PROINFLAMMATORY CYTOKINE LEVELS IN NASAL FLUID AS INDICATORS OF SEVERITY OF NASAL POLYPOSIS

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SUMMARY – The aim of this prospective study was to evaluate whether cytokine levels in nasal secretions may be clinical parameters of severity of nasal polyposis. Forty nasal polyp patients (20 asthmatic and 20 nonasthmatic) requiring surgical treatment were included. Nasal secretion samples were collected from nasal cavities of all 40 subjects. The levels of T-helper type 1 (Th1) proinflammatory cytokines IL-2, IL-12, IFN-γ, IL-1β, TNF-α and TNF-β, Th2 cytokines IL-4, IL-5 and IL-6, antiinflammatory cytokine IL-10 and chemokine IL-8 were measured using flow cytometric method. Each of the 40 patients was staged clinically according to global nasal symptom score, endoscopic score, and Lund-Mackay computed tomography (CT) score. Eosinophils were counted in hematoxylin-eosin stained sections of all nasal polyp samples. The concentrations of Th2 proinflammatory cytokines IL-5 and IL-6 were significantly higher ($P<0.05$ and $P<0.01$, respectively) in patients with nasal polyposis and asthma compared with nasal polyp patients without asthma. Positive correlations were observed between IL-2 concentration in nasal secretions and nasal symptom score, endoscopic score, and Lund-Mackay score only in nasal polyp patients without asthma. We also found positive correlation between Lund-Mackay score and the levels of IL-8, IL-4, and IL-1β in nonasthmatic patients. A positive correlation between IL-5 levels in nasal fluid and endoscopic score was found only in asthmatic patients. Eosinophil counts were higher in asthmatic patients' polyps compared with nonasthmatic ones, but without statistical significance. Nasal polyposis in asthmatic patients has different immunological patterns compared to those without asthma. The concentrations of cytokines measured in nasal fluid were not sensitive enough to be universal criteria to determine the severity of all forms of nasal polyposis.

Key words: *Nasal polyps – complications; Nasal polyps – diagnosis; Nasal polyps – etiology; Asthma – complications; Cytokines – secretion; Respiratory hypersensitivity – immunology*

Introduction

Nasal polyposis is a chronic inflammatory disease of the nasal and paranasal sinus mucosa, which is characterized by the formation of benign edematous polyps. Most often, polyps originate from the anterior ethmoid complex and from there they can descend between the middle turbinate and the lateral nasal wall into the nasal cavity causing symptoms such as nasal obstruction, anosmia, sneezing, rhinorrhea, and itching[1]. Chronic persistent inflammation is a major factor in the development of nasal polyposis[2]. Polyp tis-

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sue includes mixed inflammatory cells, predominantly eosinophils and neutrophils. They have the primary role in perpetuation of chronic inflammation[2,3]. It has been suggested that an ineffective local T-helper 1 (Th1)-based immune response in these patients is associated with increased T-helper 2 (Th2)-cytokine-based activity, which contributes to chronic infection as well as to an increased presence of eosinophils, which then lead to further polyp formation[4]. It has been proposed that the weakened Th1 response in these patients may be secondary to the down-regulation of some specific toll-like receptors involved in the innate immune response[4].

It was found that asthma was present in 29.9% of patients with nasal polyps referred to ENT departments[5]. On the other hand, 7% of asthma patients had nasal polyps[2,5]. Asthma is the most common chronic disease among children and adolescents. It is characterized by intermittent obstruction and inflammatory changes of airways and bronchial hyperresponsiveness[6]. The pathogenesis and pathophysiology of this disease are known to be associated with alterations of glucocorticoid receptor function and also with persistent pulmonary inflammation, the important mediators of which are reactive oxygen and nitrogen species[7].

Nasal secretions represent a first line defense medium, in which leukocytes probably act as an efficient part of the defense mechanism along with the mucociliary transport system and mucus biochemical properties[8]. Cellular secretory products in nasal secretions may be determined to characterize inflammatory changes of the upper respiratory mucosa[9]. Nasal secretions contain small amounts of cytokines, potent biologic factors involved in the regulation of inflammation and immune defense, and other inflammatory mediators expressed by various epithelial and nonepithelial cells[10]. It has been shown that nasal secretions reflect the inflammatory status of the nasal mucosa and the evolution of mucosal disease. However, the mechanisms of cytokine release in nasal fluid are less well known. Results published by Ohkubo *et al.*[11] show that IL-6 and IL-8 were released to the nasal fluid mainly from the migrating and epithelial cells as a result of antigen provocation, reflex action of metacholine and by direct action of histamine. As cytokines play a dominant role in the pathophysiology of airway disease, the cytokine profile in nasal secretions may help recognize the mechanisms underlying nasal polyposis. The key question in this study was: may cytokine levels in nasal fluid be indicators of the nasal polyposis severity?

