Sirs,

Erythema nodosum (EN) is the most common type of panniculitis (1). It may be idiopathic or secondary to a wide variety of diseases (2). A question still unanswered is whether polymorphisms of proinflammatory cytokine genes may mediate an abnormal inflammatory response leading to the development of EN.

In the present study we aimed to assess the potential role of the IL-6 gene (-174 G/C) promoter polymorphism in the pathogenesis of EN. Since we have previously reported some immunogenetic differences between idiopathic and secondary EN, in particular in those cases associated to sarcoidosis (3, 4), we also studied whether potential differences in the IL-6 gene (-174 G/C) promoter polymorphism might be useful to discriminate patients with EN associated to sarcoidosis from other patients presenting with EN.

As previously described (5), 100 consecutive patients with biopsy-proven EN and 118 ethnically matched controls from the Lugo region in Galicia (Northwestern Spain) were genotyped for a single biallelic (G/C) nucleotide polymorphism in the promoter region at the position -174 of the IL-6 gene by a polymerase reaction chain-restriction fragment length polymorphism method. Informed consent was obtained to perform this study.

Clinical data of the patients included in the present study have previously been reported (6, 7). Thirty-six 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 context of other conditions (n=33) such as an infectious diseases, drug-intake, and more rarely, in the setting of an inflammatory bowel disease or Sweet’s syndrome (3, 4, 6, 7).

In controls, no evidence of departure from Hardy-Weinberg equilibrium was observed. No significant differences in the allele and genotype distribution of the IL-6 gene (-174 G/C) between patients with EN and controls were observed (Table 1).

However, the genotype distribution differed significantly in patients with EN secondary to sarcoidosis from that observed in patients with idiopathic EN and EN secondary to other conditions different from sarcoidosis (p=0.036; OR: 3.90 [95%CI: 1.01-14.99]) (Table 1). In this regard, 6 of the 10 patients from the whole series of 100 biopsy-proven EN who carried the homozygous CC genotype were diagnosed with sarcoidosis (CC vs. GG+GC in the 31 patients with EN secondary to sarcoidosis compared with the remaining 69 EN patients: p=0.038; OR: 3.90 [95%CI: 1.01-14.99]) (Fisher exact test) (Table 1). Interestingly, Maver et al. showed an increased frequency of IL-6/-174CC allele and also an increased genotype frequency of IL-6/-174 CC and GC carriers among sarcoidosis patients compared to healthy controls (8). Also, Grutters et al. showed that the IL-6/174allele might have a role in the genetics underlying sarcoidosis severity or the progression towards pulmonary fibrosis in a particular subgroup of patients with sarcoidosis (9).

As observed for other gene polymorphisms (10), the clinical heterogeneity of conditions presenting with EN might explain the negative association observed between the IL-6 gene (-174 G/C) promoter polymorphism and EN when our series of unselected patients with biopsy-proven EN were assessed altogether. However, the present study does not support a role of the IL-6 gene (-174 G/C) polymorphism in the susceptibility to develop EN in patients with idiopathic (primary) EN from Northwestern Spain. In contrast, our results show that IL-6/-174 CC genotype characterizes a subgroup of patients who are at higher risk of developing EN in the setting of sarcoidosis. In any case, further controlled studies of biopsy-proven EN patients must be performed to confirm these results.

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