gene may be responsible for a relatively severe disease course with eye involvement in the elder brother, but much stronger environmental factors might be required for the development of BD in individuals carrying only the second susceptibility gene.

In conclusion, a discordant disease course up to 5 yr in these HLA-B51-negative MZ twins further supports the important role of HLA-B51 or a non-HLA gene very close to this locus in the genetic predisposition to BD. Larger series of MZ and dizygotic twins, and investigation of the multicase families, are needed to clarify the genetic component in the pathogenesis of BD.

A. Gül, M. İnanç, L. Öcal, O. Aral, M. Čarin, * M. Konice
Division of Rheumatology, Department of Internal Medicine and *Tissue Typing Laboratory, Department of Medical Biology, Istanbul Medical School, Istanbul, Turkey
Accepted 13 January 1997
Correspondence to: A. Gül.

REFERENCES

Autoantibodies Against Cardiolipin and Endothelial Cells in Takayasu’s Arteritis: Prevalence and Isotype Distribution

Sir—Takayasu’s arteritis (TA) is a large-vessel vasculitis, with a predilection for the aortic arch and its branches. The aetiology of TA is not known. Some of the current clinical and laboratory data point towards an immune basis for the disease [1–3]. In view of the potential role of antibodies to cardiolipin (aCL) and endothelial cells (aEC) in vascular damage, we considered it of interest to study in TA patients the prevalence and levels of IgG, IgM and IgA isotypes of these two autoantibodies.

The study group consisted of 30 TA patients presenting between 1994 and 1995 at a tertiary care hospital in Lucknow, India, and 44 age- and sex-matched healthy controls. TA was diagnosed according to the ACR criteria [4] and considered to be in an active stage if two or more of the following were present: (i) constitutional features, for which no other cause could be identified; (ii) painful arteries; (iii) elevated ESR (>30 mm/h); (iv) elevated CRP (>0.6 mg/dl). Thirteen patients had active disease. None of the patients had signs of the antiphospholipid syndrome.

IgG and IgM aCL and aEC were determined according to the method described previously [5]. For IgA aCL and aEC, the serum was used in a dilution of 1/30 and anti-human IgA alkaline phosphatase conjugated (α-chain specific, Sigma, St Louis, MO, USA) in a dilution of 1/1000. The cumulative intra- and inter-assay coefficients of variation were <10% and <15% for aCL and aEC, respectively. The cut-off limit for a positive value was taken as the mean +2 s.d. of the control group excluding three very high values of IgG aEC and one value of IgM aEC; these cases were, however, taken as positive.

The standardized normal deviate and Fisher exact test were used for comparing two proportions. The Mann–Whitney U-test was used for comparison of levels of antibodies between patient and controls.

Significantly higher levels of all three isotypes of aCL (P < 0.01) and of IgG (P < 0.01) and IgM (P < 0.05) isotypes of aEC were observed in patients in comparison to those in controls (Fig. 1). The prevalence of one or more isotypes of aCL was 53.3% and of aEC 36.7% in patients in comparison to 9.1% (P < 0.01) and 13.6% (P < 0.05), respectively, in controls (Table 1). Furthermore, in patients with active disease, the prevalence of aCL and aEC was 84.6 and 61.5%, respectively, in comparison to 29.4% (P < 0.05) and 17.6% (P < 0.05), respectively, in those with inactive disease. aCL and aEC co-occurred in 33% of patients.

Although aCL have an established association with recurrent venous and/or arterial thromboses [6], there are now reports of aCL in inflammatory vascular diseases, as well as one on IgG aCL in TA [7–9]. Our
observation of an association of aCL with the activity of the vasculitic disease lends further support to a close relationship of these antibodies with vascular inflammation. The unusually high prevalence (33.3%) of IgA aCL observed by us may indicate that the triggering event for the formation of these antibodies is at the mucosal level, possibly a gastrointestinal or a respiratory tract infection.

The association of aEC with disease activity may also suggest their pathogenic involvement in TA. There is only one report available on aEC in TA in which IgG aEC was studied and observed to be elevated in 94% of TA patients [10]. The disease activity status of the patients in this study was not mentioned and the very high prevalence of aEC in comparison to that observed by us could be because most of their patients may have had active disease.

**TABLE 1**
Prevalence of antibodies to cardiolipin and endothelial cells in Takayasu’s arteritis patients and in healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>aCL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>10</td>
<td>(31.3)</td>
<td></td>
</tr>
<tr>
<td>IgM</td>
<td>6</td>
<td>(20.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IgA</td>
<td>10</td>
<td>(33.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>aEC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>10</td>
<td>(33.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IgM</td>
<td>6</td>
<td>(18.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IgA</td>
<td>1</td>
<td>(3.3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

aCL, antibodies to cardiolipin; aEC, antibodies to endothelial cells.
NS, not significant (P > 0.05).

In summary, we have observed aCL and aEC in a significant proportion of TA patients with a correlation with disease activity. Further studies on the mechanisms of action and antigenic targets of the autoantibodies may shed light on their pathogenic involvement in TA.

We would like to thank Margareta Söderqvist for excellent technical assistance, S. Mandal and M. Srivastava for statistical analysis of the data, and the Obstetrics and Gynaecology Department, Karolinska Hospital, for providing the umbilical cords. This work was supported by an intramural grant, SGPGIMS, Lucknow, India, and by AFA (Labour Market Insurance Company), Nanna Svartz, Knut & Alice Wallenberg and Petrus & Augusta Hedlund foundations, Sweden.

S. NIYANAND,*‡ K. MISIRA,* S. SHRIVASTAVA,** G. HOLM,** A. K. LEFVERT‡

*Departments of Immunology and ‡Cardiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, India and †Immunological Research Laboratory and Department of Medicine, Karolinska Hospital, Stockholm, Sweden

Accepted 13 January 1997

Correspondence to: A. K. Lefvert, Immunological Research Laboratory, Department of Medicine, Karolinska Hospital, 171 76 Stockholm, Sweden.


Von Willebrand Factor Antigen and Angiotensin Converting Enzyme Levels in Takayasu Arteritis

Sir—The assessment of disease activity in Takayasu arteritis (TA) is hampered by the lack of reliable criteria and laboratory markers. Although changes in