The aim of this study was to compare the levels of these cellular secretory products in nasal secretions of asthmatic and nonasthmatic patients with nasal polyps and to correlate cytokine levels with clinical parameters of nasal polyposis severity in asthmatic and nonasthmatic patients.

Patients and Methods

Study population

Forty patients requiring surgical treatment (20 subjects with nasal polyposis and 20 subjects with nasal polyposis and concomitant asthma) were included in this prospective study, which was performed according to the Declaration of Helsinki. A written informed consent was obtained from all subjects. The study was approved by the Ethics Committee of the Military Medical Academy, Belgrade, Serbia. There were 15 male and 5 female patients in the nasal polyp group (mean age 43.27±14.72 years) and 16 male and 4 female patients in the nasal polyp with asthma group (mean age 46.52±15.31 years). The diagnosis of nasal polyposis was based on each patient's medical history and on the results of anterior rhinoscopy, nasal endoscopy and computed tomography according to the current European Guidelines[2]. Nasal polyposis, which is considered to be a subgroup of chronic rhinosinusitis, is defined as inflammation of the nose and paranasal sinuses, characterized by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior, posterior nasal drip) ± facial pain/pressure ± reduction or loss of sensation of smell and either endoscopic signs of polyps and/or mucopurulent discharge primarily from middle meatus and/or edema/mucosal obstruction primarily in middle meatus, and/or computed tomography (CT) changes showing mucosal changes within the ostiomeatal complex and/or sinuses for more than 12 weeks[2].

The diagnosis of nasal polyposis was confirmed by histopathologic analysis of nasal polyp specimens after endoscopic sinus surgery. Twenty patients had the

diagnosis of mild persistent bronchial asthma. The diagnosis of asthma was made at the time of inclusion in the study according to the Global Initiative on Asthma (GINA)[12]. Assessment of the severity of asthma was done by a pulmonologist based on the patient's medical history, clinical data and pulmonary function testing, including forced expiratory volume in 1 second (FEV1) and methacholine provocation test (Mch PD20). Only patients with polyps associated with mild bronchial asthma, without aspirin sensitivity were included in the study. The diagnosis of aspirin-induced asthma was done by a positive bronchial aspirin-provocation test. The other exclusion criteria were the presence of antrochoanal and sphenochoanal polyps, aspirin sensitivity, cystic fibrosis, and primary ciliary dyskinesia. None of the study subjects had bronchial or respiratory tract infection and none of them was treated with oral and topical corticosteroids, antibiotics and antihistamines for at least three weeks before enrolment. All patients underwent skin prick test for sensitivity to eighteen common allergens. Test result was considered positive when at least one of the induration diameters was by 3 mm higher than that in negative control. Subjects were considered allergic if they had a serum IgE level >200 IU/mL.

Clinical score

All patients were examined by the same otorhinolaryngologist. The patients were asked to assess their symptoms associated with nasal polyposis. Only subjects with nasal symptoms persisting for at least 12 weeks were included in the study. The presence of nasal symptoms associated with nasal polyposis (obstruction, anosmia, sneezing, rhinorrhea, and itching) on the day of enrolment was scored according to Tsicopoulos *et al.*[13] from 0 to 3, as follows: 0 for no symptoms, 1 for mild symptoms, 2 for moderate symptoms, and 3 for severe symptoms, so that the maximal global nasal symptom score was 15.

Nasal endoscopy was performed in sitting position with a rigid endoscope 0° and 30° (Storz, Tuttlingen, Germany). Topical anesthesia or decongestion were not used. Endoscopic physical findings were scored according to Lildholdt *et al.*[14]. The degree of nasal polyps is classified in relation to fixed anatomical landmarks in four steps: 0 = no polyposis; 1 = mild polyposis (small polyps not reaching the upper edge of the inferior turbinate); 2 = moderate polyposis (medium sized polyps reaching between the upper and lower edges of the inferior turbinate); and 3 = severe polyposis (large polyps reaching below the lower edge of the inferior turbinate). The maximal endoscopic score is 6, bilaterally.

