

# Histopathological Features of Chronic Rhinosinusitis with Nasal Allergic Polyps

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**ABSTRACT:** Chronic rhinosinusitis with nasal polyps of allergic etiology is one of the most common pathology in the ENT sphere that affect a significant percentage of population. The paper aims to establish the involvement of the allergic component in the genesis of nasal polyposis. The study included 150 nasal polyps from patients hospitalized and operated in the ENT Department of Craiova's Clinical Emergency County Hospital. The biological material was fixed in 10% buffered formalin, processed by classical paraffin embedding technique followed by hematoxylin-eosin staining and it was interpreted in the Pathology Department of the same hospital. We evaluated a number of histopathological parameters that were given severity scores. The most common changes at epithelial level were: basal layer hyperplasia observed in 87 cases (58%), goblet cell hyperplasia in 121 cases (80.66%), basal membrane thickening with values between 10-42 $\mu$ m corresponding to a number of 118 cases (78.66%). The most important stromal changes were edema in 88% and infiltration with eosinophils 100%, indicating the allergic nature of this disease.

**KEYWORDS:** Nasal polyposis, histopathology, eosinophils.

## Introduction

The pathogenesis of chronic rhinosinusitis, whether or not associated with polyps, is very complex and involves activation and migration of inflammatory cells, vasodilation, growth and changes in glandular activity, activation of nerve endings triggering neurogenic inflammation and mucosal remodeling morphologically identifiable [1].

Chronic rhinosinusitis includes multiple phenotypic expressions, but based on clinical and histological differences, four subtypes can be outlined: chronic eosinophilic rhinosinusitis with/without nasal polyps and chronic non-eosinophilic rhinosinusitis with/without nasal polyps [2,3,4,5,6,7,8].

Allergic rhinitis has different etiologies, but a common feature, represented by inflammation dominated by eosinophils, the degree of eosinophilic infiltration of tissues being an important factor in the recurrence rate of nasal polyps [9,10].

Although eosinophils dominate the inflammatory infiltrate of chronic rhinosinusitis, especially that with nasal polyps [11], many other types of inflammatory cells, including neutrophils, mast cells, lymphocytes and plasma cells also play important roles in the pathogenesis of the disease [12,13].

We followed the changes of surface epithelium and stroma of polyps in relation to their severity.

## Material and Method

The present study included 150 cases of sino-nasal polyps obtained by endoscopic polypectomy, from patients admitted and operated in the ENT (Ear Nose Throat) Department of the Clinical Emergency County Hospital of Craiova.

The surgical specimens were fixed in 10% buffered formalin, subjected to usual processing by paraffin inclusion and hematoxylin-eosin staining.

For the selected cases we assessed a series of histopathological parameters that were given specific scores according to similar studies in literature [14,15,16] (Table 1).

- epithelial compartment: basal membrane thickening: 0 (<9 $\mu$ m), 1 (10-19 $\mu$ m), 2 (20-29 $\mu$ m), 3 ( $\geq$ 30 $\mu$ m); goblet cell hyperplasia: 0 (<3 cells), 1 (3-10 cells), 2 (11-20 cells), 3 (>20 cells); epithelial infiltration with eosinophils: 0 (0 cells), 1 (1-2 cells), 2 (3-10 cells), 3 ( $\geq$ 11 cells); basal layer hyperplasia: 0 (absent), 1 (focal), 2 (zonal), 3 (diffuse); squamous metaplasia: 0 (absent), 1 (focal), 2 (zonal), 3 (diffuse); stromal edema: 0 (absent), 1 (focal), 2 (zonal), 3 (diffuse);

epithelial alteration: 0 (absent), 1 (partial denudation), 2 (complete denudation);

- stromal compartment: eosinophilic infiltration: 0 (0 cells), 1 (1-3 cells), 2 (4-15 cells), 3 (>15 cells); stromal infiltration with lymphocytes: 0 (<10 cells), 1 (11-30 cells), 2 (31-50 cells), 3 (>50 cells); stromal infiltration with plasma cells: 0 (<10 cells), 1 (11-30 cells), 2 (31-50 cells), 3 (>50 cells); stromal infiltration with macrophages: 0 (0 cells), 1 (1-2 cells), 2 (3-9 cells), 3 ( $\geq$ 10 cells).

Basal membrane thickness was evaluated at 100x objective, using the graded scale attached to Panthera L. Hyperplasia of goblet cells, epithelial infiltration with eosinophils, stromal infiltration with eosinophils, lymphocytes, plasma cells and macrophages, were evaluated with 10 fields/x100, Panthera L binocular microscope with built-in digital camera (MOTIC manufacturer) and microscope integrated

software (for mobile devices running Android and IOS for "live" viewing of the microscope image and image acquisition, morphometry and annotation).

