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Histopathologic characteristics of inferior turbinate vs ethmoidal polyp in chronic rhinosinusitis ☆

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Abstract It seems apparently that the 2 separate anatomical areas (nasal cavity and paranasal sinus mucosa) are indeed one single unit with an identical behavior during inflammatory process. Similar histopathologic evidence in long-term condition could emphasize on the concept of *rhinosinusitis* in patients with inflammatory paranasal sinus disease. Prospective study was performed on 50 consecutive patients with polyposis in 2 different groups, one with and the other without asthma. Inferior turbine and polyp with ethmoid sinus origin were selected to compare the histopathologic findings of the surgical specimens from the 2 sites (affected sinus vs apparently unaffected nose). The general degree of inflammation, epithelial thickening, and inflammatory cell count were measured. The degree of inferior turbinate inflammation correlated with that of the ipsilateral polyp of ethmoid sinus in both groups. In addition, the total inflammatory cell count was comparable. There was no statistically significant difference in total polymorphonuclear, lymphocyte, and eosinophil count between the 2 sites in each group ($P > .05$). The ethmoid sinus inflammation in polypoid chronic sinusitis is accompanied by a proportionate inferior turbinate inflammation, not only in the patients with asthma but also in those with isolated sinonasal polyposis.

Keywords: Chronic rhinosinusitis; Rhinitis; Sinusitis; Inferior turbinate; Polyp; Asthma; Histopathology

1. Introduction

Nasal polyps are hyperplastic swellings of the nasal mucous membranes. It shows, clinically, a great heterogeneity, ranging from single polyps (antrochoanal polyps) to nearly complete polypoid transformation of all paranasal sinuses. They may be seen in different conditions such as chronic rhinosinusitis, cystic fibrosis, Wegener's granulomatosis, and Kartagener's syndrome. The pathogenesis of nasal polyps has not been exactly known yet; however, allergy, infective or immunologic inflammation, and genetic predisposition are of the proposed hypotheses.

Polyps often originate from the paranasal sinuses, and yet, nasal inflammation occurs concurrently; therefore, using the term *rhinosinusitis*, which implies on more generalized inflammation, is more appropriate than sinusitis. Hence, a task force commissioned by the American Academy of Otolaryngology–Head and Neck Surgery Foundation in 1997 and the Sinus and Allergy Health Partnership proposed the application of the term rhinosinusitis instead of "sinusitis" to refer to the inflammatory paranasal sinus disease [1,2]. They noted that sinusitis is usually preceded and/or accompanied by rhinitis. Similarly, several articles [3,4] have shown the continuity and close relationship between the nasal and paranasal sinus mucosa. To support this concept, Bhattacharyya [5] assessed

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rhinosinusitis by comparing the degree of nasal inflammation and the paranasal sinuses. He noted that histopathologic evidence of rhinitis is associated with chronic sinusitis. Nasal septum was the area examined for evidence of rhinitis in his study. However, in another study of a specimen obtained from the middle turbinate instead of the nasal septum, the conclusion was identical [6]. The authors discussed that considering the middle turbine (as a part of nasal cavity) a separate entity to ethmoid sinus due to the close proximity to the ethmoid sinus and its role in the ostiomeatal unit (OMU) is negotiating. Conceptually, we selected the inferior turbine for comparison as an accessible site for biopsy. Moreover, the distance of inferior turbine to ostiomeatal complex is greater than the distance from middle turbinate to it; so its inflammation implicates on a more general inflammatory process.

We tried to demonstrate that patients with chronic inflammatory paranasal sinus disease have an inflammation of a similar degree in the ipsilateral inferior turbinate implying on similar sinonasal pathology as a single unit during inflammatory conditions. We carried out the study not only on the patients with asthma with systemic respiratory disorders but also on those with isolated polypoid chronic sinusitis (patients without asthma). Nasal involvement of the latter condition might implicate on more widespread sinonasal inflammation.