Findings on CT scans were graded according to Lund-Mackay score[15]. Mucosal abnormalities were graded as 0 (no abnormality), 1 (partial opacification), or 2 (total opacification) of the frontal, maxillary, anterior ethmoid, posterior ethmoid and sphenoid sinus, bilaterally. The ostiomeatal complexes were scored bilaterally as 0 (not occluded) or 2 (occluded). The maximal CT grading score is 24.

Sampling of nasal secretions and cytokine determination

Nasal secretion samples were collected from nasal cavities of all 40 subjects (20 patients with nasal polyposis and 20 patients with nasal polyposis and asthma) several days before endoscopic sinus surgery, using absorption technique with cotton-wool sticks (length 10 millimeters, diameter 4 millimeters; Institute of Virology, Vaccine and Sera, Torlak, Belgrade, Serbia), which were inserted into the nasal cavity for 60 seconds, as previously described[16,17]. The samples were placed in a 2-mL Eppendorf tube containing 1 mL of transfer media (phosphate-buffered saline with gentamicin 50 μg/mL, penicillin G 340 U/mL, fungizone 500 μg/mL) for 30 min to allow for diffusion of cytokines into the medium. Nasal fluids were centrifuged at 1000 g for 10 minutes to separate cellular components. After centrifugation, the supernatants were portioned and stored at -70 °C until cytokine determination. The levels of eleven cytokines (TNF-α, TNF-β, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, and IFN-γ) were measured in all 40 samples using a commercial flow cytometric kit (Flow Cytomix, Bender MedSystems GmbH, Vienna, Austria) on a flow cytofluorimeter (Beckman Coulter XL-MCL, USA), which was connected with BMS Flow Cytomix Pro 2.2 Software, according to the manufacturer's instructions. The sensitivity of detection was as follows: 22 pg/mL for TNF-α; 32 pg/mL for TNF-β; 17 pg/mL for IL-1β; 28 pg/mL for IL-2; 20 pg/mL for IL-4; 30 pg/mL for IL-5; 21 pg/mL for IL-6; 13 pg/mL for IL-8; 20 pg/mL for IL-10; 5.1 pg/mL for IL-12; and 8 pg/mL for IFN-γ.

Table 1. Characteristics of study population

	Nasal polyposis	Nasal polyposis + asthma
Patients (n)	20	20
Age (yrs)	43.27±14.72	46.52±15.31
Male/female ratio	15/5	16/4
FEV1	100.54±4.81	95.22±5.35
MchPD20 (μg)	1589.38±57.73	548.83±101.78
Allergic	8	12
Nonallergic	12	8
Nasal symptom score	10.4±2.05	11.74±2.78
Nasal endoscopic score	5.1±1.23	6.24±1.84
Lund-Mackay score	17.44±3.16	18.8±3.21

All results are expressed as mean ± SD FEV1 = forced expiratory volume in 1 second; Mch PD20 (μg) = amount of methacholine in micrograms

Tissue preparation and quantification of eosinophils

All patients were operated endoscopically (FESS) under general anesthesia by the same surgeon. Nasal polyps located in the middle meatus were surgically removed. For histologic examination, polyp specimens were fixed in 10% formaldehyde, embedded in paraffin, cut with a microtome into 5-μm sections and stained with hematoxylin and eosin. Histologic examination was performed using a digital optical microscope (Nikon Coolscope), assisted with computerized image analysis system. This system was programmed by ImageJ (Java-based image processing program)[18]. Once the glass slide was set, brightfield images could be viewed on the monitor. Eosinophils were counted at X400 magnification. The visual field was oriented along the whole length of the epithelium basement membrane. To yield the mean number of eosinophils *per* high power field (HPF), 10 randomly chosen HPFs of a single section were examined. The eosinophils in each section were counted, and the mean number of eosinophils *per* HPF was calculated.

Statistical analysis

Data were expressed as mean ± standard deviation (± SD). Statistical comparisons of the results were performed by using the nonparametric Mann-Whitney U test and χ^2-test. Correlations between different parameters were made by Pearson's correlation test. A *P* value of less than 0.05 was considered statistically significant. On statistical analysis, we used Stat Plus 2007 program as a computerized analysis system.

