.*, 1973; Schlosstein *et al.*, 1973; Aho *et al.*, 1973; Zachariae *et al.*, 1973; Woodrow, 1973). We have studied the HLA antigen frequencies in a group of adult patients with acute and chronic iridocyclitis and with chronic cyclitis to determine whether factors such as the chronicity of inflammation, the presence of associated joint or systemic disease, or the sex of the patient are specifically related to certain HLA antigen frequencies.

Materials and methods

Fifty-three unrelated patients with uveitis were typed for HLA antigens. Thirty-nine had iridocylitis of adult onset. Nineteen of these were males and 20 were females with an age range from 25 to 68 years (mean 42·6 years). Twenty of these patients had acute recurrent iridocyclitis and had characteristic symptoms at the onset of each episode including: ocular pain, conjunctival injection, photophobia, epiphora, and blurred vision. Nineteen patients had chronic iridocyclitis, although eight had initially presented with an acute episode. Patients with chronic iridocyclitis had a painless anterior uveitis of greater than six months duration which was poorly responsive to medication. Seven male and seven female Caucasian patients were thought to have chronic cyclitis; their ages ranged from 5 to 67 years (mean 26·6 years). All of these patients had an acute onset of uveitis, the most frequent chief complaint being floating spots. On ophthalmological examination patients with chronic cyclitis showed cellular opacities in the anterior vitreous, large vitreous snowballs, and 'snow banking' on the inferior pars plana.

All patients were examined by at least two examiners. The cases were classified as iridocyclitis when the inflammation was predominantly in the anterior chamber of the eye; and the diagnosis of chronic cyclitis was made by the clinical findings described above.

HLA typing was performed by the microlymphocyte cytotoxicity test for 10 HLA-A and 14 HLA-B specificities described previously (Ohno *et al.*, submitted for publication). The frequency of HLA antigens in patients with acute and chronic iridocyclitis and with chronic cyclitis of adult onset was compared with 72 normal control subjects using a chi-square test with Yates's correction.

Results

The distribution of HLA antigens among 33 Caucasian patients with acute and chronic iridocyclitis of adult onset and among normal adult control subjects is presented in Table 1. There were no statistically significant alterations in the HLA-A locus antigen frequencies in the patient versus the

This investigation was supported by a Fight for Sight Grant no. G574 and NIH Grants Nos. EY01759 and EY01597.

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control populations. Eighteen out of 33 patients (54·5%) were positive for HLA-B27, in contrast to 5 out of 72 (6·9%) normal controls ($\chi^2=27·3$, $P<0·0001$). The frequency of HLA-B27 was analysed according to the presence or absence of associated joint disease, systemic disease, and sex (Table 2). Eleven of 19 males (57·9%) were positive for HLA-B27 as were nine of 20 females (45%). In the category of ankylosing spondylitis five out of seven patients were B27 positive. Two patients with Reiter's disease, one patient with sacroiliitis, and one patient with osteitis condensans ilii were also noted to have the HLA-B27 antigen. Among 26 patients with iridocyclitis (9 males and 17 females) there were no physical or roentgenologic signs of either joint or systemic disease. Eleven of these patients (42%) also were B27 positive.

The frequency of HLA-B27 was also analysed according to the chronicity of the iridocyclitis. In acute recurrent iridocyclitis 12 out of 20 patients (60%) were positive for HLA-B27. Among patients with chronic iridocyclitis eight out of 19 (42%) were positive; this difference was not statistically significant. There was no difference in the HLA-B27 frequency between patients with unilateral versus bilateral iridocyclitis, and we did not note any significant correlations between the severity of the iridocyclitis and HLA-B27.

