Letters to the Editor

Is there an increased prevalence of C. pneumoniae and H. pylori in patients with rheumatoid arthritis?

Sirs,

Increased mortality due to cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) has been demonstrated (1). The reason for this is not fully understood. However, the inflammatory reaction seems to increase the risk (1). Chronic infections with Chlamydia pneumoniae and Helicobacter pylori have been suggested to be associated with the risk of atherosclerotic diseases (2), although the significance of this is still under debate (2, 3).

The aim of this study was to evaluate the prevalence of serologic signs of C. pneumoniae or H. pylori infection in patients with RA and age- and sex-matched controls. We also evaluated the possible associations between these infections and markers of inflammation and soluble adhesion molecules, as well as the presence of ultrasound measured atherosclerosis.

From a retrospective inception cohort (1) constituted of all patients with early sero-positive RA between 1974-79 (n = 211), all patients with a maximum age of 65 years (n = 39) were enrolled in an ultrasound study on atherosclerosis in RA (4). One year later, 30 patients (23 women, 7 men) agreed to participate in the present study together with 30 age- and sex-matched controls from the same region. The groups were similar in terms of the traditional cardiovascular risk factors (4).

Antibodies (Ab) of the IgG and IgA classes against C. pneumoniae were measured using microimmunofluorescence and DNA of the bacterium was detected with a nested polymerase chain reaction (nPCR) (5). Antibodies of the IgG class against H. pylori were measured using ELISA (Pyloreset ELA-I, III, Orion Diagnostic, Trosa, Sweden). ESR and CRP were measured by routine procedures. Other inflammatory markers (IL-6 and IL-2sRα) and soluble adhesion molecules (sICAM-1) were measured using ELISA (R&D Systems, Minneapolis, USA). We measured the disease activity over time according to an accumulated disease activity score (6). The intima-media thickness (IMT) of the common carotid arteries, as measured by B-mode ultrasound, was reported formerly (4).

Differences in continuous data between patients and controls were tested statistically with the Wilcoxon signed rank test and between sub-groups with the Mann-Whitney U-test. Category data were tested with the Chi-square test. Correlations between variables were tested for using Spearman’s rank correlation test.

<p>| Table I. Levels of ESR, CRP, accumulated disease activity score and the presence of antibodies (Ab) to C. pneumoniae and H. pylori in 30 RA patients (mean age 56 yrs, range 39-66) and 30 age- and sex-matched controls. Results presented as means (± SEM) and numbers of individuals (%), respectively. |
|----------------------------------------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Method</th>
<th>RA (n=30)</th>
<th>Controls (n=30)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR, mm/h</td>
<td>26 (± 4)</td>
<td>7 (± 1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>17 (± 3)</td>
<td>10 (± 0.1)</td>
<td>0.0002</td>
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<tr>
<td>Acc disease activity score1</td>
<td>4.54 (± 0.14)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Positive C. pneumoniae IgG-Ab2</td>
<td>14 (47%)</td>
<td>14 (47%)</td>
<td>ns</td>
</tr>
<tr>
<td>Positive C. pneumoniae IgA-Ab2</td>
<td>2 (7%)</td>
<td>1 (3%)</td>
<td>ns</td>
</tr>
<tr>
<td>Positive C. pneumoniae nPCR</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>ns</td>
</tr>
<tr>
<td>Positive H. pylori IgG-Ab3</td>
<td>11 (37%)</td>
<td>13 (43%)</td>
<td>ns</td>
</tr>
</tbody>
</table>

*Acumulated disease activity according to Baecklund et al. (6); 'A titre of ≥1/16 was used as the cut-off point; 'A titre of ≥1/20 was used as the cut-off point; ns = not significant.

There were no significant differences between patients and controls in the prevalence of antibodies against C. pneumoniae and H. pylori (Table I). Within the patient group, there were no significant differences between those positive and negative for IgG-Ab against C. pneumoniae considering any of the other measured variables. However, in the patient group we found a positive correlation between the titres of C. pneumoniae IgG-Ab and sICAM-1 (R = 0.36, p < 0.05). The two patients with high titres (≥1/64) of C. pneumoniae IgG-Ab had higher values of mean IMT of their CCA than those with negative titres (medians 1.1 mm versus 0.75 mm, p = 0.050). In H. pylori antibody positive patients, there was a direct correlation between the titre and IL-2sRα (R = 0.628, p = 0.047). Apart from these results we did not find any positive associations between titres of Ab against either of the two bacteria and IMT or any of the markers of inflammation, among the patients or controls (data not shown).