Results

Comparing two groups (nasal polyposis with asthma and nasal polyposis without asthma), we found no significant difference according to the global nasal symptom score, endoscopic score and Lund-Mackay score. Eight patients in the nasal polyp group and twelve patients in the nasal polyp with asthma group were atopic. This finding showed a higher percentage of subjects with allergy in the nasal polyp with asthma group than in the nasal polyp group ($P<0.05$; χ^2-test).

We found no significant differences in the levels of TNF-α, TNF-β, IL-1β, IL-2, IL-4, IL-8, IL-12, and IFN-γ in the nasal secretions either. The concentrations of IL-5, IL-6 and IL-10 in nasal fluid were significantly higher in patients with nasal polyposis and asthma compared to patients with nasal polyposis without asthma (635.37±585.08 pg/mL *vs.* 273.48±218.12 pg/mL, $P<0.05$ for IL-5; 284.66±235.64 pg/mL *vs.* 56.63±77.16 pg/mL, $P<0.01$ for IL-6; and 82.12±61.25 pg/mL *vs.* 35.69±47.22 pg/mL, $P<0.05$ for IL-10). Numerical cytokine levels are presented in Table 2.

Positive correlations were observed between the concentration of Th1 proinflammatory cytokine IL-2 and global nasal symptom score ($r=0.600$; $P=0.018$), endoscopic score ($r=0.544$; $P=0.036$), and Lund-

Table 2. Cytokine levels in nasal secretions

Cytokine	Nasal polyposis	Nasal polyposis with asthma	*P* value
	Mean ± SD	Mean ± SD	
IL-12	8.38±14.31	29.78±47.82	>0.05
IFN-γ	31.27±28.08	45.57±39.28	>0.05
IL-2	248.85±186.67	174.72±123.62	>0.05
IL-10	35.69±47.22	82.12±61.25	<0.05
IL-8	172.34±223.19	137.88±103.22	>0.05
IL-6	56.63±77.16	284.66±235.64	<0.01
IL-4	523.68±735.42	968.87±1328.83	>0.05
IL-5	273.48±218.12	635.37±585.08	<0.01
IL-1β	29.27±48.46	48.85±43.93	>0.05
TNF-α	26.47±24.63	36.45±41.82	>0.05
TNF-β	171.38±227.37	202.88±323.53	>0.05

All results of cytokine levels are expressed in pg/mL.
SD = standard deviation; IL = interleukin; IFN = interferon; TNF = tumor necrosis factor

Mackay score (r=0.522; P=0.046) only in patients with nasal polyposis without asthma. We also found positive correlation between Lund-Mackay score and the levels of IL-8 (r=0.522; P=0.046), IL-4 (r=0.518; P=0.048) and IL-1β (r=0.548; P=0.034) in nonasthmatic patients. Finally, our results showed positive correlation between IL-5 levels in nasal fluid and endoscopic score (r=0.578; P=0.029) only in asthmatic patients.

On histopathologic examination, in asthmatic patients' polyps, the subepithelial loose connective tissue and epithelial layer were infiltrated by numerous eosinophils. In nonasthmatic patients' polyps, the eosinophil infiltration of the epithelium and lamina propria was scarce (Fig. 1 a, b). However, there was no statistically significant difference in the number of eosinophils (asthmatics 37±8 and nonasthmatics 24±6) (Fig. 2).

