ASSOCIATION OF HLA-B27 WITH ANKYLOSING SPONDYLITIS IN ISFAHAN, IRAN

K. M. ADIB AND H. HOSSEINI

From the Immunogenetic Laboratory of Aliasghar Hospital, Isfahan University of Medical Sciences, Isfahan, Islamic Republic of Iran.

ABSTRACT

Using a standard microcytotoxicity (NIH) technique of tissue typing, the HLA-B27 antigen was identified in 30 out of 34 patients (88.2%) with classical ankylosing spondylitis (AS), compared to 6 out of 70 controls (8.6%) (P < 0.005).

We also found this antigen in 8 out of 76 (10.5%) patients with non-AS arthritis.


INTRODUCTION

A link between the HLA-B27 histocompatibility antigen and several forms of seronegative spondyloarthropathies including ankylosing spondylitis, Reiter's disease and reactive arthritis is now firmly established.1,2

Ankylosing spondylitis (AS) shows a very strong association with HLA-B27, but the extent of this association varies considerably among various racial and ethnic groups.3 The present study was performed to investigate the strength of this association in Isfahan, Iran.

PATIENTS AND METHODS

All of the patients had been referred to the immunogenetic laboratory of the Aliasghar Hospital, and had been under observation by a rheumatologist for at least two years. Some had advanced, overt disease with restriction of chest and spinal movement, while others had only lumbar and pelvic pain. The patients' radiographs were studied by rheumatologists and those having at least grade 3 bilateral sacroiliitis were accepted as definite patients.

All patients had classical clinical and radiological findings of ankylosing spondylitis according to the New York criteria.4 The patients consisted of 34 Iranian adults, 26 men (76.5%) and 8 women (23.5%), with an age range of 16 to 38 years (average 25 years). Among the patients, 62% had a raised erythrocyte sedimentation rate. 76 other patients (38 men and 38 women) who referred to the lab with arthritis due to Reiter's disease, ulcerative colitis, psoriasis, rheumatoid arthritis, and other non-AS disease were also typed for the HLA-B27 antigen.

The controls were selected from normal, symptom-free blood donors with the same range of age. Typing for human leukocyte antigens was carried out using the NIH microlymphocytotoxicity test,5 and 5 ml of defibrinated blood was collected from each person. Mononuclear cells were separated by adding 5 ml of diluted blood to Ficoll - Isopaque.6 The separated lymphocytes were washed, adjusted to 2000 cells/μl, and applied to ready-made HLA typing plates, which contained 72 different HLA-A, B and C antisera plus negative and positive controls.

RESULTS

The HLA types of patients and controls are depicted in Tables I and II. HLA-B27 was found in 30 of 34 patients (88.2%). The 4 HLA-B27 negative patients had definite ankylosing spondylitis.

6 out of 70 controls were HLA-B27 positive (8.6%).
HLA-B27 in Ankylosing Spondylitis

Table I. HLA-A and C types in patients with ankylosing spondylitis and in controls.

<table>
<thead>
<tr>
<th>HLA-A&amp;C Antigens</th>
<th>Ankylosing Spondylitis (n=34)</th>
<th>Controls (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td>HLA-A1</td>
<td>6 (17.8%)</td>
<td>18 (25.7%)</td>
</tr>
<tr>
<td>A2</td>
<td>11 (32.3%)</td>
<td>16 (22.9%)</td>
</tr>
<tr>
<td>A3</td>
<td>2 (5.9%)</td>
<td>2 (2.9%)</td>
</tr>
<tr>
<td>A9</td>
<td>12 (35.3%)</td>
<td>20 (28.8%)</td>
</tr>
<tr>
<td>A11</td>
<td>6 (17.8%)</td>
<td>14 (20%)</td>
</tr>
<tr>
<td>A23</td>
<td>2 (5.9%)</td>
<td>6 (8.6%)</td>
</tr>
<tr>
<td>A24</td>
<td>6 (17.8%)</td>
<td>16 (22.9%)</td>
</tr>
<tr>
<td>A26</td>
<td>3 (8.8%)</td>
<td>6 (8.6%)</td>
</tr>
<tr>
<td>A28</td>
<td>2 (5.9%)</td>
<td>4 (5.7%)</td>
</tr>
<tr>
<td>A29</td>
<td>- (·)</td>
<td>4 (5.7%)</td>
</tr>
<tr>
<td>A30</td>
<td>- (·)</td>
<td>3 (4.3%)</td>
</tr>
<tr>
<td>A31</td>
<td>- (·)</td>
<td>- (-)</td>
</tr>
<tr>
<td>Aw 36</td>
<td>- (·)</td>
<td>- (-)</td>
</tr>
<tr>
<td>A25</td>
<td>- (·)</td>
<td>- (-)</td>
</tr>
<tr>
<td>HLA-C Antigens</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLA Cw1</td>
<td>- (·)</td>
<td>3 (4.2%)</td>
</tr>
<tr>
<td>Cw2</td>
<td>3 (8.8%)</td>
<td>4 (5.7%)</td>
</tr>
<tr>
<td>Cw3</td>
<td>- (·)</td>
<td>2 (2.9%)</td>
</tr>
<tr>
<td>Cw4</td>
<td>8 (23.5%)</td>
<td>19 (27.1%)</td>
</tr>
<tr>
<td>Cw7</td>
<td>1 (2.9%)</td>
<td>7 (10%)</td>
</tr>
</tbody>
</table>

One of the HLA-B27 positive normal controls was found to have an increased sedimentation rate and antistreptolysin O titer on further investigation. He did not have a positive family history of definite AS, and did not give a history of rheumatic disease or recent streptococcal infection.

Among the 76 patients with other types of arthritis, 8 had the HLA-B27 antigen (10.5%). In our study, men were more often affected by disease than women, and we had a male to female sex ratio of 3.3.

**DISCUSSION**

There are marked differences in the prevalence of AS among various ethnic and racial groups. These race related differences are very obvious between white and black populations. In general, most patients with AS possess HLA-B27 and the prevalence of the disease roughly corresponds to the prevalence of HLA-B27 in the population.

The present study was performed to determine the prevalence of HLA-B27 in the normal Iranian (Isfahan) population and to compare its prevalence with that in AS patients. Aside from this, the prevalence of all HLA
group one antigens was also determined in controls and
patients.

By studying the results, one can easily claim that
there is a statistically significant difference between the
two groups in the prevalence of the HLA-B27 antigen
(P<0.005). Other HLA group one antigens were not sig­
nificantly different between the two groups.

Our finding of HLA-B27 in 88.2% of individuals
with AS in Isfahan is similar to the findings of Davatchi
and Nikhin in Iran who found HLA-B27 positivity in
92% of AS patients, and also to that of investigators in
other countries and very close to UK (88%) and the
US white population (88%). Our results are in contrast
with the findings of Sonozaki et al, from Japan who
found 67% HLA-B27 positivity among patients and 0%
HLA-B27 positivity among controls.

Our data show a male to female sex ratio of 3.3.
Carter et al. found similar results (4:1), but Polley et
al. reported a 10:1 ratio in his earlier study. However,
most investigators reported this ratio to be 3 fold
greater in males, but the importance and cause of this
finding has yet to be explained.

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