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Fc?RIIA polymorphism and anti-C1q(CLR) in SLE

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Keywords

FcR, lupus, nephritis, polymorphism

Context

Two alleles of FcR?IIA, expressed on leukocytes and platelets, are recognised: H131, which binds IgG2 more strongly, and the R131 variant. R131 homozygotes cannot bind immune complexes *in vitro*and there may be an association with susceptibility to infection and autoimmune disease. Systemic lupus erythematosus (SLE) patients with autoantibodies to the collagenous region (CLR) of C1q develop nephritis. This study assessed the frequency of Fc?RIIA R131 homozygotes to determine if there is an association between Fc?RIIA polymorphism and antibodies to the CLR of C1q in patients with SLE.

Significant findings

Of the SLE patients, 28% had anti-C1q antibody (Ab), 84% of whom had active renal disease (compared to 13% of anti-C1q negative patients), and the Ab was predominantly IgG2. Fc?RIIA genotyping showed that although allele frequencies were similar in patients and controls, in patients with anti-C1q there was an increased frequency of the R131 allele (70% cf 55% normals, $p < 0.01$). SLE patients with nephritis also expressed this allele more frequently (68%, $p = 0.01$). R131 homozygotes were as common in SLE as in normal controls (~33%) but significantly more common in patients with anti-C1q (50%, $p = 0.01$) or nephritis (48%, $p = 0.009$).

Comments

This paper provides an interesting insight into the pathogenesis of SLE. The corollary, that IgG2-deficient patients may be protected from developing lupus nephritis, would require a larger study, but would complete the picture. Analysis of FcR polymorphisms in non-caucasoid populations with an inherently greater frequency of developing lupus would also be interesting. Lack of negative feedback

caused by failure of circulating antibody to bind Fc?RIIA may play a role in the polyclonal gammopathy associated with lupus.

Methods

IgG subclasses, anti-C1q(CLR) antibodies (including IgG subclass-specific anti-C1q) and Fc?RIIA genotypes were analysed in 195 caucasoid SLE patients and 283 caucasoid normal controls.

Additional information

A paper in the same issue (Dijstelbloem HM *et al*, *Arth Rheum* 1999; **42**: 1823-1827)(abstract) examines FcR polymorphisms in Wegener's granulomatosis. Although there was no significant association between individual FcR genotype and disease susceptibility, individuals who were RIIA H131/H131 together with RIIa V158/V158 were significantly more common in Wegener's granulomatosis ($p = 0.0092$). This genotype was associated with an 83% 5-year relapse rate (cf 32%, $p < 0.01$).

References

1. Norsworthy P, Theodoridis E, Botto M, Athanassiou P, Beynon H, Gordon C, Isenberg D, Walport MJ, Davies KA: Overrepresentation of the Fc? receptor type IIA R131/R131 genotype in caucasoid systemic lupus erythematosus patients with autoantibodies to C1q and glomerulonephritis. Arthritis Rheum. 1999, 42: 1828-1832.