Table 1 *Frequency of HLA antigens in adult iridocyclitis and chronic cyclitis*

HLA antigen	*Controls (N=14)*		*Adult iridocyclitis (N=33)*		*Chronic cyclitis (N=14)*	
	No.	*%*	*No.*	*%*	*No.*	*%*
HLA—A1	20	(27·8)	6	(18·2)	6	(42·9)
HLA—A2	34	(47·2)	19	(57·6)	3	(21·4)
HLA—A3	16	(22·2)	7	(21·2)	4	(28·6)
HLA—A9	18	(25·0)	5	(15·2)	3	(21·4)
HLA—A10	9	(12·5)	4	(12·1)	4	(28·6)
HLA—A11	10	(13·9)	4	(12·1)	1	(7·1)
HLA—A28	4	(5·6)	2	(6·1)	1	(7·1)
HLA—A29	5	(6·9)	2	(6·1)	0	(0)
HLA—AW30	5	(6·9)	2	(6·1)	0	(0)
HLA—AW32	7	(9·7)	4	(12·1)	1	(7·1)
HLA—B5	6	(8·3)	2	(6·1)	1	(7·1)
HLA—B7	18	(25·0)	8	(24·2)	4	(28·6)
HLA—B8	17	(23·6)	5	(15·2)	4	(28·6)
HLA—B12	19	(26·4)	7	(21·2)	3	(21·4)
HLA—B13	3	(4·2)	1	(3·0)	1	(7·1)
HLA—B14	7	(9·7)	2	(6·1)	1	(7·1)
HLA—B18	4	(5·6)	3	(9·1)	2	(14·3)
HLA—B27	5	(6·9)	18	(54·5)*	0	(0)
HLA—BW15	7	(9·7)	4	(12·1)	1	(7·1)
HLA—BW16	3	(4·2)	1	(3·0)	1	(7·1)
HLA—BW17	6	(8·3)	1	(3·0)	1	(7·1)
HLA—BW22	3	(4·2)	0	(0)	0	(0)
HLA—BW35	8	(11·1)	5	(15·2)	1	(7·1)
HLA—BW40	10	(13·9)	4	(12·1)	2	(14·3)

*$\chi^2=27·3$, $P<0·0001$.

Table 2 *Frequency of HLA-B27 and associated diseases*

	HLA—B27 Present		*HLA—B27 Absent*		*Total*
	Male	*Female*	*Male*	*Female*	
Ankylosing spondylitis	5	0	1	1	7
Reiter's disease	2	0	0	0	2
Urethritis	0	0	2	0	2
Sacroiliitis	0	1	0	0	1
Osteitis condensuns ilii	0	1	0	0	1
No associated disease	4	7	5	10	26
Total	11	9	8	11	39

Discussion

Acute and chronic iridocyclitis of adult onset has a highly significant association with the HLA-B27 antigen in contrast to juvenile chronic iridocyclitis and chronic cyclitis (Ohno *et al.*, 1977). Brewerton *et al.* (1973) first reported the association of acute anterior uveitis and HLA-B27. They noted that 55% of 44 patients with acute anterior uveitis had HLA-B27. Twenty-nine per cent of 24 patients with acute anterior uveitis without systemic disease were also positive for B27. These findings have been confirmed in the case of acute recurrent uveitis, but not in chronic uveitis, by Ehlers *et al.* (1974). Mapstone and Woodrow (1974) studied 59 patients with acute anterior uveitis and 32 (54%) had the HLA-B27 antigen. Among 41 patients without systemic disease 17 (42%) were also positive. Similar B27 frequencies were recently reported by Brewerton and James (1975) and Woodrow *et al.* (1975).

Iridocyclitis associated with ankylosing spondylitis and with Reiter's disease has a close association with HLA-B27, because the systemic disease itself has a significant correlation with HLA-B27. Sacroiliitis seems to be one of the most important forms of arthritis associated with iridocyclitis. In both ulcerative colitis and in Reiter's disease uveitis was found more often in patients with sacroiliitis than those without it (Wright *et al.*, 1965; Oates and Young, 1959). In our series, 42·3% of the 26 patients who had no sacroiliitis or associated systemic disease had the HLA-B27 ($\chi^2=15·0$, $P<0·0001$). There was no difference in the percentage of males or females having uveitis without systemic disease.

It is possible that patients with iridocyclitis and HLA-B27 may have subclinical or asymptomatic sacroiliitis, and we suspect these patients may represent an incomplete form of the uveitis syndrome associated with ankylosing spondylitis or Reiter's disease.

Ehlers *et al.* (1974) did not find an increased incidence of HLA-B27 in chronic uveitis. In our

study there was an increased incidence of HLA-B27 (42·1%) among 19 patients with chronic iridocyclitis of adult onset which was significantly higher than that among normal controls ($\chi^2=12·4$, $0·0005 > P > 0·003$). Even among the patients whose chronic iridocyclitis never underwent acute exacerbations HLA-B27 was also significantly increased (36·4%), and this was again statistically significant ($\chi^2=5·77$, $0·02 > P > 0·015$). There appears to be a fundamental difference between adult onset iridocyclitis and chronic iridocyclitis in children or chronic cyclitis, both of which have no correlation with HLA-B27 (Ohno *et al.*, 1977). These data would suggest that there are marked differences among the anterior uveitides, although the clinical findings may be somewhat similar.

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