ARE THERE ANY CORRELATIONS AMONG HISTORIC, RADIOLOGIC, AND CYTOPATHOLOGIC FINDINGS IN NON-ALLERGIC CHRONIC RHINOSINUSITIS WITHOUT NASAL POLYPOSIS?

By

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Summary

***Purpose**: To investigate any correlations among cytopathologic, radiologic, and historic findings in non-allergic chronic rhinosinusitis without nasal polyposis.*

***Materials and Methods:** This prospective study was done on 40 adult patients who had undergone functional endoscopic sinus surgery due to chronic rhinosinusitis. Symptom, nasal smear, paranasal computed tomography, as well as histopathologic findings of uncinate process, anterior ethmoid cells, and ethmoidal infundibulum were scored. Correlations were analysed among symptom, radiologic, and cytopathologic scores.*

***Results**: While the symptom scores of patients with chronic rhinosinusitis were positively correlated with only nasal smear scores, it was not correlated with computed tomography and histopathologic scores. On the other hand, radiologic scores were correlated with tissue eosinophils scores of uncinate process, anterior ethmoidal cells, and ethmoidal infundibulum*

***Conclusions**: The correlation of symptom score to nasal smear score in chronic sinusitis may be an evidence for the positive relationship symptoms and acute inflammation. The correlation of radiologic score to eosinophilia scores of uncinate process, anterior ethmoidal cells, and infundibulum may signify the importance of tissue eosinophils in chronic sinusitis.*

***Key words**: Rhinosinusitits, nasal polyposis, non-allergic rhinosinusitis.*

Introduction

Although rhinosinusitis is a common clinical problem in general medical practice all over the world, the clinical diagnosis of rhinosinusitis is very challenging and far from accurate. The current definition of chronic rhinosinusitis (CRS) is not evidence-based but is based principally on subjective data, incorporating the use of major and minor symptoms (history) and signs that have been present for > 12 weeks.[1,2] Because of the inherent uncertainty associated with its diagnosis, more objective tools have been sought. For this reason, the use of computed tomography scans has become a useful adjunct in the diagnosis and management of this condition. One of the other objective tools in diagnosis of rhinosinusitis is nasal endoscopy; it can provide objective data regarding the condition of nasal mucosa and the presence of fluid or polyps.[3] We have reported previously that nasal smear could be used in the diagnosis and treatment follow-up of acute maxillary sinusitis.[4] The aim of this study conducted was to find out any correlations among cytopathologic, radiologic, and historic findings in non-allergic chronic rhinosinusitis without nasal polyposis.

Patients and Methods

This study was done on 40 adult patients who underwent functional endoscopic sinus surgery (FESS) due to CRS, who had insufficient clinical response to medical treatment (at least 4 weeks with antibiotics and 12 weeks with topical steroids) prospectively. Patients with nasal polyposis, allergic rhinosinusitis, cystic fibrosis, asthma (bronchial or triad), and had prior nasal and paranasal surgery were excluded from this study. Ages, sex, durations of sinusitis and smoking of them were noted. Clinical evaluation was done according to major and minor symptoms and signs (Table 1). Symptom scores were obtained by scoring major symptom two points and minor symptom one point.

Major Symptoms and signs **(2 points each)**	**Minor symptoms and signs** **(1 point each)**
Nasal obstruction	Headache
Nasal discharge	Cough
Post nasal Drainage	Halithosis
Facial pain/pressure	Dental pain
Hyposmia/anosmia	Earache

Table 1. *Major and minor symptoms and signs used in the definition and diagnosis of CRS.*

Computerized coronal tomography (CT) scans of the paranasal sinuses were undertaken for all patients before *2-3* days of surgery. One radiologist unaware of patients' clinic data reviewed all CT scans. The extent of disease in the CT scans was scored according to both Lund-Mackay (L-M) and Gliklich-Metson (G-M) CT staging systems.[5,6] Each side was scored individually, and the total possible score was 12 (all together, for both sides, 24) on the L-M staging system. Each side was scored individually and the highest possible total score was 4 points on the G-M staging system.

Nasal smears were obtained by port-cotton from the middle meatus on the same side of CRS. Scoring of nasal smear was done according to the average neutrophil number in per high-power field (0=0, 1=1 point, 2-5=2 points, 6-19=3 points, and 20-above 4 points)[11].

