Letters to the Editors

P-selectin gene -825 polymorphism is associated with risk of Henoch-Schönlein purpura nephritis

Sirs,

In recent years the morbidity of Henoch-Schönlein purpura (HSP) has risen, but its exact pathogenesis is unknown. One manifestation of HSP that can continue to cause lifelong problems is renal involvement. Some Henoch-Schönlein purpura nephritis (HSPN) patients have poor prognosis. Davin *et al*. (1) found that 20% of the patients developed chronic renal failure. Although the exact mechanisms governing the fate of renal function in HSPN are also unclear, genetic factors are presumed to participate in its development and progression. In particular, the correlations between the development of HSPN and single-nucleotide polymorphisms (SNPs) in genes that encode nephritis-related molecules have become the focus of attention (2, 3).

P-selectin is a cellular adhesion molecule belonging to the selectin family. After its activation, P-selectin molecules are released from the a-granules of platelets and participate in the rolling and tethering of platelets at the surface of endothelial cells. P-selectin is also redistributed at the cell membrane of activated endothelial cells from Weibel-Palade bodies and therefore mediates the adhesion and rolling of leukocytes on the vascular wall. P-selectin therefore plays an important role in the recruitment of leukocytes on the vascular surface at inflammatory foci, in their extravasation, and in the adhesion of platelets to the endothelium (4). Because of its biological functions, this molecule is postulated to be involved in the development of vasculitis and its complications. Supporting this concept are the observations that P-selectin inhibition has been shown to reduce glomerular leukocyte recruitment and renal injury, suggesting that P-selectin mediated rolling interactions contribute to efficient glomerular leukocyte recruitment (5, 6).

The P-selectin gene (OMIM 173610) is located on chromosome 1q21 to 1q24, a region that also shelters the E- and L-selectin genes. Although P-selectin is expressed as a functional membrane glycoprotein, a shorter, soluble isoform has been reported. Increased levels of soluble P-selectin have been observed in Henoch-Schönlein purpura nephritis (7). In this study, we investigated the association between P-selectin -825 polymorphism and HSPN.

Eighty-six patients who fulfilled the diagnostic criteria for HSP revised by the American College of Rheumatology and 70 healthy ethnically matched controls were enrolled in this study. All of the subjects were unrelated Chinese individuals of Han ethnicity.

Genomic DNA was isolated using TIANamp Blood DNA Kit (TIANGEN, BeiJing, China). The amount of DNA for each sample was determined by measuring the optical density at 260nm wavelength using a spectophotometer (Eppendorf AG, Germany). Genotyping was carried out by Polymerase Chain Reaction (PCR)- direct sequencing. To this aim, a 550bp fragment of promoter was amplified using specific primers (fw: 5'-ACAGCATTTCCTTCACCATC-3'; rev: 5'-TCAGCTGTGCTGTTAAACTG-3'). The fragment was purified and then a direct sequence was performed with an ABI PRISM 3730 gene analyser. AA and AG genotype were found, but GG genotype was not discovered.

Allele and genotype frequencies were obtained by direct counting. Hardy-Weinberg equilibrium was tested by χ^2 goodness-of-fit analysis with 1 degree of freedom. χ^2 analysis was used for comparing differences in allele and genotypic frequencies distribution. In all analyses, p-value<0.05 was considered significant.

Genotype distributions of the P-selectin -825 polymorphisms were compatible with Hardy-Weinberg equilibrium in both HSP patients and controls (χ^2<3.84, p>0.05). Genotype and allele frequencies of the P-selectin gene -825 site are shown in Table I. There were significant differences in the P-selectin -825 genotype frequency between the HSPN and the control group (χ^2=9.068, p=0.003). Significant differences were also found between the HSPN and the HSP without the nephritis group (χ^2=6.09, p=0.014). The HSPN group demonstrated an increased -825AA genotype frequency and an increased frequency of A allele compared with the HSP without the nephritis group (χ^2=6.09, p=0.014; χ^2=5.465, p=0.019).

It was revealed that the polymorphism of -825A/G in the promoter region of the P-selectin gene was significantly associated with HSPN in this study. The frequency of AG genotype was less in the patients than in the controls. Patients carrying the high frequency A allele (AA genotype) had a greater occurrence of renal involvement.

Table I. Genotype and allele frequencies of the P-selectin gene -825 site.

Group	n.	genotype, n. (%)		allele, n. (%)	
		AA	AG	A	G
Control	70	47 (67.1)	23 (32.9)	117 (83.6)	23 (16.4)
HSP without nephritis	46	33 (72)	13 (28)	79 (86)	13 (14)
HSPN	40	37 (92.5)*	3 (7.5)	77 (96.3)*	3 (3.8)

*p-value<0.05 *vs*. the control and the HSP without nephritis groups.

In summary, this study showed that the P-selectin -825 AA genotype and A allele frequencies increased in children with HSPN compared to HSP children without nephritis and healthy controls. Also, the AA genotype of the P-selectin -825A/G polymorphism was associated with an increased risk for the development of nephritis in HSP patients. This suggests that P-selectin -825A/G gene polymorphism may be associated with the development of HSPN and that A allele may be a susceptible gene of HSPN.

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