Histopathologic Relationship Between Ethmoid Sinus and Ipsilateral Middle Turbinate in Non-Polypose Chronic Sinusitis by FESS

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Abstract Chronic rhinosinusitis (CRS) is a common disease with significant effects on the quality of life. Infection was previously a common cause of rhino sinusitis, while nowadays its main cause is inflammation. Non-polypoid CRS patients who were resistant to medical treatment and underwent endoscopic sinus surgery in Ghaem and Imam Reza hospitals were studied from December 2008 to November 2009. There were 11 males and four females ranging in age from 14 to 57 years with the average age of 32.2. First, samples were taken from the ethmoid sinus and the ipsilateral middle turbinate. Then, histopathologic research on grade of inflammation, mucosal thickness, inflammatory cell count, metaplasia type, and hypersecretion was performed. Fifteen patients were studied. There were positive statistical correlations between inflammation grade, eosinophil counts and plasma cell counts in ethmoid and turbinate; but such a correlation was not found in lymphocyte and neutrophil in two sites. The prominent inflammatory cell in both areas was the same for 11 patients; whereas in other four cases, it was insignificantly different. Positive statistical correlation between the inflammation grades in two sites shows the coexistence of rhinitis and sinusitis; therefore, this proves the correct combination usage of rhinosinusitis. Prominent cells of the samples which were obtained from two places were similar for most patients, so this similarity is a sign of inflammatory process presence in both places. The prominent cells were mostly lymphocytes. There were more lymphocytes than eosinophils in non-allergic patients.

Keywords Middle turbinate · Ethmoid sinus · Chronic sinusitis · Rhinitis · Sinus endoscopy

Chronic rhinosinusitis (CRS) is a common disease with significant effects on quality of life. Chronic sinusitis is a form of sinusitis that lasts longer than 12 weeks. It may or may not include nasal polyposis [1]. Infection used to be known as the leading cause of chronic sinusitis without nasal polyposis CSwNP.¹ Thus, there was a great emphasis on the role of the osteomeatal unit (OMU); moreover, to open OMU, functional endoscopic sinus surgery was considered to be the treatment for CSwNP patients for whom medical treatment was not helpful [2, 3]. It was not unusual that the symptoms of these patients would continue after the operation and OMU opening. Although, repeated courses of systemic antibiotic therapy were palliative, they were not curative. The two mentioned points presented the inflammation instead of infectious disease as the main cause of CSwNP [4, 5]. Allergy is a common problem in chronic sinusitis patients. Most chronic sinusitis patients have another disease in other parts of the respiratory tract. A classic example is an inflammatory immunologic disease called Samter's triad characterized by asthma, chronic sinusitis, polyposis, and sensitivity to aspirin [6].

Anatomical changes in the sinuses and turbinates are the other predisposing factors of chronic sinusitis. The most common anatomical changes occur in the middle meatus, ager nasi cell, middle turbinate, uncinate process, bulla ethmoidalis, Haller cell (orbitoethmoidal cell), Onodi cell (sphenothmoidal cell), and septal deviation at the middle meatus area [7].

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¹ Chronic rhinosinusitis with nasal polyposis.

The usage of the term “rhinosinusitis” rather than “sinusitis” is due to the belief that rhinitis is a major predisposing factor for sinusitis. This idea was proved clinically and based on histopathologic findings of the septum and ethmoid sinus samples [8]. In this research, the reason for using “rhinosinusitis” is evaluated by the comparison between the histopathology of the ethmoid sinus and the middle turbinate instead of the septum.

It is better to study middle turbinate in preference to septum. The middle turbinate is a part of the OMU. The inflammatory mediators which were released from the inflammation of the middle turbinate are the factors for the beginning of the inflammation in the adjacent ethmoid sinus. Besides, the middle turbinate is involved in most cases of nasal polyposis CRS [8].

Materials and Methods

From December 2008 to November 2009, 15 CSwNP patients who were refractory to medical therapy underwent sinus surgery.