2. Materials and methods

A prospective study was conducted on 50 consecutive adult patients (age >15 years) who had chronic rhinosinusitis (CRS) with nasal polyposis refractory to any medical therapy. The study protocol was reviewed and approved by the research ethics review board at the Tehran University of Medical Sciences.

All those patients underwent endoscopic sinus surgery, and they were all initially examined in the respiratory clinic for the evaluation of asthma. Twenty-five cases (15 men and 10 women) with established mild to moderate asthma were selected as a separate group presenting systemic respiratory disorders (group 1). Asthma was diagnosed through clinical symptoms, medical history, physical findings, and the pulmonary function test based on the guidelines laid down by the Ciba Symposium in 1959 and later modified by the American Thoracic Society [7]. Patients with asthma showed a forced expiratory volume of <80% from the norm, based on the methacholine provocation test data in 1 second. They had experienced asthma symptoms for at least 5 years and had been treated with appropriate asthmatic medication for at least 36 months.

We also randomly selected 25 patients with chronic polypoid sinusitis without asthma (14 men and 11 women) as the other group (group 2). Chronic sinusitis was determined clinically as the presence of a combination of symptoms (ie, purulent rhinorrhea, postnasal discharge, headache, hyposmia, facial fullness, and nasal obstruction) along with sinonasal endoscopy and/or computed tomographic findings. Patients who had undergone surgery for fungal sinusitis, allergic fungal sinusitis, mucocele, antrochoanal polyps, acute rhinosinusitis, and underlying disorders (eg, Wegener's granulomatosis, sarcoidosis, cystic fibrosis, and Kartagener's syndrome) were excluded.

Endoscopic sinus surgery was performed by a rhinologist using the standard technique, under general anesthesia. The surgery was bilateral in all patients resulting in a total of 100 surgical sites. Ethmoidectomy and a punch biopsy of inferior turbine were performed on all patients. The surgical specimens from the ethmoid sinus (polyp) and the inferior turbinate were sent separately for pathology examinations. Sections of each formalin-fixed surgical specimen were stained with hematoxylin and eosin stain. The light microscopic findings of the following 7 histopathologic characteristics were compared between the nasal mucosa (inferior turbine) and sinus mucosa (ethmoidal polyp) both in asthmatic and nonasthmatic groups: (1) the thickness of the basement membrane, (2) goblet cell hyperplasia, (3) subepithelial edema, (4) submucous gland formation, (5) eosinophil, (6) lymphocyte, and (7) polymorphonuclear leukocyte (PMN) infiltration. These examinations were performed by one pathologist who was unaware of the clinical findings. The first evaluation was made under low-power magnification (×40) to determine the most affected regions. Each of the selected regions was then thoroughly reviewed under high-power magnification (×100 or ×400) and scored as described by Dhong HJ et al, [8,9] mentioned in the following subsections.

2.1. Thickness of the basement membrane

At a magnification of ×100, a score was assigned according to the degree of visible basement thickening, as follows:

0: none; 1: mild; 2: moderate; or 3: marked.

2.1.1. Goblet cell hyperplasia

At a magnification of ×400, a score was assigned according to the number of goblet cells visible, as follows:

0: <3 cells; 1: 3-10 cells; 2: 11-20 cells; or 3: >20 cells.

2.1.2. Subepithelial edema

At a magnification of ×100, a score was assigned according to the degree of subepithelial edema, as follows:

0: none; 1: mild; 2: moderate; or 3: marked.

2.1.3. Submucous gland formation

At a magnification of ×100, a score was assigned according to the number of submucous glands visible in a section, as follows:

0: <3 glands; 1: 3-10 glands; 2: 11-30 glands; or 3: >30 glands.

2.1.4. Eosinophil infiltration

At a magnification of ×400, the number of eosinophils present within epithelial cells and in the submucosa was scored as follows:

0: none; 1: 1 or 2 eosinophils; 2: 3-10 eosinophils; 3: 11-30 eosinophils; or 4: >30 eosinophils.

