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Allergic nasal polyps under scanning electron microscope

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SUMMARY

The study material consisted of 18 patients (10 men, 8 women, aged 26-66 years), suffering from recurrent nasal polyps and bronchial asthma. Nine patients manifested intolerance to aspirin and non-steroid anti-inflammatory drugs (NSAIDs). The polyps removed during one of polypectomies were analysed with the help of scanning electron microscope (SEM) in order to evaluate the morphology of their surface. All the specimens displayed the increase in areas of cilium-free epithelium, covered with short microvilli and squamous epithelial cells. The arrangement of these changes was irregular and they were more pronounced in patients with intolerance to aspirin and NSAIDs. Apart from this, there were no other differences which would allow to differentiate in SEM investigation between polyps derived from patients with and without tolerance to NSAIDs.

BACKGROUND

Morphological and clinical criteria for the diagnosis of nasal polyps and their qualification for surgery have been strictly determined [1–5], while their aetiology and pathomechanisms still remain unclear.

Many patients develop polyps in the course of allergic diseases such as bronchial asthma, particularly with coexisting intolerance to non-steroid anti-inflammatory drugs (NAIDs) [1,6–10]. In some cases, nasal polyps precede the occurrence of full clinical picture of these diseases. Sin et al. [11] prove that 50% of polyps have an allergic background, IgE-dependent mechanism and frequently, the allergy to dust mites. In histological terms, the polyps vary in respect of the dominance of neutrophil or eosinophil reaction. One should also remember that apart from allergy, there may be different causes for polyps development [4,12].

One of important reasons to investigate the issue of recurrent nasal polyps is the search for optimal treatment method to prevent polyp recurrence which may greatly affect respiratory function and necessitate reoperation.

The purpose of this paper was to investigate the morphology and surface of nasal polyps under scanning electron microscope (SEM) in patients who manifested good tolerance or intolerance to NSAIDs. The study may contribute to optimisation of diagnostic and therapeutic management of patients with nasal polyps.

MATERIAL AND METHODS

Eighteen (18) patients with recurrent nasal polyps were included in the study. The analysis of clinical material is demonstrated in table 1.

At initial stage of polypectomy, one of the polyps was removed without pre-treatment with topical adrenaline so as to avoid the damage of polyp surface. This procedure was approved of by the pa-

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Table 1.

Number of analysed patients:	18 (8 women, 10 men)
Age:	26 - 66 years, mean age 48 years
Number of patients with:	
bronchial asthma:	18 patients
intolerance to NSAIDs:	9 patients
Number of patients	
without symptoms of allergy:	9 patients
Mean polyp size:	6 x 8 x 14 mm

tients included in the analysis. The polyp located closest to the ostium was removed first.

Analysed polyps were fixed through the immersion in 5% glutaraldehyde solution in cacodylate buffer 0.2 M, pH 7.4. Then, the specimens were flushed several times in cacodylate buffer 0.2 M and dehydrated in the increasing concentrations of ethyl alcohol. After passage through absolute acetone the specimens were dried at critical point CO_2. Having coated the preparations with gold in JEE-4x sputter coater (Jed. Tokyo, Japan), the polyps were analysed under scanning electron microscope JSM-35--CF (Jed, Tokyo, Japan) at accelerating voltage of 25 KV.

The study material was processed and then analysed in the Laboratory of Scanning Microscopy, Department of Otolaryngology CM UJ in Kraków. Having analysed the whole surface of each polyp under SEM, three representative areas recorded on photographs at magnifications of 1000x and 2000x were randomly selected in order to make the evaluation standardised and objective.

The photographs were coded so as to make the evaluation of the material more objective. The photographic documentation was used to analyse epithelial cells covering polyps and proportional area covered by various types of cells with cilia, microvilli and squamous epithelial cells. The area of each cilium-free cell was calculated with planimeter.

In each specimen, the area occupied by the cells with long and short microvilli as well as squamous epithelial cells was calculated, after which a proportional assessment of the area occupied by each cell type was performed.

The numbers obtained were added up separately for the patients with intolerance to aspirin and other NSAIDs and separately for those with good tolerance of these drugs. Then, mean area occupied by various cell types was calculated for both analysed groups. Considering the fact that not all cell types were found simultaneously on the surface of analysed polyps, 100% value quoted in results section applies to the surface of those polyps only, where a given epithelial cell was present.

