HLA antigens in acute anterior uveitis in South African blacks

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SUMMARY Fifty-three black patients with acute nongranulomatous anterior uveitis (AAU) were tissue typed and the results compared to those from a panel of 200 healthy unrelated black volunteers. No statistically significant deviation from the norm with regard to the frequencies of 38 HLA antigens could be observed.

The striking association between HLA B27, acute anterior uveitis (AAU), certain rheumatic disorders like ankylosing spondylitis, Reiter's disease, reactive arthritis, and juvenile rheumatoid arthritis has been described by several authors and is well documented (Brewerton et al., 1973a, b; Schlosstein et al., 1973; Caffrey and James, 1973; Brewerton et al., 1974; Rachelefsky et al., 1974; Brewerton, 1975; Mapstone and Woodrow, 1975; Zervas et al., 1977; Ohno et al., 1977).

However, in several series of patients investigated for AAU there was a considerable number of patients who possessed the antigen HLA B27 but did not show rheumatic or any other systemic disorders, the percentages of this type of patient ranging from 30% to 45%. The frequency of the antigen in the relevant control groups ranged from 4% to 8% (Brewerton and colleagues, 1974; Mapstone and Woodrow, 1975; Zervas et al., 1977; Brewerton and James, 1975). All these investigations were undertaken in white patients, in whom it is now generally accepted that idiopathic AAU, that is, without rheumatic or other obvious systemic diseases, shows a significant association with the antigen HLA B27.

Perkins (1976) observed the absence of AAU due to rheumatic conditions in immigrant negroes from West Africa living in London and related this finding to the reported absence of HLA B27 in this ethnic group. Ayarru (1977) also reported the rarity of acute nongranulomatous anterior uveitis associated with rheumatic diseases among Nigerian patients and attributed this to the absence of the genetic marker HLA B27 among Africans. In his series most of the cases showed posterior uveitis, anterior uveitis being relatively rare.

In contrast Freedman (1974) observed a different distribution in South African blacks, as most of his 355 cases suffered from anterior uveitis, and posterior uveitis was seen far less commonly. Furthermore the rate for anterior uveitis among the South African blacks, 24 per 100 000, was significantly higher than the rate of 12 per 100 000 found in Rochester. During his investigation into the aetiology of uveitis in Bantu adults Freedman (1976) observed 2 patients out of 311 in whom ankylosing spondylitis was the associated disease and described these patients as being unique, ankylosing spondylitis being extremely rare among South African blacks (Baum and Ziff, 1970).

Though the antigen HLA B27 is not altogether absent in South African blacks, it does occur at a very low frequency of 0.6% to 0.7% (Hammond et al., 1977; David et al., 1979). It is completely absent in the normal healthy Japanese population (Tsui and Fukunishi, 1973). Yet when Sonozaki et al. (1975) investigated 27 Japanese patients who presented with ankylosing spondylitis they found the antigen present in 67% of their cases.

It was of interest, therefore, to investigate whether the association of HLA B27 and AAU, with or without systemic disease, as reported in white populations, would also hold true for a black population group.

Patients and methods

PATIENTS Fify-three black patients suffering from acute non-
granulomatous anterior uveitis were chosen for this study out of hundreds of uveitis cases seen at the St John's Eye Hospital, Baragwanath, during the years 1976 and 1978. All the patients were examined by 2 of the authors (B.M. and J.F.), and the particulars were recorded indicating history, age, sex, clinical description of the disease, and results of laboratory investigations. Diagnosis was based on clinical symptoms such as pain, photophobia, lacrimation, and recurrence, and signs such as circumcorneal injection, keratic precipitates (not mutton fat), cells and flare in the anterior chamber, and increased intraocular pressure.

All the patients underwent the routine battery of investigations adopted for uveitis which includes: x-rays of the chest, sinuses, and sacroiliac joints, full blood count, erythrocyte sedimentation rate, antistreptolysin titre, blood sugar level, gonococcal complement fixation test, toxoplasma dye and complement fixation tests, serum protein electrophoresis, fluorescent treponemal antibody test, Rose latex test for arthritis, and a delayed hypersensitivity skin test for tuberculosis. The control panel consisted of 200 healthy unrelated black volunteers belonging to various Southern African tribes.

