Prednisone, IL-6

Among the three during an increase afterwards. Occurred dose (mg/day) were significantly reduction globin, fibrinogen and CRP. Values In the shown). Compared with the values observed before the reduction of prednisone, while IL-6 values were significantly increased (p = 0.04) (table 2). Among the same nine patients, only two had an ESR ≥ 30 mm/1st h, and two had CRP concentrations ≥ 10 mg/l, while four had IL-6 concentrations ≥ 5 pg/ml at clinical relapse. In all patients experiencing clinical relapse, symptoms were controlled after the dose of prednisone was increased again. Among the three patients with giant cell arteritis, two had no relapse and did not have increased concentrations of IL-6. No unexpected increase in IL-6 concentration occurred in patients without relapse: the IL-6 value in this group of patients was 7 (20) pg/ml before reduction of the dose of prednisone, and 5 (10) pg/ml one month afterwards.

These preliminary data have demonstrated an increase in the plasma concentration of IL-6 during clinical relapses of polymyalgia rheumatica and giant cell arteritis, while ESR, CRP, haptoglobin, orosomucoid, and fibrinogen showed minimal variations.

Additional studies are required to determine the further potential usefulness of IL-6 in the management of polymyalgia rheumatica and giant cell arteritis.

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Role of androgens in the aetiology of rheumatoid arthritis

It is likely that the gender difference in the occurrence of rheumatoid arthritis (RA) can be explained, at least in part, by the effects of sex hormones, with both increased concentrations of progesteron and decreased concentrations of androgen being implicated.1 Androgen concentrations also appear to be regulated by genes encoded within the HLA region, with lower concentrations reported among men who are HLA-B15 positive2, and women who are HLA-DR4 positive.3 Other data supporting the hypothesis that androgen concentrations influence the onset of RA are based on the observation that siblings of probands are more likely to be female.4

Table 1 Clinical features of patients with or without clinical relapse

<table>
<thead>
<tr>
<th>Without clinical relapse</th>
<th>With clinical relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>75.1 (8.2)</td>
</tr>
<tr>
<td>Sex ratio (M:F)</td>
<td>1:10</td>
</tr>
<tr>
<td>Diseases</td>
<td>9 PMR</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>57.8 (51.4)</td>
</tr>
<tr>
<td>Prednisone dose (mg/day)</td>
<td>2 GCA</td>
</tr>
<tr>
<td>Initial</td>
<td>19-7 (6-8)</td>
</tr>
<tr>
<td>Before reduction</td>
<td>0-29 (1-9)</td>
</tr>
<tr>
<td>After reduction</td>
<td>1-8 (1-1)</td>
</tr>
</tbody>
</table>

Values are mean (SD).
PMR = Polymyalgia rheumatica; GCA = giant cell arteritis.

Table 2 Results of laboratory tests in nine patients before prednisone reduction and at clinical relapse

<table>
<thead>
<tr>
<th>Before prednisone reduction</th>
<th>At clinical relapse</th>
<th>Wilcoxon test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR (mm/1st h)</td>
<td>20 (14)</td>
<td>25 (16)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>9 (8-3)</td>
<td>15 (12-7)</td>
</tr>
<tr>
<td>Orosomucoid (g/l)</td>
<td>0.85 (0-21)</td>
<td>0.91 (0-24)</td>
</tr>
<tr>
<td>Haptoglobin (g/l)</td>
<td>1.41 (0-63)</td>
<td>1.64 (0-92)</td>
</tr>
<tr>
<td>Fibrinogen (g/l)</td>
<td>4 (0-8)</td>
<td>4.5 (0-9)</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>4 (12)</td>
<td>14 (23)</td>
</tr>
</tbody>
</table>

Values are mean (SD).
ESR = Erythrocyte sedimentation rate; CRP = C reactive protein; IL-6 = interleukin-6.

Reduction of their prednisone dose (data not shown). In the nine patients with clinical relapse, ESR, CRP, orosomucoid, haptoglobin, and fibrinogen each showed a non-significant increase at clinical relapse compared with the values observed before the reduction of prednisone, while IL-6 values were significantly increased (p = 0.04) (table 2). Among the same nine patients, only two had an ESR ≥ 30 mm/1st h, and two had CRP concentrations ≥ 10 mg/l, while four had IL-6 concentrations ≥ 5 pg/ml at clinical relapse. In all patients experiencing clinical relapse, symptoms were controlled after the dose of prednisone was increased again. Among the three patients with giant cell arteritis, two had no relapse and did not have increased concentrations of IL-6. No unexpected increase in IL-6 concentration occurred in patients without relapse: the IL-6 value in this group of patients was 7 (20) pg/ml before reduction of the dose of prednisone, and 5 (10) pg/ml one month afterwards.

These preliminary data have demonstrated an increase in the plasma concentration of IL-6 during clinical relapses of polymyalgia rheumatica and giant cell arteritis, while ESR, CRP, haptoglobin, orosomucoid, and fibrinogen showed minimal variations. Additional studies are required to determine the further potential usefulness of IL-6 in the management of polymyalgia rheumatica and giant cell arteritis.

It is feasible that the sex ratio of siblings may be associated with the development of autoimmune disease, as hormone concentrations are believed to affect the sex of offspring.3 Therefore, parents with low testosterone concentrations may be more likely to have female children, with these children being at an increased risk of developing RA because of their inherited tendency for low testosterone concentrations.

If this hypothesis were true, it would also be expected that women with RA would themselves be more likely to have daughters instead of sons. Indeed, Deighton et al have previously reported such a finding,1 though numbers were small (16 daughters and 2 sons). We have therefore investigated this relationship among a larger group of 94 women with RA. These women had provided pregnancy information and undergone HLA-DR typing for the purpose of another study (submitted for publication). The hypothesis was that if women with RA experience reduced concentrations of androgens, they might be expected to have an excess of daughters. Given that androgen concentrations may be partially regulated by HLA-DR status, the analysis was conducted separately for HLA-DR positive and negative women.

Overall, the 94 women had 202 children: 99 girls and 103 boys. The observed proportion of children that were daughters (0.49) was the same as that expected. When considered separately by HLA-DR status, however, there was an excess of sons among the HLA-DR4 negative mothers, and an excess of daughters among the HLA-DR positive mothers (table). The observation associated with being HLA-DR4 positive and bearing a daughter was 2:1 (95% confidence interval 1:1 to 4:2). This therefore does appear to provide tentative evidence of a link between HLA-DR status and the gender of offspring, supporting a role for androgens in the aetiology of RA. However, these observations need to be repeated in other populations.

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Role of androgens in the aetiology of rheumatoid arthritis.

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