Samples were taken from the ethmoid sinus and ipsilateral middle turbinate in all patients. Informed consent was obtained from all subjects prior to any investigations, and this study was approved by the Mashhad University of Medical Sciences ethics committee, Mashhad, Iran. Thirty slides were totally reviewed. The surgical specimens of the ethmoid sinus and the middle turbinate were submitted separately for histopathologic evaluation and were stained by hematoxylin and eosin (H–E) stain. The overall histopathologic severity of inflammation was graded with a five point ordinal scale of 0–4 (normal, very mild, mild, moderate, and severe) by examining the slides under low-power magnification ($\times 40$). High-power magnification ($\times 400$) was used to measure the thickness of the pseudostratified ciliated columnar epithelium and the number of each inflammatory cell type (eosinophils, lymphocytes, plasma cells, and neutrophils). Each epithelial cell diameter of was $5\ \mu$.

Metaplasia and hypersecretion (dilatation of the gland and increase in mucinous secretion) were detected. The measurement of the epithelial thickness and the cell count were carried out at the site of maximal inflammation. The measurements and counts were performed twice on each slide by the same examiner.

Bivariate correlation was analyzed by using Spearman's ρ coefficient to determine the relationship of the inflammation degree between the ethmoid sinus and the ipsilateral middle turbinate specimen. Paired t test was done in order to find out the differences of cell counts and epithelial thickness between the sinus and the ipsilateral middle turbinate specimens. The correlation among cell count for

specific inflammatory cell type, total inflammatory cell count, and epithelial thickness between the paired ethmoid and middle turbinate specimens was calculated with the Pearson correlation coefficient. Statistical significance was set at $P < 0.05$.

Result

Fifteen CSwNP patients, including one with asthma, four with allergic rhinitis and no one with revision sinus surgery were studied. The patients consisted of nine males and six females ranging in age from 14 to 57 years with an average age of 32.2.

The mean inflammation grade in the ethmoid sinus was 2.73 ± 0.961 (range 1–4) and in the ipsilateral middle turbinate was 2.93 ± 0.799 (range 1–4). The significant positive correlation between inflammation grade of ethmoid sinus and middle turbinate (Spearman's ρ coefficient = 0.529, $P = 0.043$) has been shown in Fig. 1.

There was a correlation between the thickness of the columnar epithelium in the ethmoid sinus and middle turbinate (Pearson correlation = 0.620, $P = 0.014$) (Fig. 2).

In the ethmoid sinus samples 28.2% of inflammatory cells were eosinophils (SD = 26.87, range 0–75%) while in middle turbinate samples 34.8% of inflammatory cells were eosinophils (SD = 31.93, range 0–80%), so there was a statistical correlation between the eosinophils cells count in two sites (Pearson correlation = 0.609, $P = 0.016$) (Fig. 3).

Plasma cells count was 13.1% (SD = 7.18, range from 5 to 30%) in the ethmoid sinus, and it was 14.6% (SD = 9.53, range from 0 to 30%) in the middle turbinate.

Fig. 1 Scattered diagram of the relationship between the inflammatory grade in the middle turbinate and ethmoid sinus for 30 paired samples (Spearman's ρ coefficient = 0.529, $P = 0.043$)

Fig. 2 Correlation between a thickness of the columnar epithelium in the ethmoid sinus and middle turbinate (Pearson correlation = 0.620, $P = 0.014$)

Fig. 4 Correlation between the plasma cells count in two sites (Pearson correlation = 0.580, $P = 0.024$)

Fig. 3 Correlation between the eosinophils cells count in two sites (Pearson correlation = 0.609, $P = 0.016$)

Fig. 5 Correlation between the lymphocyte cells count of ethmoid sinus and middle turbinate (Pearson correlation = 0.283, NS)

Consequently, there was a statistical correlation between the plasma cell count in two sites (Pearson correlation = 0.580, $P = 0.024$) (Fig. 4).

There was not any statistical correlation between the lymphocyte cell count of the ethmoid sinus and middle turbinate (Pearson correlation = 0.283, NS). Lymphocyte cell count was 55.0% (SD = 26.99, range from 10 to 90%) in the ethmoid sinus, and it was 48.6% (SD = 27.61, range from 10 to 90%) in the middle turbinate (Fig. 5).

There was not any statistical correlation between the neutrophil cell count in the ethmoid sinus and middle turbinate (Spearman's ρ coefficient = 0.353, NS) (Fig. 6). The correlation between inflammatory cell type in ethmoid sinus and middle turbinate appears in Table 1.