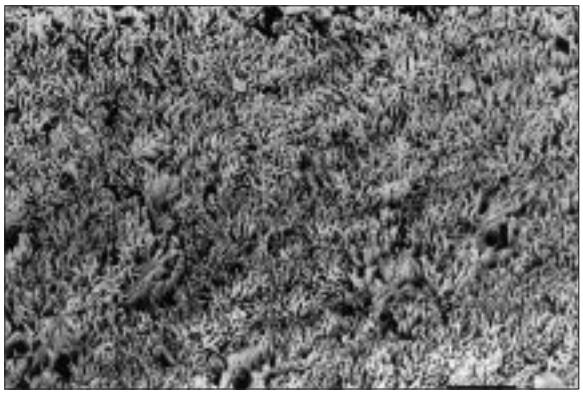

Figure 1. Epithelium with cilia, typical for normal surface of nasal mucosa. Scale = 10 μm.

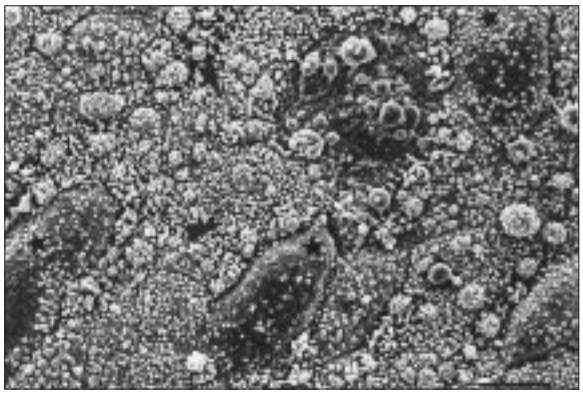

Figure 2. Surface of nasal mucosa covering polyp in analysed patients. Cells with smooth surface with few, very short microvilli. Scale = 10 μm.

RESULTS

The analysis of polyps under SEM allowed to visualise the details of its surface. Polyp epithelium covered with cilia on over 50% of polyp surface, typical for normal nasal mucosa (Figure 1) was observed in 12 analysed specimens (5 of them were obtained from patients with intolerance to NSAIDs and 7 from patients with good tolerance of these drugs). In the remaining polyps, derived from 4 patients with intolerance to NSAIDs and 2 subjects with tolerance to NSAIDs, cilium-free cells prevailed in the epithelium covering polyp surface (Figure 2).

The number of cilium-free cells on the surface of one polyp ranged between 89 and 119 (mean value: 109). All the analysed polyps had the areas of cilium-free epithelium with irregular arrangement.

Among patients with good tolerance to NSAIDs, the areas of cilium-free epithelium consisted mainly of the cells with long villi, while the cells with short microvilli and squamous epithelium were less frequent. On the other hand, in patients with intolerance to NSAIDs, the areas with cilium-free epithelium were dominated by the cells covered with short microvilli, followed by the cells with long microvilli and squamous epithelial cells. In these polyps, there were single areas ('islets') covered with cilia. All epithelial cells had regular arrangement, without a clear predominance of any of these on each polyp wall, its top or peduncle.

Apart from epithelial cells covered with cilia, long or short microvilli and squamous epithelial cells, the polyps were also analysed in terms of glandular ostia and goblet cells.

In the polyps derived from patients with good tolerance to NSAIDs and undergoing simultaneous antiallergic treatment, the microvilli found on cilium-free cells were shorter. Dense concentration of microvilli on to of the polyps tended to vary. In isolated cases, microvilli densely covered the whole cell surface. The cells without microvilli made exfoliating squamous epithelium, which were oval or convex in shape as well as having completely flat forms.

DISCUSSION

The analysis of the structure of polyp surface with the use of scanning electron microscope did not show any significant differences in the surface of epithelium covering polyps obtained from patients with good tolerance to NSAIDs and those who did not tolerate those drugs.

Nevertheless, it was only an overall assessment of detailed cell structure which allowed for the detection of some minor differences between those groups. These findings correspond to the results published by other authors who analysed polyp surface under SEM and did not observe characteristic differences between polyps derived from these groups of patients [8,13,14].