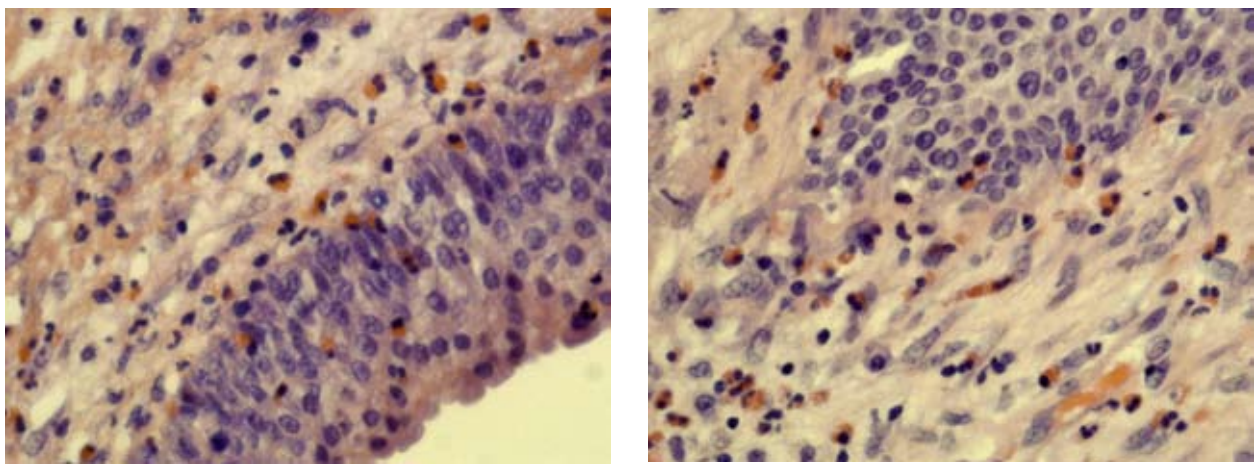

Fig. 1. In the polyps of asthmatic patients (a) the lamina propria and epithelium were infiltrated by numerous eosinophils, whereas in nonasthmatic patients' polyps (b) this eosinophil infiltration was scarce (H & E staining, X00).

Discussion

According to our results, the presence of asthma does not modify the symptoms, endoscopic and radiographic characteristics of nasal polyposis. However, we found significant influence of asthma on the cytokine profiles in nasal fluid. Hamilos *et al.*[19] found significantly higher levels of IL-5 in nasal polyp tissue from asthmatic than those from nonasthmatic subjects. The results of our research also showed a significantly higher concentration of Th2 cytokines (IL-5 and IL-6) in nasal secretions from patients with nasal polyposis and asthma than in those without asthma. These findings underline local Th1/Th2 balance as a key factor that governs local inflammation, implying that there is a different mechanism in nasal polyp evolution in asthmatic and nonasthmatic patients.

Previous data point to IL-5 as one of the key proteins in the pathomechanism of tissue eosinophilia, enhancing the differentiation, activation, expansion, mobilization, and *in situ* survival of eosinophils[20]. It is widely accepted that IL-5 plays an important role in the pathogenesis of bronchial asthma, where IL-5 induces eosinophil mobilization, B-cell growth and differentiation[20]. Eosinophils and mast cells have been reported as the main sources of IL-5[20,21]. Preliminary findings reported by Fan *et al.*[21] suggest that T-cell-derived IL-5 and autosecretion of IL-5 from activated eosinophils could be the reasons for the extension and persistence of eosinophil inflammation in nasal polyps. Although we did not find statistically significant difference, the number of eosinophils was evidently higher in lamina propria of asthmatic patients' polyps than in nonasthmatic ones. Therefore, the presence of fields of epithelial eosinophil infiltration is a clear confirmation of higher aggressiveness of eosinophilic inflammatory process in asthmatic patients. As IL-5 is a key inflammatory mediator in the development of nasal polyps associated with asthma and allergy, these findings could be an explanation of the positive correlation between IL-5 levels in nasal fluid and endoscopic score as an indicator of the spread of nasal polyps. Although an increased number of IL-5 mRNA was found in the ethmoid sinus mucosa at the time of surgery in patients that did not respond to surgical intervention[22], Drviš *et al.*[23] found a positive correlation between baseline IL-5 level in sinus lavage and improvement rate of the sinusitis symptom score. Their results showed the increased IL-5 levels in sinus fluid to predict good response to endosinusal steroid/antibiotic treatment.

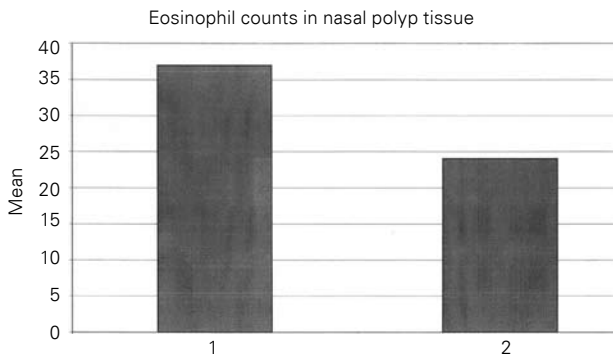

Fig. 2. The eosinophil count was higher in the polyp tissue samples from asthmatic patients (1) than in samples from nonasthmatic ones (2), but the difference was not statistically significant.