2.1.5. Lymphocyte infiltration

At a magnification of ×400, the number of lymphocytes present in the submucosa was scored as follows:

0: <20 lymphocytes; 1: 21-50 lymphocytes; 2: 51-80 lymphocytes; 3: 81-120 lymphocytes; 4: >120 lymphocytes.

2.1.6. PMN infiltration

At a magnification of ×400, the number of PMNs present in submucosa was scored as follows:

0: none; 1: 1 or 2 PMNs; 2: 3-10 PMNs; or 3: >10 PMNs.

2.2. Statistical analysis

SPSS (version 15.0; SPSS Inc., Chicago, IL, USA) was used for analyzing the data. Based on Kolmogorov-Smirnov Z test, data distribution was not normal, so we compared the data using Wilcoxon test. Statistical significance was defined as $P < .05$.

3. Results

A total of 50 patients with polypoid CRS (21 women and 29 men) were enrolled in this study, with a mean age of 41.3 years (range, 15 to 78 years). Twenty-five subjects had asthma, and 25 were isolated polypoid CRS. No one had previous sinus surgery. The mean computed tomographic Lund-MacKay score was 10.4 (range, 8 to 14). A total of 100 paired slides of samples were studied and included in our results.

Duration of the disease in patients with asthma was 4.6 ± 0.6, and for the other group was 5.8 ± 0.5, which did not show a significant difference ($P = .71$).

The mean histopathologic score of inflammation (basal membrane thickness, subepithelial edema, submucosal gland hyperplasia) among 2 groups at the 2 anatomical sites was shown in Tables 1 and 2. There was not a statistically significant difference between the mean score of inflammation in the ethmoid sinus and the ipsilateral inferior turbinate specimens in each group ($P > .05$).

Table 1
The histopathologic characteristics between nasal biopsy compared with ethmoidal polyp in patients without asthma

Histologic parameters	Inferior turbinate	Ethmoid polyp	P
Basal membrane thickness	1.1 ± 0.5	1.2 ± 0.7	.23
PMN infiltration	1.5 ± 0. 4	1.8 ± 0.5	.06
Subepithelial edema	1.6 ± 0.6	1.4 ± 0.6	.16
Eosinophil infiltration	1.0 ± 0.5	0.9 ± 0.6	.09
Lymphocyte infiltration	1.4 ± 0.7	1.6 ± 0.8	.35
Submucosal gland hyperplasia	1.4 ± 0.7	1.4 ± 0.6	.07
Goblet cell formation	1.3 ± 0.5	1.3 ± 0.8	.09

Table 2
The histopathologic characteristics between nasal biopsy compared with ethmoidal polyp in patients with asthma

Histologic parameters	Inferior turbinate	Ethmoid polyp	P
Basal membrane thickness	1.5 ± 0.6	1.4 ± 0.8	.1
PMN infiltration	1 ± 0.04	0.6 ± 0.07	.22
Subepithelial edema	1.8 ± 0.6	2.0 ± 0.7	.08
Eosinophil infiltration	1.7 ± 0.8	1.6 ± 1.0	.32
Lymphocyte infiltration	2.4 ± 0.7	2.2 ± 0.7	.3
Submucosal gland hyperplasia	1.6 ± 0.8	1.9 ± 0.6	.076
Goblet cell formation	1.7 ± 0.7	1.7 ± 0.8	.065

In addition, the total inflammatory cell count per high-power field was comparable in the ethmoidal sinus polyp and inferior turbinate specimens in both groups (Tables 1 and 2). On the other hand; there was not a statistically significant difference in the number of 3 inflammatory cell types (eosinophils, PMNs, and lymphocytes) between the 2 anatomical sites in each group ($P > .05$).

