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Complement deficiency in an arthritis animal model

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Keywords

C3, collagen-induced arthritis, complement, factor B

Context

Complement activation has previously been observed in conjunction with the development of rheumatoid arthritis and previous experiments have demonstrated that complement deficiency in animal models of arthritis can confer some degree of resistance to disease. In order to investigate the role of the early components of the complement cascade, the authors have investigated the effect of C3 and factor B (FB) deficiency in a collagen-induced mouse model of arthritis.

Significant findings

C3-deficient mice were almost completely resistant to the development of arthritis from a single immunization. However the incidence of disease increased after repeated immunization, although disease severity remained low. The severity of arthritis was reduced in FB-deficient animals compared to controls, however there was a 100% incidence of disease 23 days after repeated immunization. Histological analysis demonstrated that in contrast to control mice, the C3-deficient mice were protected from infiltration of inflammatory cells and joint destruction. FB-deficiency was only partially protective, as a slight thickening of the synovium was observed after repeated immunization. Although both C3- and FB-deficient mice had a reduced antibody response to primary immunization, with IgG1 and IgG2a being the predominant isotypes produced respectively, IgG levels were similar to control mice following repeated immunization.

Comments

Components of the complement cascade are clearly important to the development of arthritis. Although both C3 and FB appear to play a role in mediating the inflammatory infiltration, joint destruction and a normal antibody response, the specific mechanisms by which this occurs have not been addressed. Due to the increased incidence and severity of disease in the complement-deficient animals with repeated immunization, the authors suggest that inhibition of complement might increase the threshold for the development of arthritis. These particular components of the complement cascade may therefore be of therapeutic interest in the early stages of arthritic disease, however the effect of inhibition of the complement cascade on established disease needs to be elucidated.

Methods

Collagen-induced model of arthritis, ELISA, histopathology, polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP) genotyping.

References

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