Infecrive endocarditis, rheumatoid factor, and anticardiolipin antibodies

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Abstract

Serum samples from 22 patients with infective endocarditis were analysed for the presence of antibodies to cardiolipin, false positive Venereal Disease Research Laboratory (VDRL) test, and rheumatoid factor in order to determine the prevalence of anticardiolipin antibodies, their level, and to ascertain whether there was any correlation with the presence of rheumatoid factor. Although the latex test was positive in 10/22 (45%) patients, anticardiolipin antibodies, usually of a low level, were raised in only four (18%), and the VDRL test was positive in two patients in whom other antibodies were negative. These results show a clear discordance between these three tests, indicating that B-cell production of these antibodies is separate and distinct. As with other infections which result in anticardiolipin antibody production, no thrombotic events were encountered.

In a recent study reported in this journal we encountered a problem in two patients with systemic lupus erythematosus, valve lesions, and increased anticardiolipin antibodies, in whom the diagnosis of superimposed infective endocarditis was suspected. Because of significant increases of the anticardiolipin antibodies in both, the question as to whether infective endocarditis could be associated with these increases arose. We have attempted to answer this question by analysing a group of patients with infective endocarditis for the presence of these antibodies. We also analysed the sera for rheumatoid factor to ascertain whether there was any correlation between its presence and the demonstration of anticardiolipin antibodies.

Materials and methods

Serum samples were collected from 12 patients with infective endocarditis, who had presented at the Baragwanath Hospital, Johannesburg, South Africa, and from a further 10 patients attending St Thomas’s Hospital, London, United Kingdom. Patients were deemed to be suffering from infective endocarditis because of: (a) clinical features suggestive of infective endocarditis; (b) positive blood cultures; (c) echocardiographic features in keeping with ‘vegetations’; and (d) vegetations seen during surgery. All serum samples were collected within 48 hours of admission to hospital. Patients had been ill for up to four weeks before collection of serum samples and before treatment was started.

Antibodies to cardiolipin were detected by an enzyme linked immunosorbent assay (ELISA) as described by Gharavi et al.; IgG and IgM isotypes were determined. The Venereal Disease Research Laboratory (VDRL) test, Treponema pallidum haemagglutination test, and latex test for rheumatoid factors were performed according to standard techniques. The lupus 'anticoagulant' was not measured routinely as this test requires plasma and these analyses were performed on stored serum samples.

Results

Ten patients were completely negative for all immunological tests performed, while 12 showed positivity in one or another test. The table shows the results for these 12 patients. Patients with raised anticardiolipin antibody levels were culture positive (Streptococcus viridans (two), Escherichia coli (one)). The fourth patient (No 11) developed a candida endocarditis on a prosthetic valve replacement.

The VDRL test was positive in two patients only (1/4), but the latex test for rheumatoid factor was positive in 10 of the 22 patients. Anticardiolipin antibodies were positive in four—a low level of IgM anticardiolipin antibodies in three (accompanied by moderate increases of IgG anticardiolipin antibodies in one) and a moderate increase of IgG anticardiolipin antibodies in one. There was no association between increased antibodies and the false positive VDRL test present in the two patients. The prevalence of positive anticardiolipin antibodies in this group of patients with infective endocarditis, consisting of low levels of IgM anticardiolipin antibodies (13%) and moderate increases in IgG anticardiolipin antibodies (9%).

Serological features of the 12 patients with seropositive infective endocarditis

<table>
<thead>
<tr>
<th>Patient No</th>
<th>RA* latex test</th>
<th>VDRL* test</th>
<th>IgG aCL* antibodies</th>
<th>IgM aCL* antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
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<td>5</td>
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<td>Mod</td>
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<tr>
<td>12</td>
<td>+</td>
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</tr>
</tbody>
</table>

*RA= rheumatoid arthritis; VDRL= Venereal Disease Research Laboratory; aCL= anticardiolipin.
Discussion
The spectrum of valvular heart disease in systemic lupus erythematosus has undergone major and significant changes over the past few years. This is due both to an increased awareness of the clinicians and the improved methods of detection available today.\(^3\)\(^-\)\(^8\) The Libman-Sacks type of endocarditis\(^9\) as originally described is still often encountered at necropsy and is haemodynamically insignificant. Significant valve lesions, predominantly regurgitant, have been reported increasingly often, some requiring valve replacement.\(^10\)\(^-\)\(^12\)

The problem of infection superimposed on damaged valves with resultant bacterial endocarditis has been well reviewed by Lehman et al\(^13\) and others.\(^14\) A variety of infections have been associated with increases of antishupholipid antibodies, including infectious mononucleosis and AIDS.\(^15\)\(^-\)\(^16\)

The not infrequent association of false positive VDRL tests with antiphospholipid antibodies,\(^17\) the well known occurrence of false positive VDRL tests as well as rheumatic complaints and rheumatoid factors in patients with infective endocarditis,\(^18\)\(^-\)\(^22\) and the recent problem we had encountered\(^1\) all prompted us to undertake this limited study. Rheumatoid factor was present in 10 of 22 (45%) patients studied.

High levels of antishupholipid antibodies were not encountered in this study and therefore any large increases of these antibodies found in patients with valve lesions and systemic lupus erythematosus may be attributed to the underlying lupus process itself and not to the endocarditis.

17 Harris E N, Gharavi A E, Wasley G D, Hughes G R V. Use of an enzyme linked immunosorbent assay and of inhibition studies to distinguish between antibodies to cardiolipin from patients with syphilis or autoimmune disorders. J Infect Dis 1982; 146: 586-90.
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