Association between human leukocyte antigens (HLAs) and human neutrophil antigens (HNAs) and autoimmune neutropenia of infancy in Danish patients

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Abstract

Autoimmune neutropenia of infancy (AIN) is a relatively frequent cause of neutropenia in children. The disease is caused by antibodies recognizing membrane antigens of neutrophils, mostly located on immunoglobulin G (IgG) Fc receptor type 3b (FcγIIIb receptor). In this study, we investigated the possible association of human neutrophil antigens (HNA), human leukocyte antigen (HLA)-DR and HLA-DQ alleles with AIN and the association of these genotypes with the presence of anti-HNA-1a autoantibodies. Eighty AIN cases with a median age of 13.5 months were included in this study. Controls were healthy unrelated Danish blood donors. Anti-HNA-1a autoantibodies were detected using a flow cytometric granulocyte immunofluorescence test (Flow-GIFT). Molecular determination of HNA genotypes was determined using real-time polymerase chain reaction (q-PCR). High-resolution HLA-DR and HLA-DQB1 were determined by next-generation sequencing. Antibodies against HNA-1a were detected in 51% (n=41) of AIN patients, and anti-HNA-1b was detected in 3% (n=2) of cases. FCGR3B*01+,*02-,*03- was more common (odds ratio, 6.70; $p < 0.0001$), and FCGR3B*01-,*02+,*03- was less common (odds ratio, 0.30; $p < 0.0001$) among AIN cases. HNA-1a antibodies were significantly more frequent among AIN cases with the FCGR3B*01+,*02-,*03- genotype (odds ratio, 3.86; $p < 0.007$). The HLA-DR*14 and HLA-DQB1*05:03 alleles were significantly more common (odds ratio, 7.44; $p < 0.0001$ and odds ratio, 2.50; $p < 0.0001$, respectively) in AIN patients. In conclusion the HLA haplotype HLA-DR*14- DQB1*05:03 is associated with Danish AIN cases. Among Danish AIN patients, anti-HNA-1a is the most common autoantibody, and the antibody is more common in cases with the FCGR3B*01-,*02+,*03- genotype.

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