The statistical analysis was performed using the incidence tables and the chi-square comparison test ( $\chi^2$ ) within Microsoft Excel 2010, the p values under 0.05 being considered significant. The study was approved by the Ethical Committee of U.M.F. of Craiova, and the patients/or their caretakers gave a written informed consent regarding the publication of the data.

## Results

The present study included 150 cases of allergic polyps, for which we assessed a series of histopathological parameters at both lining epithelium and stromal level (Table 1).

**Table 1. Distribution of cases by lining epithelium and stromal changes.**

Histopathological parameters		No. cases	The degree of injury			
			0	1	2	3
Epithelial changes	Hyperplasia of the basal layer	87	63	51	21	15
	Squamous metaplasia	15	135	9	6	0
	Goblet cell hyperplasia	109	41	58	43	8
	Alteration of the epithelium	44	106	32	12	0
	Infiltration with eosinophils	16	134	11	4	1
	Thickening of basal membranes	118	32	89	27	2
Stromal changes	Edema	132	18	40	57	35
	Infiltration with eosinophils	150	0	71	62	17
	Lymphocyte infiltration	74	76	42	32	0
	Plasma cells infiltration	89	61	52	32	5
	Macrophage infiltration	11	139	7	3	1

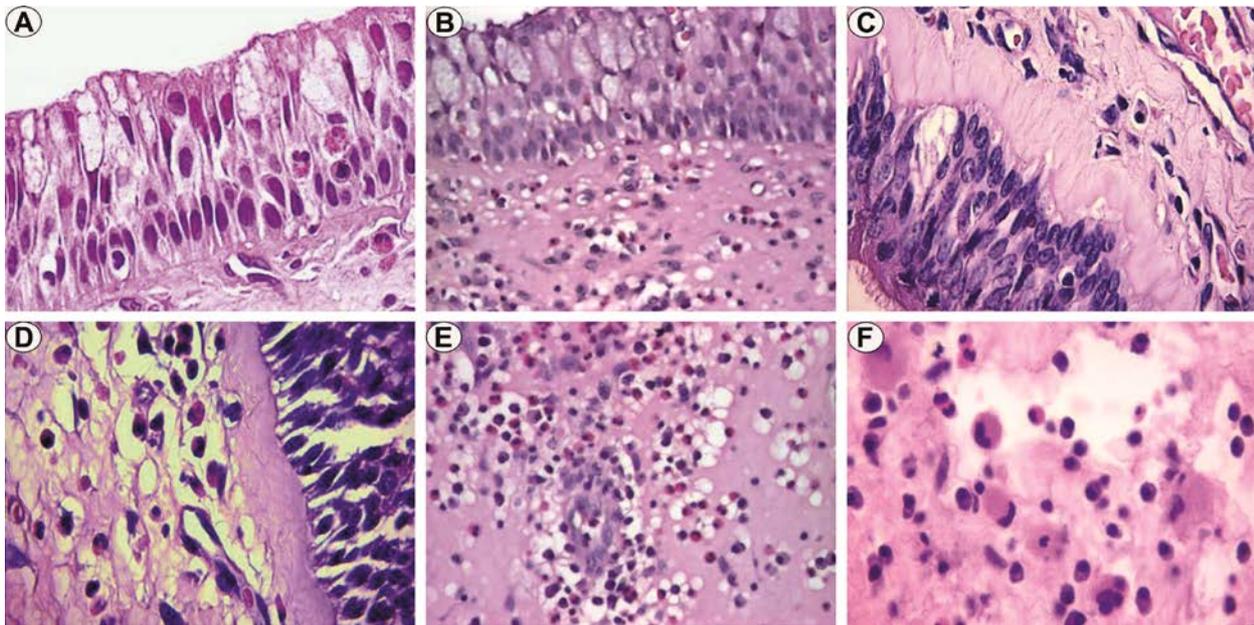
Regarding the changes produced at the surface epithelium, we found that most of the polyps analyzed were covered by cylindrical pseudostratified epithelium, but we frequently observed aspects of basal layer hyperplasia (58%), often with focal pattern, but also with epithelial denudation frequently on restricted areas (29.3%), and less frequently squamous metaplasia (10%) with focal pattern.

Also, we found in more than three quarters of cases the goblet cell hyperplasia (72.6%)

frequently moderate and rarely with formation of intraepithelial glands or even small mucous cysts (Figures 1A-B).

Another frequently observed change was the slight thickening of the basal membranes in more than half of all cases (78.6%) (Figures 1A-D).

Only rarely have we seen epithelial infiltration with eosinophils (10.6%), predominantly with low intensity.



