CYTOKINES AND PROLIFERATION MARKER KI-67 IN CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

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Chronic rhinosinusitis (CRS) is described as an inflammation of nasal cavity and paranasal sinuses. Overall prevalence of CRS, based on diagnostic criteria, is estimated to be around 5% a third of whom also have nasal polyps present. Presence of nasal polyps are the basis for CRS division into two categories chronic rhinosinusitis with (CRSwNP) and without (CRSsNP) nasal polyps.

Although a lot remains unknown about the aetiology of nasal polyps, in recent years research has been steered towards rather understanding underlying inflammatory mechanisms in CRSwNP affected mucosa. Research on interleukins found in nasal mucosa has helped to characterize type 2 and non-type 2 CRS inflammation and led to use of biological medication.

Aim of our research is to characterize appearance of cytokines IL-1α, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12 and proliferation marker Ki-67 in CRSwNP affected nasal mucosa and compare differences to a control group of healthy nasal mucosa.

Materials and methods

Study group consisted of 48 patients with CRSwNP. Samples of nasal polyps were taken during routine functional endoscopic nasal surgery. 29 patients with primary nasal polyps that experienced surgical treatment for the first time and 19 patients with recurring nasal polyps who have had surgery previously. The control group consisted of 17 otherwise healthy individuals with isolated nasal septum deviation with no history of CRS. Mucosa samples were taken during septoplasty from inferior nasal turbinates. Tissue of the samples was stained immunohistochemically for IL-1α, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12 and proliferation marker Ki-67. Results were evaluated by using semi- quantitative method. Non-parametric Mann–Whitney U test was used.

Results

Samples of all nasal polyps showed a decreased number of positive structures in epithelial cells and an increased number in subepithelial connective tissue. Number of Ki 67 positive structures were significantly decreased in epithelium of nasal polyps ($p<0.001$) but no significant differences were observed in subepithelial connective tissue. Number of IL-1α, IL-4, IL-6, IL-7, IL-8, IL-10 and IL-12 positive structures were significantly decreased in epithelial tissue of nasal polyps when compared to control samples ($p<0.001$). In nasal polyp subepithelial connective tissue significantly increased number of structures were found in case of IL-1α, IL-6, IL-7, IL-8, IL-12 ($p<0.001$) and IL-4 ($p=0.006$), but no significant changes were detected with IL-10 ($p=0.074$).

When comparing samples of recurrent nasal polyps and primary nasal polyps differences were observed between both epithelial and connective tissue IL-1α and connective tissue IL-10. Number of positive structures was increased in epithelial IL-1α ($p=0.047$) connective tissue IL-1α ($p=0.036$) and

connective tissue IL-10 ($p=0.018$) in patients with recurring nasal polyps in comparison to primary nasal polyps.

When comparing individual groups of primary and recurrent nasal polyps with control samples minor differences were observed. Epithelial number of positive structures remained significantly increased in both primary group samples IL-1α ($p<0.001$), IL-4 ($p<0.001$), IL-6 ($p<0.001$), IL-7 ($p<0.001$), IL-8 ($p<0.001$), IL-10 ($p<0.001$), IL-12 ($p<0.001$), Ki 67 ($p<0.001$) and recurrent group samples IL-1α ($p<0.001$), IL-4 ($p<0.001$), IL-6 ($p<0.001$), IL-7 ($p<0.001$), IL-8 ($p<0.001$), IL-10 ($p<0.001$), IL-12 ($p<0.001$), Ki 67 ($p=0.001$) when compared to control samples. In subepithelial connective tissue increased number of positive structures were observed in samples of primary polyps IL-1α ($p<0.001$), IL-4 ($p=0.007$), IL-6 ($p<0.001$), IL-7 ($p=0.001$), IL-8 ($p<0.001$), IL-12 ($p<0.001$) and samples of recurrent nasal polyps IL-1α ($p<0.001$), IL-4 ($p=0.042$), IL-6 ($p<0.001$), IL-7 ($p<0.001$), IL-8 ($p<0.001$), IL-10 ($p=0.005$), IL-12 ($p<0.001$) when compared to control samples. Major difference was in number of IL-10 positive structures of subepithelial connective tissue that was significantly increased with samples of recurrent nasal polyp samples ($p=0.005$), but no significant difference was observed with primary polyp samples ($p=0.475$) when compared to control samples.

Conclusions

Decreased appearance of IL-1α, IL-4, IL-6, IL-7, IL-8, IL-12, Ki 67 in epithelial cells and increased appearance of IL-1α, IL-4, IL-6, IL-7, IL-8, IL-12 in connective tissue are associated with dysfunctional epithelial barrier of nasal polyps.

Recurrent nasal polyp samples can be characterised with more severe inflammation due to increase in anti-inflammatory IL-10 and alarmin IL-1α.