IL-6 is an important proinflammatory Th2 type cytokine involved in the induction of IgE synthesis as well as in mast cell proliferation and maturation[20,24]. IL-6 also stimulates fibroblast proliferation and collagen synthesis[20,24]. Immunohistochemical staining and in situ hybridization also indicated that macrophages, eosinophils, fibroblasts, and lining epithelium were the main sources of IL-6[20,24]. The pathogenesis of nasal polyposis involves nasal polyp fibroblasts through synthesizing IL-6 to modulate the activation of immune responses (plasma cell formation) and synthesis of stroma[20,24]. Van Zele *et al.*[25] demonstrated an increased colonization of nasal polyps by *Staphylococcus aureus* and presence of specific IgE directed against *Staphylococcus aureus* exotoxins in nasal polyp tissue. The rate of colonization and IgE presence in nasal polyp tissue were increased in subjects with nasal polyposis and asthma comorbidity[23]. Hellings *et al.*[26] demonstrated the nasal application of *Staphylococcus aureus* exotoxin B in mice to be capable of aggravating experimental allergic rhinitis and asthma, paralleled with an increase in bronchial and systemic Th2 cytokine levels. IL-10 is an anti-inflammatory Th2 cytokine produced by T-lymphocytes, monocytes and macrophages. It is considered to inhibit the release of IFN-γ and cytokine synthesis of monocytes, and leads to marked immunosuppression[27].

Positive correlations between IL-4, IL-1β, and IL-8 levels in nasal secretions and Lund-Mackay score can be explained by several recently published findings. Eosinophil infiltration is regulated by numerous chemokines and adhesion molecules such as eotaxin, regulated on activation normal T cell expressed and secreted (RANTES), and vascular cell adhesion molecule (VCAM)-1[20,28]. In order to infiltrate the sites of inflammation, eosinophils leave the bloodstream and pass through the endothelium in four steps, namely rolling, adhesion, transendothelial migration, and chemotaxis[20]. Adhesion molecules, such as VCAM-1, play an important role during adhesion to endothelial cells[20].

Among other Th2 cytokines, IL-4 has been shown to deliver signals that support or cause selective influx of eosinophils[20,28]. It has been speculated that IL-4 may be involved in the induction of VCAM-1 expression on microvascular endothelium in nasal polyps[20,28]. A study performed by Yoshifuku *et al.*[28] showed that IL-4 increased the secretion of eotaxin and VCAM-1 from cultured nasal polyp fibroblasts.

IL-1β has a crucial role in the pathogenesis of chronic rhinosinusitis and nasal polyps. This strong Th1 proinflammatory cytokine secreted by epithelial cells, monocytes, macrophages and fibroblasts upregulates the expression of E-selectin and intercellular adhesion molecule-1 (ICAM-1) in vascular endothelial cells, and thereby induces extravascular transmigration of neutrophils[29]. The emigrated neutrophils then secrete IL-1β, which amplifies the expression of E-selectin and ICAM-1, resulting in further neutrophil infiltration[29]. IL-1β can lead to increased transendothelial migration of eosinophils[30]. Results published by Saji *et al.*[30] suggest that nasal polyp fibroblasts play an important role in inducing eosinophilic infiltration, through IL-1β induced production of RANTES in nasal polyp fibroblasts. *In vitro* effects of RANTES on eosinophils include chemotaxis, transendothelial migration, induction and production of reactive oxygen, and the release of eosinophil cationic protein (ECP)[30]. IL-8, a potent neutrophil and also eosinophil chemoattractant and activating factor, is known to be released by monocytes, macrophages and airway epithelial cells[20,27]. Recent data have shown that airway fibroblasts are also important sources of this chemokine[20,27]. IL-8 is a very important chemokine regarding its chemotactic activity for neutrophils (and also eosinophils) in all types of rhinosinusitis and nasal polyposis. This chemotactic factor, released in nasal discharge from nasal gland duct cells and epithelial cells, attract neutrophils out of the mucosa[27]. The neutrophils that have migrated into the sinus effusion secrete IL-8. This induces further neutrophil accumulation in the sinus effusion[27].

