ASSOCIATIONS OF *ELANE* AND *IL6* PROMOTER POLYMORPHISMS WITH THE CLINICAL COURSE OF BRONCHIECTASIS IN CHILDREN

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Abstract. Objective. To evaluate the associations of the *ELANE* −903 T>G, *ELANE* −741 G>A and *IL6* −174 G>C promoter polymorphisms with the presence of bronchiectasis, disease burden, lung function, quality of life and markers of neutrophilic inflammation in children.

Materials and methods. The genotyped subset comprised 87 children: 48 with non-cystic fibrosis bronchiectasis, 21 with cystic fibrosis-associated bronchiectasis and the control group of 18. Genotype and allele distributions, Hardy–Weinberg equilibrium, the frequency of antibiotic-treated exacerbations and hospitalizations, spirometry results, BC-QoL-UA scores, and serum interleukin-6 and neutrophil elastase concentrations were assessed. Between-group comparisons, Spearman correlation analysis, genetic model analyses, multivariable linear and negative binomial regression adjusted for cystic fibrosis, age and sex, and multiple-comparison correction were used.

Results. In non-cystic fibrosis bronchiectasis group, carriage of the C allele of *IL6* −174 G>C was associated with fewer antibiotic-treated exacerbations (1.0 [0.0; 2.0] vs 2.0 [1.0; 3.0] episodes/year; p = 0.004; q = 0.032) and hospitalizations (0.0 [0.0; 1.0] vs 1.0 [1.0; 2.0] episodes/year; p = 0.001; q = 0.022). The C-allele dose correlated inversely with exacerbations (ρ = −0.42) and hospitalizations frequency (ρ = −0.46). In the multivariable model, C-allele carriage remained associated with a lower hospitalization rate (incidence rate ratio 0.48; 95% confidence interval 0.25–0.94; p = 0.031). Carriage of the G allele of *ELANE* −903 showed a trend towards lower forced expiratory volume in one second and forced vital capacity, whereas no statistically significant associations with quality of life were identified.

Conclusions. *IL6* −174 G>C may modify the clinical course of non-cystic fibrosis bronchiectasis in children. Carriage of the A allele in patients with the NE −741 G>A genotype was associated with the presence of bronchiectasis, with an odds ratio (OR) of 3.11 (95% CI: 1.04–9.28; p = 0.061). Given the small subgroups, multiplicity of analyses and deviation from Hardy–Weinberg equilibrium, these findings are hypothesis-generating and require independent prospective replication.

Key words: children, bronchiectasis, cystic fibrosis, *ELANE*, *IL6*, neutrophil elastase, interleukin-6, genetic polymorphism.