Interleukin-1 beta gene polymorphism in patients with biopsy-proven erythema nodosum

Sirs,

Erythema nodosum (EN), the most common cause of inflammatory nodules, is generally a benign and self-limiting hypersensitivity reaction characterised by multiple and bilateral non-ulcerating tender lesions (1). Biopsy shows acute or granulomatous septal panniculitis with primary leukocyte infiltration around the veins of the septal system (1). EN may be idiopathic or secondary to a broad variety of conditions (1, 2).

Susceptibility to EN and associated clinical heterogeneity in patients with this condition may be conferred by a number of genetic loci. The interleukin-1 (IL-1) family of proteins has a major role in the inflammatory response. IL-1 promotes leukocyte extravasation by inducing the expression of adhesion molecules such as ELAM-1 (E-selectin) and ICAM and induces the production of IL-8 by endothelial cells (3). Upregulated expression of proinflammatory cytokines such as TNF, IL-6 and IL-1 has been reported in vasculitis syndromes.

Several single nucleotide polymorphisms have been found in the IL-1beta gene. A biallelic polymorphism in the IL-1beta gene at position -511 has been described (4). This (-511C/T) polymorphism in the IL-1beta gene is thought to influence IL-1 beta production and it has been assessed in autoimmune and non-inflammatory conditions (5). In this regard, an association of this polymorphism with severe renal manifestations and renal sequelae in patients with Henoch-Schönlein purpura was reported (6). Also, the IL-1 beta promoter (-511C/T) polymorphism was found to be an independent risk factor for association with Alzheimer’s disease (7). This proinflammatory polymorphism in the IL-1 beta promoter gene is also associated with increased host susceptibility to Helicobacter pylori infection in Chinese people (8), and increased risk of reflux esophagitis in Taiwanese individuals (9). Also an epistatic interaction between IL-1beta (-511C/T) and interleukin-1 receptor antagonist gene polymorphisms was found to confer protection against gastric cancer in a low-risk Italian population (10). However, this IL-1beta promoter polymorphism was not associated with the development of amyloidosis in familial Mediterranean fever patients (11).

In the present study we have examined for the first time the potential influence of IL-1 beta gene (-511C/T) polymorphism in a series of patients with biopsy-proven EN from a well-defined population (12). Ninety-nine consecutive patients with biopsy-proven EN and 148 ethnically matched controls from the Lugo region in Galicia (Northwestern Spain) were genotyped for IL-1beta gene (-511C/T) polymorphism by a polymerase chain reaction-restriction fragment as previously reported (6). Clinical data of the patients included in the present study have previously been described (12, 13). Thirty-five patients were diagnosed as having idiopathic EN. The remaining 64 patients were diagnosed with EN secondary to sarcoidosis (n=31) or developed EN in the setting of other conditions (n=33). Informed consent and ethical approval was obtained.

Controls* EN EN EN EN due to EN secondary to other conditions

<table>
<thead>
<tr>
<th>Allele</th>
<th>Controls'</th>
<th>EN 'Total'</th>
<th>EN 'Idiopathic'</th>
<th>EN 'Secondary'</th>
<th>EN 'due to Sarcoidosis'</th>
<th>EN secondary to other conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>196 (66%)</td>
<td>146 (74%)</td>
<td>51 (73%)</td>
<td>95 (74%)</td>
<td>46 (74%)</td>
<td>49 (74%)</td>
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<tr>
<td>T</td>
<td>100 (34%)</td>
<td>52 (26%)</td>
<td>19 (27%)</td>
<td>33 (26%)</td>
<td>16 (26%)</td>
<td>17 (26%)</td>
</tr>
</tbody>
</table>

Genotype

| CC   | 67 (45%) | 57 (58%) | 21 (69%) | 36 (56%) | 12 (39%) | 11 (33%) |
| CT   | 62 (42%) | 32 (32%) | 9 (26%)  | 23 (36%) | 5 (8%)   | 2 (6%)   |
| TT   | 19 (13%) | 10 (10%) | 5 (14%)  | 5 (8%)   | 8 (2%)   | 3 (9%)   |

‘No statistically significant differences between the whole group of EN patients and controls was found.

References

6. AMOLI MM, CALVIÑO MC, GARCIA-PORRUA C,
Letters to the Editors


