References


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Similiarity of the genetic background in rheumatic diseases between northern Italian and Israeli patients

Sir, We read with interest the paper by Tishler et al on the association between HLA-B35 and sodium aurothiomalate-related mucocutaneous toxicity in Israeli rheumatoid patients and would like to comment on it.

Firstly, we have observed a low degree of association between B35 and dermatitis in rheumatoid patients treated with sodium aurothiomalate, but a stronger one was found in those who had received tiopronin as a remission inducing drug. Secondly, in our region of northern Italy we are dealing with a rheumatoid population in which the level of DR4 is similar to that in controls (DR4: 15-27% in rheumatoid arthritis v 12-3% in controls). Similar findings were reported by Brautbar et al. Only when the patients were divided into those with and those without extra-articular manifestations did we observe some associations —namely, between DR3 and extra-articular features and between DR1 and arthritis without extra-articular disease. The lack of any significant association between DR4 and rheumatoid arthritis contrasted, though a comparison of the Israeli and Italian control series shows a different prevalence of three DR antigens—namely, DR2, DR3, and DR4 (Table 1).

Further data suggest a similarity between the two populations. As described in Israeli patients with Reiter’s disease we also found a lower than expected prevalence of B27 in 17 patients typed so far. This prevalence was 29-4%, which compares with 29% reported by Ben-Cherit et al.

We recently observed that patients with systemic lupus erythematosus also differ immunogenetically from several populations reported in published work as no relation has been found with DR2 or DR3. A strong association was observed, however, between DR7 and anticoagulopin antibodies. It would be very interesting to know whether in Israeli patients with systemic lupus erythematosus such an association also holds true.

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Table 1 Prevalence of DR antigens in Israeli and Italian controls. *Values are percentages

<table>
<thead>
<tr>
<th></th>
<th>DR1</th>
<th>DR2</th>
<th>DR3</th>
<th>DR4</th>
<th>DR5</th>
<th>DRw6</th>
<th>DR7</th>
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<td>14-2</td>
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<td>42-5</td>
<td>15</td>
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<tr>
<td>Italian</td>
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<td>25-1</td>
<td>18-4</td>
<td>12-3</td>
<td>48</td>
<td>16-4</td>
<td>24-7</td>
<td>4-5</td>
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*Data are from references 3 and 4.
Anticardiolipin versus lupus anticoagulant tests: no final judgment

Sir, I think it important to correct some statements made in a recent paper by Derksen and colleagues. Their study was a correlation of various lupus anticoagulant tests and their anticardiolipin (aCL) test with thrombosis and fetal loss in 111 lupus patients. In their discussion they implied that their group with systemic lupus erythematosus (SLE) was similar to the population of patients reported by our group in a previous study. This is incorrect. Our study looked at 121 patients with varying levels of aCL antibodies irrespective of underlying diagnosis. One third of the patients had normal aCL levels and only about 60% of the high positive group had SLE. The high percentage of patients with thrombosis and fetal loss in our report was largely influenced by the number of high aCL positive patients with these complications. Now that standard sera are available, and with improvements in the aCL test, our own and other reputable groups with similar experience continue to find that moderate to high positive aCL test results will identify a population (both SLE and non-SLE) with a high incidence of thrombosis and fetal loss. This statement will be tested further in a prospective study planned by the Kingston antiphospholipid study (KAPS) group.

Dr Derksen also stated that 'sera exchanged between his laboratory and that of the Lupus Research Laboratory were concordantly classified as negative, low, medium, or high positive for anticardiolipin antibodies'. Dr Derksen participated in the International Anticardiolipin Standardisation Workshop and had a valid assay, but this need not imply in any way concordance of test results between his laboratory and our own. Since the standardisation workshop there has been no formal study conducted between Dr Derksen's laboratory and our own that involved an exchange of sera and tests for concordance of our results. Indeed, such a process is only now being attempted at an international level by the KAPS group. In reviewing Dr Derksen's aCL assay method I must emphasise that the particular units and serum dilutions he used were his own and not those of the international workshop. In addition, in assays performed by the Lupus Research Laboratory (and now by my own laboratory in Louisville) the cut off level of low positive results (20 GPL or 20 MPL units) is well above 2SD of normal controls. Despite our efforts to standardise the aCL test my experience suggests that concordance between laboratory results in the absolute terms used by Dr Derksen will prove a difficult goal indeed.

In 1983 Doctors Gharavi and Hughes and I made the decision to set up an anticardiolipin test after it was found that lupus anticoagulant tests performed routinely in our hospital were not sufficiently sensitive and reproducible to identify patients whom we believed to have the lupus anticoagulant syndrome. Over the last five years and in the course of working in three very different institutions I remain convinced that our original decision was correct. We have managed to identify a substantial number of patients using the aCL test alone. My most recent experience in Louisville, Kentucky is a case in point. My laboratory has measured aCL levels in about 300 sera and found nine sera with moderate to high positive results. Seven of these sera were from patients with recurrent fetal loss or thrombosis, or both. Despite the fact that these patients had markedly raised IgG or IgM concentrations on several occasions I obtained a positive lupus anticoagulant test result on only two occasions. It is probable that the lupus anticoagulant test performed by the laboratory to which we send our plasma has an insensitive test. In busy outpatient settings in large institutions it is practically impossible for clinicians to meet the technicians performing coagulation tests, much less to have technicians perform the numbers of tests for the lupus anticoagulant outlined by Derksen and colleagues. The requirements that plasma specimens be platelet-poor and be freshly prepared (or stored at −70°C) impose further constraints. In addition, standardisation of the lupus anticoagulant test and measurement of these test results are difficult tasks and are only now being addressed by some international groups, including the KAPS group.

At a time when we are still improving both solid phase antiphospholipid tests and standardising lupus anticoagulant tests sweeping statements such as that made by Derksen and colleagues in the title of their paper are premature. The recent creation of the KAPS group in Jamaica was designed to address some of the issues raised by Derksen and colleagues. Until we know better, wisdom suggests that both tests be performed, if possible.

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References