AUTOANTIBODIES AGAINST THE COMPLEMENT REGULATOR FACTOR H IN NEUROMYELITIS OPTICA PATIENTS

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Introduction: Neuromyelitis optica (NMO) is an autoimmune inflammatory disorder of the central nervous system (CNS), characterized by pathogenic, complement-activating autoantibodies against the main water channel in the CNS, aquaporin 4 (AQP4), and lesions in the CNS that contain complement activation products. NMO is frequently associated with other autoantibodies and antibody-mediated diseases. Because complement is implicated in the pathogenesis of NMO, the aim of this study was to evaluate the presence of autoantibodies against the complement regulator factor H and the alternative pathway C3 convertase components C3b and factor B in the serum of NMO patients.
Methods: Serum samples of 45 NMO patients, who were all seropositive for AQP4 autoantibodies, were screened by ELISA for autoantibodies against C3b, factor B, and factor H. Recombinant fragments of factor H and recombinant factor H-related proteon 1 (FHR1), expressed in insect cells, were used in ELISA to map the binding sites of the autoantibodies. Serum FHR1 was analyzed by Western blot. The presence of factor H–antibody complexes in the sera were analysed after IgG precipitation and Western blotting. The avidity of the antibodies were measured in ELISA using NaSCN as chaotrop salt.
Results: Four of 45 NMO patients (~9%) had factor H autoantibodies and none had antibodies to C3b and factor B. The factor H autoantibody titers were low in three and high in one of the patients' sera. The avidity indexes calculated for the four autoantibodies were low. We could also detect factor H-IgG complexes using a monoclonal antibody to factor H as a capture antibody in ELISA and in the IgG fractions by Western blot. The autoantibodies bound to factor H domains 19-20, and also recognized the homologous protein FHR1. This binding pattern was similar to pathogenic factor H autoantibodies associated with atypical hemolytic uremic syndrome (aHUS), used as positive controls in the assays. However, in contrast to the majority of autoantibody-positive aHUS patients, these NMO patients did not lack FHR1.
Conclusions: Our results demonstrate that factor H autoantibodies are not uncommon in NMO. Our data also suggest that generation of antibodies against complement regulating factors among other autoantibodies may contribute to the complement-mediated damage in NMO.

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