The analysis of the study material revealed epithelial areas void of normal cilia. Likewise, Mygind et al. [15] and Larsen et al. [16] claim that the areas of polyp covered with squamous epithelium clearly predominate in patients with intolerance to NSAIDs when compared to subjects who tolerate these medicines [7,8]. In our study, there were similar epithelial areas covered solely with cilium-free cells and these included mainly the cells with short microvilli or squamous epithelium cells.

It seems that the classification of polyps proposed in 1970s into eosinophilic and neutrophilic ones [13,16–18] on the basis of cytological smear obtained from polyp surface and histopathological investigation is more useful for therapeutic purposes. Eosinophilic polyps resistant to treatment usually require the administration of corticosteroids. Some authors assume that eosinophilic polyps [11,19] are the result of allergic tissue inflammation which often co-occurs with other allergic diseases. Patient's medical history, allergological tests and allergological laboratory assessments often allow to identify responsible allergen.

However, the causal relationship between eosinophilic inflammation of tissue, allergy and the development of polyps is difficult to establish and this truth is supported by a bulk of evidence. One should not forget that allergic reaction in nasal mucosa even in patients with something as typical as allergy to pollen, may trigger eosinophilic reaction in some subjects, eosinophilic-neutrophilic reaction in others and still in others – an acute allergic reaction to pollen manifested in non-infectious neutrophilic reaction [20].

It is also a well-known fact that patients with atopy (allergy to pollen or dust mites) develop nasal polyps extremely rarely, despite the presence of eosinophilic reaction in nasal mucosa. Just as in patients with non-allergic rhinitis with eosinophilia (NARES syndrome), this complication is not common.

The results presented in our paper as well as the data quoted in literature on the subject suggest that although patients with intolerance to aspirin and other NSAIDs often develop eosinophilic polyps, eosinophilic reaction may also occur in subjects with good tolerance to these drugs.

The studies conducted by many investigators [11,18,22,23] stress the fact that cytological smear obtained from polyp surface and histopathological investigations confirm a considerable share of eosinophils in the inflammatory reaction in nearly 50%

of cases. On the other hand, Sinn [11] observed a similar proportion of patients (50%) with IgE-dependent allergy in both types of polyps: eosinophilic and neutrophilic ones.

The results of polyp surface assessment with the help of SEM as well as the studies of cytokine content in nasal polyps carried out by Lee et al. [24] did not show the presence of characteristic features typical for patients with and without tolerance to NSAIDs as well as for eosinophilic and neutrophilic polyps.

Therefore, it seems right to postulate that the development of polyps results from the intensification of inflammatory process in nasal mucosa which leads to epithelial damage as well as chronic oedema in submucous tissue, while it does not depend on the very factor triggering inflammation.

The intensification of eosinophilic reaction in polyp structure might be induced by the predominance of eosinotactic factors, e.g. interleukin 5 [22,25]. Thus, the identification of a factor responsible for triggering and maintenance of a chronic inflammatory process is significant for the selection of effective pharmacological and preventive treatment.

Since some authors claim that allergic background of nasal polyps and the correlation between the reaction and IgE may be determined in nearly 50% of cases, irrespective of histopathological picture and NSAIDs tolerance [11,18,21,23], the identification of allergen type would make it possible to isolate the patient from the cause of allergy. The determination of inflammatory cytokine profile would be helpful in optimal selection of pharmacological prophylactics which would allow for effective inhibition of the inflammation induced by a given allergen. Steroid aerosols, cromones and anti-mediator drugs (e.g. cetirizine) may be particularly useful in the selection of effective pharmacotherapy in these patients. One should also remember about the significance of possible improvement in self-purification of mucosa through its flushing and climatotherapy. Epithelial damage observed in our study greatly impairs physiological self-purification mechanisms of nasal mucosa and thus, intensifies harmful effects of the environment.

CONCLUSIONS

1. Polyp surface in patients with intolerance to NSAIDs is covered predominantly by the cells with short microvilli and squamous epithelial cells when compared with the surface of polyps in patients with tolerance to NSAIDs.
2. Apart from this, there were no other differences in surface morphology of nasal polyps in patients with intolerance to NSAIDs which would allow for their clear differentiation from the polyps derived from patients tolerating NSAIDs, with the help of scanning electron microscopy.

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