Clinical Research

Anti-cytomegalovirus antibodies and other atherosclerosis risk factors in patients with cardiovascular diseases

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Objective To determine anti-cytomegalovirus (CMV) antibodies along with anti-Chlamydia pneumoniae (CP) antibodies in comparison with inflammatory markers and other risk factors of atherosclerosis in patients with selected cardiovascular diseases (CVD). Methods A total of 228 patients with coronary heart disease (CHD) and/or hypertension (HT), and those who underwent reconstructive vascular surgery (RVS) on carotids or abdominal aorta were tested for the presence of anti-CMV IgG and IgM antibodies as well as anti-CP IgA antibodies, C-reactive protein (CRP), and interleukin-6 (IL-6). Other risk factors for atherosclerosis, namely age, gender, smoking, hypercholesterolemia, and diabetes mellitus were also analyzed. Results Anti-CMV IgG antibodies were found in 204 patients sera (89.5%), compared with 46 positive of 68 sera in the controls (67.6%), whereas anti-CMV IgM antibodies were detected in 4 of 54 sera of patients tested (7.4%), but not in the controls. The highest proportion of positive sera with not only anti-CMV IgG antibodies (95.6.7%), but also anti-CP IgA antibodies (78.3%), IL-6 (84.8%) and CRP (97.8%), was observed in patients with RVS. The results obtained corresponded to age, hypercholesterolemia, and diabetes. Conclusions The presence of anti-CMV antibodies together with antibodies to CP and markers of inflammation (CRP and IL-6) in our study was associated with CVD, primarily in elderly patients who underwent RVS.(J Geriatr Cardiol 2007;4:131-134.)

Key Words cytomegalovirus; chlamydia pneumoniae antibodies; inflammatory factor; atherosclerosis; cardiovascular disease
(chosen for their possible connection with persistent CP infection) were assessed by the SeroCP-IgA ELISA kit (Savyon Diagnostics Ltd, Israel) with optical density 1.1 as a cut-off value. Detection of IL-6 was performed by an IL-6 ELISA kit (Immunotech, France) with a positive value 3 ng/L. CRP was detected by C-reactive Protein ELISA (Immundiagnostik, Germany) with a positive value 3 mg/L. All ELISA analyses were performed and calculated according to the manufacturer’s instructions. Cholesterol levels were evaluated by a standard method on the biochemical analyser vitros 250 with a value 4.5 mmol/L being positive.

For the statistical analysis, \( \chi^2 \) test and Fischer exact test in a contingency table was employed.

**Results**

As follows from Table 1, analysis of some atherosclerosis risk factors has shown that the proportion of males and smokers in all patients and controls was similar, except for patients with RVS, where both males and smokers prevailed (76.1% and 59.0%, respectively). The latter group consisted of elderly patients (93.5%) which contained the highest proportion (39.1%) of patients with diabetes, whereas none of the control group exceeded the age of 60 years and had diabetes. Moreover, hypercholesterolemia occurred in 100.0% of the patients with RVS, 82.9% of the total CVD patients, but only in 14.7% of the controls.

As shown in Figure 1, the presence of anti-CMV IgG and anti-CP IgA antibodies as well as IL-6 and CRP was significantly higher in all groups of patients as compared to the control group. Anti-CMV IgG antibodies were found in 68.7% of all 228 patients with CVD. From this group, in 105 patients with CHD, the anti-CMV IgG antibodies were detected in 89.5%, and in 77 patients with HT the detection rate was 85.7%. The highest proportion of sera with IgG anti-CMV antibodies was found in 46 patients (95.6%) with RVS. At the same time, these antibodies were detected in 67.6% of 68 control serum samples.

Similar results were obtained when testing anti-CP IgA antibodies, IL-6, and CRP. Positive samples containing anti-CP IgA antibodies were found in about two-thirds of patients as compared to less than half of the controls, being the most frequent (73.9%) in patients with RVS.