All FESSs were performed under local anesthesia with premedication according to Messerklinger technique. In twenty-eight of 40 patients, FESS were performed bilaterally and the remaining patients were performed unilaterally. Sixty-eight biopsy specimens (mucosa and piece of bone) from each of the uncinate process, anterior ethmoid cells, and ethmoidal infundibulum; 36 specimens from each of frontal recess and posterior ethmoid cells; and 4 specimens from sphenoid sinus were obtained. However, histopathologic findings of uncinate process, anterior ethmoid cells, and ethmoidal infundibulum were evaluated for this study. First, pieces of bone were decalcified and then all specimens were embedded in paraffin blocks, serially cut into 5µm-thick sections, and put on glass slides. These sections from each region were stained with hematoxylin-eosin (H&E) and were examined with light microscope under high-power magnification (X400). A pathologist unaware of patients' clinic data investigated parameters of inflammation *in* the sections as seen Table 2. The presence of each histopathologic parameter was scored as one point and sum pathologic score was counted. In addition to, if oesinophil in the lamina propria were detected they were classified as follows: 1-2; minimum (1 point), *3-10;* mild (2 points). 11-20; intermediate *(3* points), and 21-above; severe (4 points). Mean histopathologic scores were used for patients with bilateral CRS.

In this study, correlations between the symptomatic, radiologic, and cytopathologic parameters were investigated with each other. Spearman correlation test was used in statistical analysis. An *r* value of 0-0.25 denotes no, an *r* of 0.26-0.50 denotes weak, an *r* of 0.5 1-0.75 good or strong, and an r> 0.765 denotes excellent or very strong correlation. Mann-Whitney U test was used for comparisons.

Surface epithelial desquamation	1	0
Submucosal g1anc11ar hyperplasia	1	0
Polypoid mucosa	1	0
Osteitis or osteomyelitis	1	0
Edema	1	0
Hypertrophy of Goblet cells or cystic dilatation	1	0
Lymphocyte	1	0
Plasma cell	1	0
Fosinophil	1	0
Neutrophil	1	0

Table 2. Histopathologic parameters of CRS

Results

Forty patients (28 male and 12 female) aged 17-50 years (mean age 28.07 ±9.16 years) were included in this study. While 4 patients had 5 points that was the

lowest symptom score, 5 patients had 13 points that was the highest symptom score. Eight patients had 4 points that was the lowest L-M CT score and also, a patient had 22 points that was the highest L-M CT score. On the other hand, the lowest and highest G-M CT scores were respectively one and 4 points; 10 patients had one point and 8 patients had 4 points. Nine patients had 3 points and 31 patients had 4 points in view of nasal smear scores. The histopathologic scores of uncinate process, anterior ethmoid cells, and ethmoidal infundibulum were respectively ranged between 3 and 9, 2 and 9, and 3 and 7 points. Tissue eosinophilia as a histopathologic parameter was detected in the uncinate processes of 24 of 40 patients. Ten patients had one point and 2 patients had 4 points according to tissue eosinophil severe score in uncinate process (Table 3).

Anatomic Regions	**Number of patients**	**1**	**2**	**3**	**4**
		+ eosinophils Point			
Uncinate process	24 patients	10	*4*	*8*	2
Anterior ethmoid cells	30 patients	16	3	9	2
Ethmoidal infundibulum	23 patients	6	12	5	0

***Table** 3. Severity scores of tissue eosinophils according to anatomic region.*

Positive correlations of patients were given in Table 4. The symptom scores of patients with CRS were correlated positive with only nasal smear scores (Table 4; no.1). L-M CT scores were correlated well with tissue eosinophil scores of uncinate process (Table 4; no.5).

Discussion

The definition of chronic rhinosinusitis is based on subjective information, and it is important to reveal if this data is correlated with objective findings obtained with endoscopy, nasal smear and CT. Since patients meeting the definition of chronic rhinosinusitis, a symptom-based definition, several weeks of antibiotic treatment is prescribed rather than surgery. New parameters to guide the prospective treatment strategy must be developed in order to build up an evidence based, objective approach. Therefore, the correlation between these parameters should be searched.

L-M CT scoring system is used for evaluation of sinus mucosal thickening, extent of sinus opacification, and the ostieomeatal complex is whether obstracted or not [5]. Another CT scoring system is G-M grading system, which is designed according to the unilateral or bilateral sinus pathology and anatomic variations on CT findings.[6] These systems are commonly used and approved systems in reporting extent of sinus disease and treatment outcomes. [7-11] In this study, we used these two scoring systems in evaluating disease on CT. We found an excellent correlation between L-M and G-M CT scores in this study. This result confirmed that the two

CT staging systems are useful to detect the extent of disease in the patients with CRS.

