Lack of association between Toll-like receptor 4 gene polymorphism and Henoch-Schönlein purpura

Sirs,

Henoch-Schönlein purpura (HSP) is the most common type of primary small-sized blood vessel vasculitis in children and a rare entity in adults (1, 2). Infections are report- ed to be precipitating factors in at least 50% of the cases (1, 2). Infectious agents are also involved in the modulation the innate immune system, and low-grade chronic or recurrent infections and several infectious agents have been proposed to play a role in autoimmunity.

Genetic factors may determine the immunological and inflammatory response to unknown antigens in patients with HSP. Previous studies have shown that different genes may influence the phenotype and the outcome of HSP (3, 4). Human toll-like receptors (TLRs) participate in the innate re- sponse and signal the activation of adaptive immunity. TLRs are classified into four subfamilies (6). The TLR4 gene is involved in innate immune recognition, with subsequent proinflamma- tory cytokine release (6). A single nucle- otide polymorphism-SNP (+896 A/G) result- ing in the amino acid substitution Aspartic acid/Glycine (Asp299Gly) (rs4986790) in high linkage disequilibrium with other non- synonymous polymorphisms of TLR4 in Caucasian population, has been proposed to influence the susceptibility to HSP (7). The mutant allele (G) of this variant, which occurs with an allelic frequency of less than 6% in most European populations (7), was associated with decreased susceptibility to some autoimmune disorders such as rheumatoid arthritis (8).

Taking into account all these considera- tions, the present study was sought to determine the potential implication of the TLR4 (+896 A/G) gene polymorphism in the susceptibility to HSP.

Patients with cutaneous vasculitis that ful- filled classification criteria for HSP (1, 2) were recruited from the Divisions of Pedi- atrics and Rheumatology of the Hospital Xeral-Calde (Lugo, northwest Spain). Sixty HSP patients (47 children [≤20 years] and 13 adults; 30 males) with at least 2 year’s follow-up were studied. All patients pre- sented palpable purpura. Forty-two had ar- thralgias and/or arthritis, 48 suffered several gastrointestinal manifestations (gastroin- testinal bleeding and/or bowel angina) and 39 haematuria with or without proteinuria. After a minimum of 2 year’s follow-up (me- dian 8 years) only 12 (20%) had persistent renal involvement, mainly hematuria.

Age and sex and ethnically matched controls without history of cutaneous vasculitis or any other autoimmune diseases (n=234) were also studied.

DNA from patients and controls was obtained from peripheral blood samples. Single nucleo- types for the TLR4 (+896 A/G) (rs4986790) gene polymorphism by polymerase chain re- action, using a pre-designed TaqMan allele discrimination assay (7). Informed consent and ethical approval was obtained.

No evidence of departure from Hardy-Wein- berg equilibrium was observed in controls. No significant differences for this biallelic polymorphism were observed between HSP patients and controls (Table 1). It was also the case when patients were stratified by the presence of severe gastrointestinal manifestations, nephritis or persistent renal involvement (data not shown).

Table 1. Genotypic and allelic frequencies of TLR4 rs4986790 polymorphism in patients with HSP and controls.

<table>
<thead>
<tr>
<th>TLR4</th>
<th>HSP patients n (%)</th>
<th>Controls n (%)</th>
<th>p-value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs4986790 n=60</td>
<td>n=234</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genotype</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>A/A</td>
<td>54 (90.0)</td>
<td>208 (88.9)</td>
<td>0.81</td>
<td>1.02 (0.4-2.5)</td>
</tr>
<tr>
<td>A/G</td>
<td>5 (8.3)</td>
<td>25 (10.7)</td>
<td>0.60</td>
<td>0.90 (0.3-2.3)</td>
</tr>
<tr>
<td>G/G</td>
<td>1 (1.7)</td>
<td>1 (0.4)</td>
<td>0.30</td>
<td>3.90 (0.4-38.2)</td>
</tr>
<tr>
<td>Allele</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>113 (94.2)</td>
<td>441 (94.3)</td>
<td>0.98</td>
<td>0.90 (0.4-2.1)</td>
</tr>
<tr>
<td>G</td>
<td>7 (5.8)</td>
<td>27 (5.7)</td>
<td>0.98</td>
<td>1.11 (0.5-2.5)</td>
</tr>
</tbody>
</table>

No significant association between interleukin-4 gene polymorphism in patients with HSP and controls (7).

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References