Association between ABH secretor status and autoimmune neutropenia of infancy in Danish patients

Kirstine Kloeve-Mogensen[1], Rudi Steffensen[1], Tania Nicole Masmas[2], Henrik Hasle[3], Andreas Glenthøj[4], Kaspar René Nielsen[1]

Affiliations

[1] Department of Clinical Immunology, Aalborg University Hospital, Aalborg, Denmark

[2] Pediatric Hematopoietic Stem Cell Transplantation and Immunodeficiency, The Child and Adolescent Clinic, Copenhagen University Hospital, Rigshospitalet, Denmark.

[3] Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark.

[4] Center for Hemoglobinopathies, Department of Hematology, Copenhagen University Hospital, Rigshospitalet, Denmark

Background

Autoimmune neutropenia of infancy (AIN) is a frequent cause of neutropenia in children. The disease is caused by antibodies against epitopes on the immunoglobulin G (IgG) Fc receptor type 3b (FcγIIIb). Several studies have shown associations of the *ABO, FUT2* (Secretor) and *FUT3* (Lewis) genes with susceptibility or resistance to various infectious and inflammatory diseases.

Aims

Establish the association between ABH secretor status and AIN in Danish pediatric patients.

Methods

One hundred and forty-three AIN cases diagnosed before age five, were included. The control group consisted of 400 healthy and unrelated Danish blood donors. Molecular determination of *ABO* types was analyzed in all AIN cases with polymerase chain reaction (PCR) testing three SNPs (rs8176719, rs7853989 and rs8176743). For the control group the ABO phenotype was determined by serology. ABH secretor status types was determined as the combination between ABO and five SNPs, one in the *FUT2* gene G428A (rs601338) and four in the *FUT3* gene*:* T59G (rs28362459), T202C (rs812936), C314T (rs778986) and T1067G (rs3894326). These five SNPS were determined with PCR or Sanger Sequencing. Statistic p-values were calculated as Chi-squared test and odds ratio with 95 % confidence interval.

Results

Individuals who are both blood type O and secretors, indicating that these individuals are expressing H antigen both in blood and in body fluids like saliva and mucus, are significant different in the distribution in AIN cases compared to the control group (Table 1). The odds ratio indicates that ABH secretors are more protected against AIN than individuals who are either not secretors or express A or B antigens in their secretions.

Summary

The ABH secretor status are associated with AIN, and H substance secretors have a lower risk of attracting the disease. The mechanism underlying the association between autoimmunity and the epistasis effect between the ABO, secretor and Lewis genes have not yet been elucidated, but several studies indicates a connection to the gut microbiota.

Table 1 Frequencies of ABH secretor status

ABO type	Lewis phenotype	Secretor	Cases n = 143 (%)	Controls n = 400 (%)	P value	OR (95% CI)
O	**Le(a-b-)**	**No**	4 (2.8)	13 (3.3)	0.790	0.86 (0.27-2.67)
O	**Le(a+b-)**	**No**	13 (9.1)	34 (8.5)	0.829	1.08 (0.55-2.10)
O	**Le(a-b+)**	**Yes**	36 (35.0)	140 (47.5)	**0.032**	0.62 (0.41-0.96)
A	**Le(a-b-)**	**No**	4 (2.8)	10 (2.5)	0.847	1.12 (0.35-3.64)
A	**Le(a+b-)**	**No**	14 (9.8)	31 (7.8)	0.449	1.29 (0.67-2.50)
A	**Le(a-b+)**	**Yes**	53 (51.5)	123 (41.7)	0.167	1.33 (0.89-1.98)
B	**Le(a-b-)**	**No**	1 (0.7)	2 (0.5)	0.784	1.40 (0.13-15.57)
B	**Le(a+b-)**	**No**	3 (2.1)	8 (2.0)	0.943	1.05 (0.27-4.01)
B	**Le(a-b+)**	**Yes**	9 (8.7)	24 (8.1)	0.900	1.05 (0.48-2.32)
AB	**Le(a-b-)**	**No**	1 (0.7)	1 (0.25)	0.466	2.81 (0.17-45.22)
AB	**Le(a+b-)**	**No**	0 (0.0)	6 (1.5)	0.291	0.21 (0.01-3.78)
AB	**Le(a-b+)**	**Yes**	5 (4.9)	8 (2.7)	0.321	1.78 (0.57-5.52)