There is not a consensus in the literature regarding correlation between sino-nasal symptoms and CT scan evidence of paranasal sinus disease. Kenny et al[10] reported that except for the severity of facial pain or pressure and headache, the severities of five symptoms (fatigue, lack of a good night's sleep, nasal discharge or postnasal drip, stuffy blocked nose and decreased sense of smell) were found to be correlated with severity of diseases on CT scan. Arongo and Kountakis[7] found statistically significant difference between the symptom scores of patients with positive CT findings and negative CT findings. Although they detected major, minor and overall symptoms scores were correlated with the extent of the disease on CT, the correlation in each patient failed to achieve statistical significance.

Bhattacharya et al[12] used the Sino-Nasal Outcome test (SNOT)-20 symptom survey and LM CT scoring system in their 221 patients. They did not find any correlation between symptom severity and CT score. Steward et al.[7] compared patients with chronic rhinosinusitis using both the chronic rhinosinusitis survey and the SNOT-20 survey for symptom evaluation and the Harvard and Lund systems for CT scoring and they found no significant correlation.

On the other hand, Mudgil et al.[13] reported no correlation between localized facial and/or head pain and findings on CT. They suggested that findings on CT sinus imaging do not routinely correlate with patients' presumed sino-nasal symptoms of facial and/or head pain. The diagnosis ol rhinosinusitis is clinically based, sinus CT studies should probably be reserved for patients who have symptoms additional to pain alone and/or physical findings that also support paranasal sinus disease. This study was performed on selected patients with - histopathologically confirmed- chronic rhinosinusitis. All patients underwent complete coronal paranasal CT imaging. The CT score was expected to be higher when the sum of symptom scores is high. Although there was evidence of sinus disease on CT for all the patients, we did not find any statistically significant correlation between the sum of symptom scores and neither LM, nor GM CT scores.

In one of the recent studies, Kutluhan et al[16] demonstrated that neutrophils in thc nasal smear of patients with acute maxillary sinusitis could give clues in the diagnosis and followup. In this study, inflammatory cells (lymphocyte, eosinophils, plasma cell, neutrophils, mast cell) seen in histopathologic findings of chronic rhinosinusitis were also investigated in nasal smears of the same patients. While lymphocyte, plasma cell, mast cell and basophils were totally absent in nasal smears, a few eosinophils were encountered in 8 of 40 patients. Bosinophils detected in the nasal smears were insufficient to be significant for statistical studies, On the other hand, neutrophils were seen in the nasal smears of all patients. Thirty- one of overall patients scored as 4 points and 9 patients scored as 3 points according to neutrophils count. There was a weak correlation between symptom scores and nasal smear scores in this study. This

finding shows that some patients may be at the acute or subacute stage inflammation at operation time. Therefore, for chronic sinusitis patients who are planned to undergo surgical treatment, nasal -smears may be a good measure for duration and dose of antibiotic treatment.

Chronic rhinosinusitis is histopathologically characterized with mucosal thickening, destruction of the epithelial layer, goblet cell hyperplasia, subepithelial fibrosis, and persistent inflammation)[17,18] Lymphocytes and activated eosinophils are prominent more than neutrophils in the sinus mucosa of patients with chronic rhinosinusitis[19]. In this study, samples of uncinate process, anterior ethmoid cells, and ethmoidal infundibulum obtained during FESSs performed on 40 patients with CRS were examined histopathologically. Although osteitis-osteomyelitis is not demonstrated in any sections of any regions mentioned above, at least a few pathologic mucosal changes of CRS were seen in all sections. Histopathologic scores of uncinate process correlated weakly with anterior ethmoid cells and ethmoidal infundibulum and there was no correlation between histopathologic scores of anterior ethmoid cells and ethmoidal infundibulum. This result suggests that CRS is an ostiomeatal complex disease. On the other hand, there were no significant correlations between symptom scores and histopathologic scores of uncinate process, anterior ethmoidal cells and infundibulum. Presumably, the formation of symptoms is induced by some other factors rather than histopathologic changes.

