Letters to the Editors

Lack of association of epithelial cell-derived neutrophil-activating peptide (ENA)-78 gene polymorphism with susceptibility to biopsy-proven giant cell arteritis

Sirs,

Giant cell arteritis (GCA) is the most common systemic vasculitis in individuals over the age of 50 years in Western countries (1, 2). GCA is a polygenic disease and different genes may influence the phenotype and the outcome of this condition (3).

Inflammatory cytokines, such as interferon-gamma (IFN-γ), play a role in the pathogenesis of GCA (4). A CA repeat polymorphism in the first intron of the IFN-γ gene was associated with the development of visual ischemic manifestations in biopsy-proven GCA patients (5). Chemokines are chemotactic cytokines of 70-130 amino acids characterized by the presence of conserved cysteines linked by disulfide bonds (6). They activate and direct the migration of leukocytes acting on responsive leukocyte subsets through G-protein-coupled transmembrane receptors (7). Hence, chemokines and chemokine receptors are involved in the leukocyte trafficking across different compartments from the tissue of origin and the blood to sites of homing, host defense, or disposal. Because of that, they are implicated in many pathological conditions including inflammation and autoimmunity (8).

In the present study we have examined the influence of the polymorphism of epithelial cell-derived neutrophil-activating peptide (ENA) -78 (CXC chemokine) gene in the susceptibility and clinical expression of patients with GCA. Fifty-three biopsy-proven GCA patients and 107 ethnically matched controls from Lugo (North West Spain) were studied.

Molecular analysis of ENA-78 gene polymorphism: DNA was extracted from anticoagulated blood collected in EDTA. Assays were designed for detection of the promoter polymorphism (-156 C/G) using the ABI PRISM SNapshot ddNTP primer extension Kit (9). The genomic DNA was amplified using the following primers: Forward 5'-ACT CCC TTC TAG CTG GAG CC-3'. Reverse 5'-GTG CCT TCT GCA CTC CTT TT -3' as previously reported (9). A PCR product of 246 bp was visualized on a 3% agarose gel stained with ethidium bromide. The probe used for the single nucleotide extension in the primer extension kit was 5'-CAG ACA ATG GGA ACT GGT-3'. After extension and purification, the product was electrophoresed on a 3100 ABI analyzer and the results were analyzed with Genescan software.

Table I. Frequency of ENA-78 polymorphism in biopsy-proven giant cell arteritis (GCA) patients with and without polymyalgia rheumatica (PMR) or visual ischemic complications and controls*.

	Controls	GCA (Total)	GCA with PMR manifestations		GCA with visual ischemic manifestations	
			Yes	No	Yes	No
No. patients	(N = 107)	(N = 53)	(N = 25)	(N = 28)	(N = 13)	(N = 40)
Allele						
G	86	92	90	95	92	93
C	14	8	10	5	8	7
Genotype						
GG	74	85	76	89	85	85
GC	23	15	24	11	15	15
CC	3	0	0	0	0	0

*No statistically significant differences between biopsy-proven GCA patients and controls were found.

In controls and biopsy-proven patients GCA patients no evidence of departure from Hardy-Weinberg equilibrium was observed (p = N.S.).

When the allele and genotype frequencies of ENA-78 polymorphism in GCA patients were compared to those of controls no significant differences were found (Table 1). In this regard, allele G frequency was marginally increased in biopsy-proven GCA patients (92%) compared with controls (86%), but the difference remained slightly out of the levels of significance (p = 0.07; OR: 2.08 [95% CI: 0.92- 4.69]) (Table I). Likewise, allele G frequency was increased in biopsy-proven GCA without associated PMR (95%) compared to controls (86%), but this increase was also slightly out of the range of significance (p = 0.07; OR: 2.99 [95% CI: 0.88- 10.18]) (Table I). No association of this polymorphism with the development of visual ischemic manifestations of GCA was found (Table I).

In a former study, we observed that in Northwest Spanish the regulated upon activation normal T-cell expressed and secreted (RANTES) (CC chemokine) gene polymorphism was associated with the susceptibility to isolated PMR (10). However, no implication of RANTES gene polymorphism with biopsy-proven GCA was found (10). The present study extends the analysis of the potential influence of other chemokine gene polymorphisms to GCA.

Our results do not support a role of the ENA-78 chemokine gene polymorphism in the susceptibility to biopsy-proven GCA in Northwest Spain. Since this study is the first aiming to address this potential association, further studies in populations with different genetic background are required to exclude completely the implication of this chemokine gene polymorphism in the pathogenesis of GCA.

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