**HLA TYPING**

Tissue typing was performed at the Tissue Bank of the South African Institute for Medical Research in Johannesburg. The method used was the Standard 2 Stage NIH Lymphocyte Microcytotoxicity test at an incubation temperature of 37°C throughout the test, trypsin blue as the indicator dye. A total of 174 different typing sera were used to identify 38 HLA antigens: 17 of the A locus, 18 of the B locus, and 3 of the C locus. Although the first group of 16 patients were investigated in 1976 and the remaining patients in 1978, the range of antiserum remained essentially the same. The exception was the introduction of antisera against Aw30, Aw31, and Aw33. For the typing of the first group only antisera with the specificity Aw30/Aw31 were available, whereas for the 1978 group antisera which allowed differentiation between Aw30 and Aw31 and later on Aw33 were at the typing team's disposal. The statistical evaluation of the results was performed by employing the $\chi^2$ test with Yates's correction.

**Results**

There were 28 males and 25 females among the patients. The mean age of the males was 35.5 years and that of the females was 31.1 years.

Twenty of the patients, on questioning, reported previous episodes of ocular symptoms which might from the patients' descriptions have been attacks of acute anterior uveitis. None of the 53 patients had any overt clinical evidence of rheumatic or other systemic disease. Ten patients had a raised ESR, 6 had a positive serological test for syphilis, 3 had a positive test for toxoplasmosis, 3 had a raised antistreptolysin titre, 1 had active sinusitis radiologically, and 5 had a positive skin test for tuberculosis but no evidence of active tuberculosis.

None of the 3 HLA B27 carriers, 2 males and 1 female, showed any of the above clinical findings.

The frequencies of 38 HLA antigens in 53 black South African patients suffering from acute, nongranulomatous anterior uveitis, as compared to 200 controls, are presented in Table 1.

**Discussion**

The antigen HLA B27 was represented slightly more frequently in the patient group (3/53) than in the control group (2/200). However, this did not reach statistically significant proportions. None of the

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<table>
<thead>
<tr>
<th>HLA-A1</th>
<th>Controls (No. = 200)</th>
<th>AAU patients (No. = 53)</th>
<th>$\chi^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2</td>
<td>7.0</td>
<td>13.2</td>
<td>1.38</td>
<td>NS</td>
</tr>
<tr>
<td>A3</td>
<td>10.0</td>
<td>0.0007</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>A9</td>
<td>18.0</td>
<td>18.9</td>
<td>0.0029</td>
<td>NS</td>
</tr>
<tr>
<td>A10</td>
<td>0.0</td>
<td>0.0007</td>
<td>-</td>
<td>NS</td>
</tr>
</tbody>
</table>

1Tested 62. 2Tested 37. 3Tested 23.
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remaining antigens showed any statistically significant deviation from the norm.

Antigen frequencies of the A, B, and C locus of the major histocompatibility complex of man vary between different racial groups (Payne et al., 1977). The same applies to the linkage disequilibria which have been found to exist between these antigens (Ward and Biegel, 1976; Hammond et al., 1977). Positive or negative linkage disequilibria occur when antigens of the different HLA loci are found together more frequently, or less frequently, on the same chromosome than would be expected by the frequency of the single antigen alone in a given population group. The association of HLA B27 or any other HLA antigen with a certain disease has been attributed tentatively to the location, on the genome, of specific immune response (Ir) genes in close proximity to the gene coding for HLA B27, or to the indicted HLA antigen, and to the occurrence of positive linkage disequilibria between these HLA markers and the, in man as yet, hypothetical Ir genes (Brewerton and James, 1975; Dausset and Hors, 1975; Svejgaard et al., 1975).

Should this hypothesis be true, it is conceivable that the linkage disequilibria found in one racial group are not repeated in another racial group, consistent with the established racial variations in linkage disequilibria between antigens of the A, B, and C locus. This could be one reason why this study has not revealed an association between AAU and any of the HLA antigens in a group of 53 black patients. In this connection it is interesting to mention the well documented association of HLA B17 with psoriasis in whites (Russel et al., 1972; White et al., 1972). B17 is the antigen with the highest frequency, 33%–41%, on the B locus in blacks (Payne et al., 1977; Hammond et al., 1977; David et al., 1979). Yet psoriasis is hardly present in the blacks of South Africa.

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References


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