The prominent cell types were lymphocyte and eosinophil in all samples. The cell types were similar in both the ethmoid sinus and middle turbinate for 11 subjects; however, in four subjects they were different in two sites. Two patients had more lymphocytes in the ethmoid sinus than in middle turbinate, and vice versa.

No metaplasia was found in the ethmoid sinus samples, but it was seen in the middle turbinate of 33% of patients. Moreover, hypersecretion was found in the ethmoid sinus and all parts of the middle turbinate samples in 86% of patients.

Discussion

Chronic sinusitis is a common disease which has different etiologies. Some of its predisposing factors are correctable,

Fig. 6 Correlation between the neutrophil cells count in ethmoid sinus and middle turbinate (Spearman's ρ coefficient = 0.353, NS)

Table 1 The correlation between inflammatory cell type in ethmoid sinus and middle turbinate

The inflammatory cell type in ethmoid sinus	The inflammatory cell type in middle turbinate		
	Eosinophil	Lymphocyte	Sum
Eosinophil	3	1	4
Lymphocyte	3	8	11
Sum	6	9	15

and it can be treated by eliminating those factors. The etiology that is responsive to medical therapy, and does not require any surgical treatment, is rhinitis. Thus, rhinitis diagnosis and treatment are the most important steps toward sinusitis treatment. The biopsy which is taken from different areas of the nasal mucosa including septum mucosa, inferior turbinate, and middle turbinate is used to assess rhinitis [9]. The purpose of this research is to evaluate the effects of rhinitis on sinuses; therefore, samples were taken from the mucosa of the middle turbinate that is the nearest area to the sinuses.

The middle and inferior turbinates are histologically different. There are more mucous glands in the middle turbinate, probably due to its function. Serous glands are normally more numerous than mucous acini in both middle and inferior turbinates [10]. Venous sinuses are larger and more numerous in the inferior turbinate; thus, the inferior turbinate plays a primary role in nasal air flow. Owing to this point, and the fact that anatomical changes in the middle turbinate are effective on the osteomeatal complex, partial resection of the middle turbinate does not interfere in nasal air flow [6].

Recent histopathologic studies on the mucous of the nose and sinuses has revealed new information about the

pathogenesis of the sinusitis. The inflammatory cell type can be a clue to the persistence of the symptoms after the surgery. For example, an increase in goblet cells was associated with congestion, rhinorrhea, headache, and cough, but it was not associated with PND and smell abnormalities. Increased subepithelial thickness was associated with PND, but its relationship with congestion, rhinorrhea, and cough was negative. An increase in mast cells was associated with an increase in PND and decrease in rhinorrhea and cough after post-operatively. It had no relationship with nasal itching, sneezing, headache, and smell abnormality. An increase in eosinophils was not related to any increase in symptoms [10].

Previous studies showed that children with a histopathology of sinusitis were different. In contrast to adults, eosinophils were less, the prominent cell was the lymphocyte, basement membrane was thinner, and sub mucosal glands were more numerous. Therefore, it indicates different CRS pathogenesis for different ages [11].

In this study, there was a significant relationship between the inflammation grade in ethmoid sinus and in middle turbinate. This suggests the direct relationship between rhinitis and sinusitis, so the usage of “rhinosinusitis” is definitely correct.

The similarity of the inflammatory cell type in both biopsies of most subjects reveals a common process in two areas, although it was different in some cases. This was probably due to cytokines releasing from the middle turbinate that affect the nearby ethmoid sinus and leads to infiltration of inflammatory cells in the ethmoid sinus. To prove this, it is necessary to do research on cytokines.

In our study, the lymphocyte was the prominent cell in most subjects. This may suggest that in CSwNP, the inflammatory process is caused by lymphocytes. Since the prominent cell in the non-allergic process is the lymphocyte (contrary to the allergic process where the prominent cell is eosinophil), the allergic process has a smaller role as the predisposing factor of sinusitis in this study. More research is needed to evaluate this suggestion. On the other hand, as the inflammatory process was severe in the middle turbinate, partial middle turbinectomy may be beneficial to the patients who have recurrent sinusitis.

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