**Figure 1. Allergic polyp: A. Hyperplasia of the basal layer, goblet cell hyperplasia and eosinophil infiltration, HE staining, x100; B. Hyperplasia of the basal layer and basal membrane (BM) thickening, HE staining, x40; C. Hyperplasia of the basal layer and BM thickening, HE staining, x100; D. Hyperplasia of the basal layer, BM thickening and stromal infiltration with eosinophils, HE staining, x100; E. Edema and inflammatory infiltrate with eosinophils, lymphocytes and plasma cells HE staining, x40; F. Edema and inflammatory infiltrate with eosinophils, plasma cells, lymphocytes and macrophages, HE staining, x100.**

Stromal changes were represented by edema and inflammatory cells infiltration.

The stromal edema frequently observed (88%) had different degrees, but frequently more pronounced subepithelial (Figures 1E-F).

Stromal eosinophilic infiltration was consistently present, often with moderate or reduced intensity.

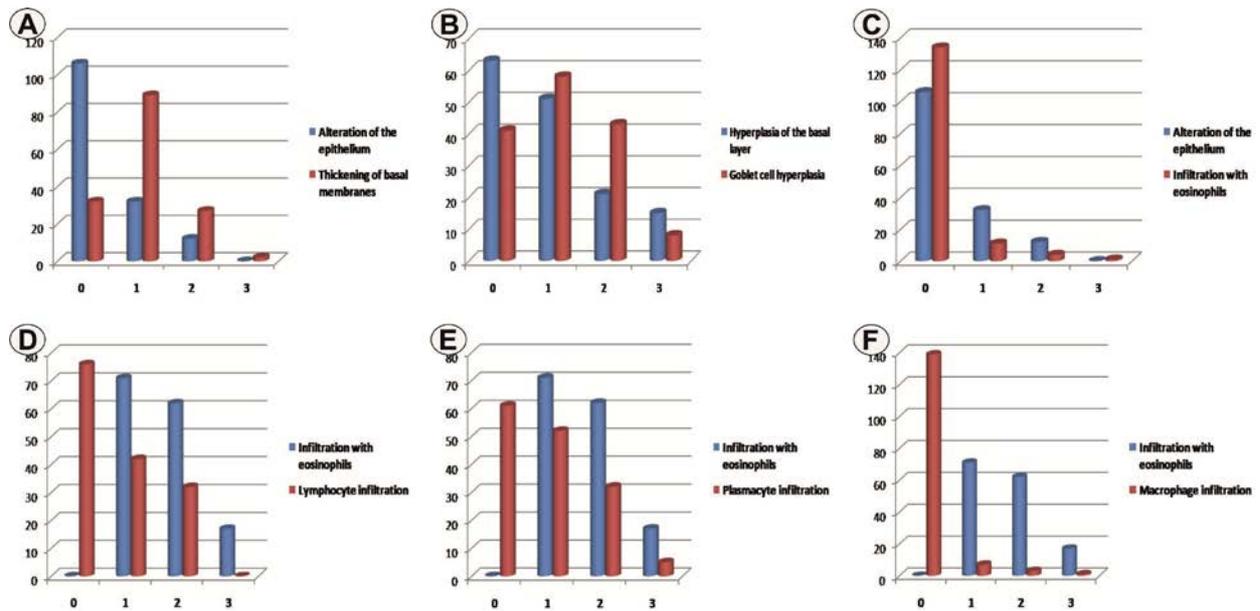
Along with eosinophils, we also noticed other inflammatory cells such as plasma cells (59.3%) and lymphocytes (49.3%) and only rarely macrophages (7.3%) (Figures 1D-F).

The analysis of the distribution of cases with respect to epithelial changes indicated statistically significant differences of the alteration of the epithelium and thickening of basal membranes ( $p < 0.001$ ,  $\chi^2$  test) in the sense of the predominance of the first parameter for

negative scores (score 0) and of the second one. second parameter for positive scores (score 1-3) (Figure 2A).

The analysis of the distribution of hyperplasia of the basal layer and goblet cell hyperplasia indicated the predominance of the basal changes for the negative or maximum scores, respectively scores 0 or 3 and of the changes related to the goblet cells for the intermediate scores, respectively scores 1-2. ( $p = 0.002$ ,  $\chi^2$  test) (Figure 2B).

Epithelial infiltration with eosinophils predominated for the negative cases (score 0), while alteration of the epithelium was more frequent for the positive cases (score 1-3), differences that were statistically significant ( $p < 0.001$ ,  $\chi^2$  test) (Figure 2C).