Positive correlations between the concentration of IL-2 and nasal symptom score, endoscopic score and Lund-Mackay score in nonasthmatic nasal polyp patients is difficult to explain. IL-2 is an essential growth factor for T-cells and it acts in an autocrine fashion to stimulate T-cell proliferation and also serves to regulate immunoglobulin production and the growth of cytotoxic T-lymphocytes and natural-killer cells[6]. It has been suggested that nasal polyps present a mixed Th1 type and Th2 type cytokine profile[4]. We speculate that IL-2 as a strong Th1 cytokine maybe have predominant role in the pathogenesis of nonasthmatic patients' polyps, where the presence of atopy is not dominant. However, its role in the development of nasal polyposis is unclear and presents a topic for further investigation.

Conclusion

Our results demonstrated the presence of Th2 cytokines, especially IL-5 and IL-6 in nasal fluid in nasal polyp patients to be a prominent feature related to the increased inflammatory process. Our findings also suggest that up-regulation of Th2 cytokines is a more significant characteristic of nasal polyposis in asthmatic than nonasthmatic patients. These results showed that these patients with similar clinical findings had significantly different mediator profiles in their nasal secretions, implying clear differences in the pathogenesis of their nasal polyps. The concentrations of IL-4, IL-8 and IL-1β correlated with Lund-Mackay CT score as an indicator of the disease severity only in nonasthmatic nasal polyp patients. In asthmatic nasal polyp patients, IL-5 levels in nasal fluid correlated with endoscopic clinical findings. In different types of nasal polyposis (asthmatics and nonasthmatics), different cytokines correlated with different clinical parameters. Although the concentrations of cytokines measured in nasal fluid were not sensitive enough to

determine the severity of all types of nasal polyposis, evaluation of local immune reaction mediators in nasal secretions could be an accessible and valuable path in monitoring these patients and evaluating the pathogenesis of this disease.

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Sažetak

KONCENTRACIJE PROUPALNIH CITOKINA U NOSNOM SEKRETU KAO INDIKATORI TEŽINE NOSNE POLIPOZE

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Cilj ove prospektivne studije bio je ispitati mogu li koncentracije citokina u nosnom sekretu poslužiti kao klinički parametri za procjenu težine nosne polipoze. U studiju je bilo uključeno 40 bolesnika s nosnom polipozom (20 astmatičnih i 20 neastmatičnih) u kojih je bilo potrebno kirurško liječenje. Uzorci nosnoga sekreta bili su sakupljeni iz nosnih šupljina svih 40 bolesnika. Koncentracije T pomoćničkih-1 (Th1) proupalnih citokina IL-2, IL-12, IFN-γ, IL-1β, TNF-α i TNF-β, Th2 citokina IL-4, IL-5 i IL-6, protuupalnog citokina IL-10 i hemokina IL-8 mjerene su primjenom metode protočne citometrije. Svaki od 40 bolesnika klinički je klasificiran prema zbiru nosnih simptoma, endoskopskom zbiru i Lund-Mackayevu zbiru. Eozinofili su se brojili u uzorcima nosnih polipa obojenim tehnikom hematoksilin-eozin. Koncentracije Th2 proupalnih citokina IL-5 i IL-6 bile su statistički značajno više u astmatičnih nego u neastmatičnih bolesnika s nosnom polipozom (P<0,05, P<0,01). Nađena je pozitivna korelacija između koncentracije IL-2 u nosnom sekretu i zbira nosnih simptoma, endoskopskog zbira i Lund-Mackayeva zbira samo u neastmatičnih bolesnika. Također su utvrđene pozitivne korelacije između Lund-Mackayeva zbira i razina IL-8, IL-4 i IL-1β u neastmatičnih bolesnika. Pozitivna koralacija između koncentracije IL-5 u nosnom sekretu i endoskopskog zbira nađena je samo kod astmatičnih bolesnika. Broj eozinofila bio je veći u tkivu nosnih polipa astmatičnih bolesnika nego u neastmatičnih, ali bez statističke značajnosti. Nosna polipoza u astmatičnih bolesnika ima drugačiji imunološki tijek u usporedbi s neastmatičnim bolesnicima. Koncentracije citokina mjerene u nosnom sekretu nisu dovoljno osjetljiv pokazatelj da bi bile univerzalni kriterij za procjenu težine svih oblika nosne polipoze.

Ključne riječi: *Nosni polipi – komplikacije; Nosni polipi – dijagnostika; Nosni polipi – etiologija; Astma – komplikacije; Citokini – lučenje; Respiracijska preosjetljivost - imunologija*