

Letters to the Editors

IL18 gene polymorphisms in Henoch-Schönlein purpura

Sirs,

Henoch-Schönlein purpura (HSP) is the most common type of primary small-sized blood vessel leukocytoclastic vasculitis in children and a rare entity in adults (1, 3). The cytokine interleukin-18 (IL-18), a member of the IL-1 superfamily, elicits several biological activities that initiate and promote host defense and inflammation following infection or injury (4). This cytokine plays an important role in chronic inflammation and autoimmune disorders. IL-18 is biologically and structurally related to IL1beta (4). We previously reported an association between IL1beta gene and IL-1 receptor antagonist gene polymorphisms with severe renal involvement in patients with HSP (5, 6).

In the present study we sought to establish the potential role of three polymorphisms (-137,-607,-1297) within the promoter of the IL18 gene in the susceptibility to HSP.

Sixty-two patients (48 children [≤ 20 years] and 14 adults; 30 males) with cutaneous vasculitis that fulfilled American College of Rheumatology and the Michel *et al.* classification criteria for HSP (7) were recruited from Hospital Xeral-Calde, Lugo, Northwest Spain (2, 3). All patients presented palpable purpura, 44 arthralgias and/or arthritis, 48 gastrointestinal bleeding and/or bowel angina and 41 nephritis. After a minimum of 2 year's follow-up (median 8 years) only 12 (20%) had persistent renal involvement, mainly hematuria.

Two hundred age- and sex- and ethnically-matched controls without history of cutaneous vasculitis or any other autoimmune diseases were also studied.

DNA was obtained from peripheral blood mononuclear cells. The genotyping of the IL18 polymorphisms was performed using a pre-designed TaqMan SNP Genotyping Assays (Applied Biosystems, Foster City, CA) as previously reported (8).

No evidence of departure from Hardy-Weinberg equilibrium was observed in controls. In assessing the IL18-137(G->C)(rs187238) gene polymorphism we observed that IL18 -137 allele G frequency was increased in HSP patients compared to controls ($p=0.04$; OR: 1.71; 95% CI 1.01-2.92). It was due to a marginally increased frequency of homozygosity for the IL18 -137 G/G genotype in patients with HSP compared to controls (IL18-137 G/G versus IL18-137 C/G plus IL18-137 C/C genotypes: $p=0.06$; OR: 1.73; 95% CI 0.93-3.24)

No significant differences between HSP patients and controls for the IL18 -607 C>A (rs1946518) and the IL18-1297 T>C (rs360719) gene polymorphisms were observed (Table I). Also, there were not significant differences between HSP patients

Table I. IL-18 gene polymorphisms in HSP patients and healthy controls.

IL-18	HSP patients n=62 (%)	Controls n=200 (%)	p-value	OR (95% CI)
-137 (G->C) (rs187238)*				
G/G	39 (62.9)	99 (49.5)	0.06	1.73 (0.93 – 3.24)
C/G	23 (37.1)	90 (45.0)	0.27	0.72 (0.38 – 1.35)
C/C	0 (0.0)	11 (5.5)	0.07	0.00 (0.0 – 1.49)
G	101 (81.5)	288 (72.0)	0.04	1.71 (1.01 – 2.92)
C	23 (18.5)	112 (28.0)	0.04	0.59 (0.34 – 0.99)
-607 (C->A) rs1946518				
C/C	23 (37.1)	69 (34.5)	0.70	1.12 (0.59 – 2.11)
C/A	32 (51.6)	108 (54.0)	0.74	0.91 (0.49 – 1.67)
A/A	7 (11.3)	23 (11.5)	0.96	0.98 (0.36 – 2.57)
C	78 (62.9)	246 (61.5)	0.77	1.06 (0.69 – 1.64)
A	46 (37.1)	154 (38.5)	0.77	0.94 (0.61 – 1.46)
-1297 (T->C) rs360719				
T/T	38 (61.3)	117 (58.5)	0.69	1.12 (0.60 – 2.10)
T/C	24 (38.7)	75 (37.5)	0.86	1.05 (0.56 – 1.97)
C/C	0 (0.0)	8 (4.0)	0.20	0.00 (0.00 – 2.16)
T	100 (80.6)	309 (77.3)	0.42	1.23 (0.72 – 2.10)
C	24 (19.4)	91 (22.8)	0.42	0.81 (0.48 – 1.38)

*Genotype distribution for the IL18-137 (G->C) polymorphism: $p=0.06$

with or without nephritis or with or without gastrointestinal manifestations of the disease (data not shown).

A recent study has shown that IL-18 promoter -137 G / C polymorphism influences IL-18 levels and the occurrence of coronary artery disease in Chinese individuals. However, no significant association between the IL18-137 G>C (rs187238) and the IL18-607 C>A (rs1946518) gene polymorphisms and the susceptibility to Crohn's disease or ulcerative colitis was found (10). These different results in terms of disease susceptibility mediated by the IL18 gene polymorphisms in different autoimmune diseases support the notion that different pathogenic mechanisms are involved in the development of polygenic diseases.

In conclusion, the present study shows, for first time, a potential role of the IL18 gene promoter polymorphism in the susceptibility to HSP.

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