**Figure 2. Cases distribution depending on: A. alteration of the epithelium and thickening of basal membrane; B. hyperplasia of the basal layer and goblet cell hyperplasia; C. alteration of the epithelium and infiltration with eosinophils; D. infiltration with eosinophils and lymphocyte infiltration; E. infiltration with eosinophils and plasma cells infiltration; F. infiltration with eosinophils and macrophage infiltration.**

In the stromal compartment, we observed the predominance of eosinophils in relation to lymphocyte infiltration ( $p < 0.001$ ,  $\chi^2$  test) (Figure 2D), eosinophils infiltration ( $p < 0.001$ ,  $\chi^2$  test) (Figure 2E) and macrophage infiltration ( $p < 0.001$ ,  $\chi^2$  test) (Figure 2D), for all positive scores (scores 1-3).

In this study, the alteration of the epithelium, thickening of the basal membrane, hyperplasia of the basal layer and goblet cell hyperplasia, along with eosinophilic infiltration at the epithelial and stromal level seem to be the most specific changes of the allergic nasal polyps.

## Discussions

The allergic polyp is the most common variety of nasal polyp, present in 86% of cases, histologically characterized by pronounced hyperplasia of the goblet cells, thickening of the basal membrane with hyalinization, presence of eosinophils and mast cells in stroma, together with edema [17,18,19].

The covering epithelium of the allergic-type nasal polyps may be a normal respiratory mucosa or it may be partially or completely denuded [20].

In addition, it may express various changes such as basal layer hyperplasia, squamous metaplasia, goblet cell hyperplasia and infiltration with inflammatory cells, especially with eosinophils [18,21,22].

The aspects described in literature were identified in the studied cases, the most frequent being hyperplasia of the basal layer, hyperplasia of goblet cells and thickening of the basal membrane.

The association of basal hyperplasia and squamous metaplasia with nasal polyps is frequently mentioned in different studies, sometimes even with dysplasia-type changes [23].

In our study the hyperplasia of the basal layer was found in more than half of cases, but squamous metaplasia appeared only in a small number of cases with focal pattern.

Goblet cell hyperplasia together with squamous metaplasia are among the most common epithelial changes in nasal polyps [24,25,26,16,27].

Regarding the analysis of goblet cells, we found a great variation of associated phenomena, starting from rare mucous cells to a true formation of intraepithelial glands or cystic mucosal formations.

Alteration of the epithelium by superficial or complete erosion, up to the basal membrane level, has often been mentioned in different studies [28].

In the present study, we noticed the alteration of epithelium covering the polyps from its partial to complete denudation.

In only 16 cases (10.6%), we noticed the infiltration of the epithelium with eosinophils from those analyzed, with a frequency of a limited number of 1-2 cells/x100 corresponding to grade 1.

The thickening of basement membrane is the result of a dense fibrosis that occurs primarily in the lamina reticularis [29]. This configuration was encountered in 118 cases (78.6%), the thickness of the basal membrane varying between 10-42 $\mu$ .

In another study, thickening of the basement membrane was frequently identified in patients with chronic rhinosinusitis, in 95% of patients the thickening of the basement membrane was >20 $\mu$ m [30].

There were no apparent differences in the severity of epithelial lesions and the thickening of basement membrane in the allergic patients compared to the non-allergic ones, nor the differences between the patients with or without asthma [30].

In this study at the epithelial level, the thickening of the basement membrane predominated in relation to the alteration of the epithelium, goblet cell hyperplasia in relation to hyperplasia of the basal layer and the infiltration of eosinophils in relation to the alteration of the epithelium.

The major changes identified in the stroma of the nasal polyps are inflammatory infiltrate into the lamina propria and stromal edema, sometimes associated with focal fibrosis [31,32].

In our study we found the presence of stromal edema in 88% of cases, more pronounced below the epithelium and in a moderate quantity.

In a different study, the authors reported similar aspects, more than half of cases presenting moderate edema [16].

In all the cases analyzed with different characteristics we found the presence of stromal infiltration with eosinophils, which predominated in relation to infiltration with lymphocytes, plasma cells and macrophages. In the normal nasal mucosa there are no eosinophils or they are very rare, but in literature, there is no consensus on the value of normal tissue eosinophilia.

However, several studies consider that the minimum number for eosinophilia is 5 eosinophils/x40 in absolute quantification, and 5% as a percentage compared to the control group, which presented on average below 2 eosinophils/x 400 [33,34,35].

The density of these cells varies for different polyps, and even in different areas of the same polyp and this variability is in accordance with the dynamics of the polyp process [36].

## Conclusions

The histopathological analysis allows the detailed highlighting of the heterogeneity of epithelial and stromal changes, especially of different populations of inflammatory cells involved in the pathogenesis of this disease.

The most important stromal changes were edema and eosinophilic infiltration, in accord with the allergic nature of the disease.

The presence of intraepithelial as well as stromal eosinophils probably plays a role in the process of remodeling the mucosa of chronic rhinosinusitis with nasal polyps.

Further studies are needed to understand the correlations between histopathological features and the evolution of the disease.

## Conflict of interests

None to declare.

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