A lot of studies are reported about correlations between CT scan findings and histopathologic changes in the paranasal sinuses of patients with CRS. Although the degree of mucosal changes on CT scan findings has failed to correlate with patient-based reports of paranasal Sinus symptoms, some radiologists believe that radiographic changes may he demonstrative of inflammatory disease within the sinuses. Many CT staging systems (LM5, GM6 and Jorgensen 20)) for CRS have been developed as a method to quantify sinus disease.

The greater the inflammation in the histologic specimen, the more edematous and thickened the sinus mucosa would be in the gross specimen. Biedlingmaier and Trifillis[21] compared CT scan and electron microscopic findings on harvested middle turbinate from patients with CRS. They found that as the severity of disease as demonstrated by CT scan increased, mucosal changes progress. Baroody et a1[22] noted a correlation between severity of disease on CT scan and blood serum 1gE levels. But Cousin et a1[23] reported that their study did not support the theory and they suggested that the severity of sinus disease based on preoperative CT scan does not correlate with the histologic degree of disease. Goldwyn et al 24 also found no significant correlation between cell count and extent of disease as demonstrated by CT scan. We did not find any correlation between L-M and G-M CT scores and histopathological scores of uneinate process, anterior ethmoidal cells, and infundibulum, either. Consequently, we can say that

each inflammation may not lead to edema and mucosal thickening.

It is thought that tissue eosinophils may have a central role in the pathogenesis of chronic rhinosinusitis. Several authors have found that tissue eosinophilia is more prevalent in the mucosa of patients with CRS than controls 18, 25. It is known that eosinophils influence the mucosal response to allergens and infection as a source of immunomodulators and cellular byproducts [26] In this study, tissue eosinophilia in uncinate process, anterior etmoid cells, and ethmoidal infundibulum were not detected in all patients (Table 3). Therefore, tissue eosinophils is not the only pathogenetic factor by itself in CRS without nasal polyposis. Even though tissue eosinophilia have not been shown to be correlated with symptom and histopathologic scores, it has been correlated with L-M and G-M CT scores. These results may show that the more the tissue eosinophilia. the more extensive is the disease on CT scans. Radiologically extensive CRS in CT scans may possibly have a high number of tissue eosinophils.

Conclusions - The correlation of symptom score to nasal smear score in chronic sinusitis may be an evidence for the positive relationship symptoms and acute inflammation. The correlation of radiologic score to eosinophilia scores of uncinate process, anterior ethmoidal cells, and infundibulum may signify the importance tissue eosinbphils in chronic sinusitis.

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Table 4. Positive correlations among findings of chronic rhinosinusitis.

No.	Correlations	r values	Significance
1.	Between clinic symptom and nasal smear score	.33785	Weak
2	Between L-M and G-M CT scores	.872	Excellent
3	Between L-M CT scores and histopathologic scores of anterior ethmoid cells	.39675	Weak
4	Between L-M CT scores and histopathologic scores of uncinate process	.36167	Weak
5	Between L-M CT scores and tissue eosinophil scores of uncinate process .	.560	Good
6	Between L-M CT scores and tissue eosinophil scores of anterior ethmoid cells	.455	Weak
7	Between L-M CT scores and tissue eosinophil scores of ethmoidal infundibulum	.364	Weak
8	Between G-M CT scores and eosinophil scores of uncinate process tissue.	.415	Weak
9	Between G-M CT scores and eosinophil scores of anterior ethmoid cells tissue	.288	Weak
10	Between G-M CT scores and tissue eosinophil scores of ethmoidal infundibulum	268	Weak
11	Between cytopathologic scores of uncinate process and anterior ethmoid cells	.493	Weak
12	Between histopathologic scores of uncinate process and ethmoidal infundibulum .	.316	Weak
13	Between histopathologic scores of uncinate process and tissue eosinophil scores of uncinate process	.562	Good
14	Between histopathologic scores of uncinate process and tissue eosinophil scores of anterior ethmoid cells	.416	Weak
15	15 Between histopathologic scores of anterior ethmoid cells and tissue eosinophil scores of anterior ethmoid cells	.5212	Good
16	16 Between histopathologic scores of anterior ethmoid cells and tissue eosinophil scores of uncinate process	419	Weak
17	Between tissue eosinophils scores of uncinate process and anterior ethmoid cells	.837	Excellent
18	Between tissue eosinophils scores of uncinate process and ethmoidal infundibulum	.627	Good
19	Between tissue eosinophil scores of anterior ethmoid cells and ethmoidal infundibulum	.574	Good