There is an increasing body of evidence that chronic infections may be associated with atherosclerosis (2). We found no increased prevalence of C. pneumoniae or H. pylori infection in patients with RA. However, patients with high titres of C. pneumoniae IgG-Ab, i.e., a sign that may indicate a chronic infection (2), had higher levels of mean IMT-CCA than those patients with low titres. IMT is regarded to be a sensitive marker of the early sub-clinical phase of atherosclerosis (7). We also found a correlation between the titre of C. pneumoniae IgG-Ab and sICAM-1 in patients with RA. In one report C. pneumoniae was shown to induce ICAM-1, as well as other adhesion molecules, on endothelial cells in vitro (8). In our earlier study on the prevalence of atherosclerosis in RA, we demonstrated increased levels of sICAM-1 in patients with atherosclerotic plaque (4). Furthermore, sICAM-1 has been shown to predict future myocardial infarction in healthy females (9). Taken together, these facts give some support to a relationship between infection with C. pneumoniae and endothelial cell activation leading to atherosclerosis in patients with RA.

The correlation between titres of H. pylori and IL-2sRa among the patients could be expected since IL-2sRα is raised in patients with autoimmune inflammation or infection (10). Since the present study is relatively small, and very few of the patients had clinical manifestations of atherosclerosis, further investigations are needed to clarify these observations.

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References


6. BAECKLUND E, EKROM A, SPAREN P, FEL-
Spondyloepiphyseal dysplasia tarda simulating juvenile chronic arthritis

Sirs.

We describe three patients with spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA) in two Turkish families who had earlier been mistakenly diagnosed as having juvenile chronic arthritis (JCA).

Case 1, the sister of Case 2, first developed pain and stiffness in her finger joints at the age of 13 years. She underwent corrective surgery for coxa vara at age 15. Involvement of the phalangeal epiphyses was evident along with osteoarthritic changes being present in the interphalangeal joints.

Spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA) was described as an inherited skeletal dysplasia with striking progressive impairment of joint mobility, osseous swelling of the joints, best seen in the fingers and short stature in older patients (1, 2). Autosomal recessive, autosomal dominant, and X-linked recessive patterns of inheritance in SED have been reported (3). Gedeon et al. showed that the X-linked form of spondyloepiphyseal dysplasia tarda (SEDL) is caused by mutations in the SEDL gene (4). El-Shanti et al. showed strong evidence for localisation of a gene for SEDT-PA to chromosome 6q (5). Although we could not perform any genetic analysis in our cases, based on clinical, laboratory and radiological findings, our cases were concluded to bear typical features of SEDT-PA.

Although the first two cases had non-inflammatory synovial fluid and synovial hypertrophy in both knees, we were unable to support the presence of an inflammatory condition in our cases. Previous reports also emphasised that SEDT-PA may present with soft tissue swelling in association with effusions (6). Effusions are usually reported to be non-inflammatory unless calcium pyrophosphate dihydrate crystals are present (1). We were unable to show any crystals in synovial fluid in our cases. The disorder is more frequent in Arabic countries, the reason being the large family sizes and high consanguinity rate (7). There have been several reports of cases with SEDT and SEDT-PA in Turkey up to the present time (8, 9), even though we are unsure of its prevalence yet. Still, because consanguinity rate is also rather high in our country (1-47%) (10), prevalence of SEDT-PA might actually be more common than it is thought in Turkey. So, we could expect more cases of SEDT-PA provided that atypical rheumatoid arthritis cases are fully reviewed and more precise diagnoses are made.

SEDT-PA might be mistaken for JCA, which could result in overtreatment with immunosuppressive drugs. Therefore, we suggest that SEDT-PA also be considered for the differential diagnosis of JCA particularly in countries with high consanguinity rate.

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References

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