4. Discussion

The definition of CRS continues to change. Earlier articles focused on infection as the primary cause, so they put emphasis on the role of the OMU. Hence, endoscopic sinus surgery for opening the OMU was considered as the management for the cases not responding to medical therapy [10-12]. However, it is common to encounter patients with persistent symptomatic CRS despite surgery and patent OMU. In addition, repeated courses of systemic and topical antibiotics can be palliative rather than curative in several CRS cases. This has led researchers to adopt the concept of *CRS* as primarily an inflammatory rather than infectious disease [1,2]. As such, the concept is supported by several reasons. Allergy is common in patients with CRS. Chronic rhinosinusitis might have been accompanied with disease in other regions of the respiratory tract. A classic example of an inflammatory-immunologic disease is Samter's triad (asthma, CRS with nasal polyposis, and aspirin sensitivity). Ultimately, histopathology of surgical specimens from the paranasal sinuses often shows tissue eosinophilia and other features of inflammation.

The use of the term rhinosinusitis rather than sinusitis was based on the fact that sinusitis in most patients is preceded by or accompanied with rhinitis. Such a concept was supported by clinical rather than histopathologic data [6]. There are few studies in the medical records to histologically assess such accompanying. Bhattacharyya [5] addressed the histopathologic basis for the use of the term rhinosinusitis by examining nasal septum and ethmoid sinus specimens. His data noted inflammation at both sites, and he concluded that the use of the term is appropriate. This concept was supported in another survey, which was done by Busaba et al [6]. The middle turbinate was the site for comparison in this study. They

dedicated this site is more relevant because of the close proximity to the ethmoid sinus and its role in the OMU.

In our survey, inflammatory cells including neutrophils, eosinophils, and lymphocyte cells were noted in comparable numbers at inferior turbinate and ethmoid. In addition, basal membrane thickness, subepithelial edema, and submucosal gland hyperplasia as histopathologic characteristics of long-term inflammation in the obviously affected sinus area (ethmoid sinus) was comparable with the apparently healthy nasal mucosa (inferior turbine) in both groups. Our study aimed at further studying the concept of rhinosinusitis by comparing the histopathology of the ethmoidal sinus polyp to that of the ipsilateral inferior turbinate instead of the septum [5] and middle turbinate [6]. Inferior turbinate rather than septum specimen can be more appropriate in such analysis for several reasons. It is more accessible with less morbidity for histologic evaluation of the sinonasal inflammation; because of proximity to OMU, it is more likely affected by the similar condition rather than septum. Comparing with middle turbinate again, it is more accessible with less morbidity for evaluation. In addition, the inferior turbinate does not seem clinically involved in most cases of chronic rhinosinusitis with nasal polyposis; therefore, its microscopic involvement support the term of rhinosinusitis than sinusitis more than septum and middle turbinate.

Our data showed that inflammation in the ethmoid sinus was associated with a commensurate inflammation in the ipsilateral inferior turbinate in patients with and without asthma who suffer intractable CRS. There was a strong correlation between the grades of inflammation in the ethmoid sinus and the ipsilateral inferior turbinate in our patients, and hence, the findings support the concept of rhinosinusitis in these cases.

Our data, like the study of Busaba et al [6], showed a correlation between the total numbers of inflammatory cells and the numbers of specific inflammatory cells at the 2 different anatomical sites; however, the nasal inferior turbinate and ethmoidal sinus appearance were completely different (clinically). Furthermore, we compared 2 groups of patients from the point of histologic characteristics of CRS. Sinus and nasal similarity for microscopic involvement was seen not only in the patients with asthma but also in the cases with isolated polyposis. This finding, consequently, implies greatly on the term of rhinosinusitis rather than sinusitis alone.

5. Conclusion

The term of rhinosinusitis is appropriate in referring to patients with inflammatory paranasal sinus disease. The ethmoid sinus inflammation is accompanied by a simultaneous and commensurate inflammation of the ipsilateral inferior turbinate in patients who undergo surgery for refractory polypoid CRS.

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