IL-6 was detected in 81.1% of all patients with CVD as compared to controls (57.3%), with some variation between the groups of patients (from 77.1% in CHD to 84.8% in those with HT and RVS). On the other hand, much higher differences were found when detecting CRP. It concerns not only CVD patients in all (69.7%) and controls (20.6%), but also differences among the patients groups, i.e., 64.8% for patients with CHD, 59.7% with HT, and 97.8% for those with RVS. The mean CRP values were also higher in CVD patients in all (8.1±7.8 mg/L) than in the controls (4.9±1.4 mg/L).

More detailed analysis revealed that all factors studied, i.e., anti-CMV IgG, and anti-CP IgA antibodies together with inflammatory markers (IL-6 and CRP) occurred in 51.3% of patients with CVD, but only in 4.4% of the controls. Again, the highest proportion (77.1%) of sera containing all antibodies and inflammatory markers was in the group of patients with RVS. Of interest was also analysis of the highest anti-CMV IgG antibody values (0.8 IU/ml). They were found only in 29.4% of control sera, but in 46.7% of total patients sera, and even in 54.3% of sera with RVS. As to the anti-CMV IgM antibodies, they were demonstrated in 4 sera (7.4%) of 54 patients (one with CHD, two with HT, and one with RVS), but not in the controls.

**Discussion**

The role of inflammation and infection in CVD has been discussed at length by many authors, but the participation of the infectious agents in the pathogenesis of atherosclerosis still remains a controversial issue. Although there are data connecting the presence of anti-CMV antibodies with CVD, other studies do not confirm this relationship. Moreover, some authors found an association of CMV seropositivity with the presence of CRP or IL-6 response. However, adjusting for known risk factors can profoundly alter the association between CMV and atherosclerosis. The situation with CP is even more complicated; a recent microreview accumulated all possible arguments against a casual relationship between CP and atherosclerosis.

In our study we found an association of infectious agents (anti-CMV IgG and anti-CP IgA antibodies) and inflammatory markers (IL-6 and CRP) with CVD, which was most expressed in the patients with RVS. They also matched together in more than half of CVD patients, in more than 75% of pa-

Table 1. Age, gender, smoking, hypercholesterolemia, and diabetes in patients with CVD and in the control group

<table>
<thead>
<tr>
<th>Patients(n)</th>
<th>Age ≥60 years</th>
<th>Men</th>
<th>Smokers</th>
<th>Hypercholesterolemia</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD(228)</td>
<td>57.9</td>
<td>62.1</td>
<td>42.1</td>
<td>82.9</td>
<td>11.4</td>
</tr>
<tr>
<td>CHD(105)</td>
<td>55.2</td>
<td>57.1</td>
<td>37.1</td>
<td>78.1</td>
<td>2.9</td>
</tr>
<tr>
<td>HT only(77)</td>
<td>40.3</td>
<td>62.3</td>
<td>39.0</td>
<td>80.5</td>
<td>6.5</td>
</tr>
<tr>
<td>RVS(46)</td>
<td>93.5</td>
<td>76.1</td>
<td>59.0</td>
<td>100.0</td>
<td>39.1</td>
</tr>
<tr>
<td>Controls(68)</td>
<td>0</td>
<td>58.8</td>
<td>48.5</td>
<td>14.7</td>
<td>0</td>
</tr>
</tbody>
</table>
tients with RVS, and corresponded also to other risk factors, namely age, hypercholesterolemia, and diabetes. The highest association with patients with RVS can be attributed to their higher vulnerability connected with their age, and also to the higher possibility of reactivation of CMV infection. One can only speculate whether this was the case in 4 patients with anti-CMV IgM antibodies detected in our study. CMV is an omnipresent pathogen, with a seroprevalence among adults of 50-100%. It corresponded in our study to 67.6% positivity of IgG antibodies in controls; these were, however, significantly younger than CVD patients. Therefore, when evaluating the difference observed between controls and CVD patients, the role of age should also be considered. When linking CMV serology with endothelial function, selection of older subjects with CHD could account for the difference between the findings in different studies.

Though our findings of anti-CMV and anti-CP antibodies, IL-6, and CRP in CVD patients contributed to similar previous observations, their role in the development of atherosclerosis will be the purpose of further studies.

Acknowledgement

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References


