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The correlation of clinical measures with the histopathological findings in nasal polyposis

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Abstract

Objective: The aim of this study was to outline the histopathological findings of nasal polyposis and to investigate whether these findings were associated with the severity of the disease and co-existing morbidities as well as hematological parameters.

Methods: Seventy-seven nasal polyposis (52 male, 25 female; mean age: 46.99±13.27 years) patients who underwent endoscopic sinus surgery between 2007 and 2011 were included in the study. Data was extracted from medical files and endoscopy scores, and Lund-Mackay Computed Tomography scores, Nasal Obstruction Symptom Evaluation (NOSE) scales, presence of allergy and asthma, and blood eosinophil levels were noted. Correlation of this data with histopathological findings (such as basement membrane thickness, goblet cell hyperplasia, subepithelial edema, submucous gland formation, eosinophilic infiltration, lymphocytic infiltration and polymorphonuclear leukocyte infiltration) was analyzed.

Results: Analysis of our findings yielded that the only statistically significant finding was the correlation of eosinophilic infiltration with the blood eosinophil level ($p<0.01$). No other statistically significant differences were found between histopathological findings and accompanying clinical or hematological parameters under investigation.

Conclusion: Results of the current study have shown that histopathological features of nasal polyposis do not exhibit correlation with the severity or extent of the disease.

Keywords: Nasal polyposis, histopathology, eosinophilia, severity, correlation.

Özet: Nazal polipoziste histopatolojik bulgular ile klinik ölçütler ile arasındaki ilişki

Amaç: Bu çalışmada nazal polipozisli hastalarda histopatolojik bulguların detaylı olarak tanımlanarak bu bulguların hastalığın şiddeti ve astım, alerji ve kan eozinofil düzeyi gibi bazı eşlik eden faktörlerle ilişkisinin araştırılması amaçlanmıştır.

Yöntem: Çalışmada 2007–2011 yılları arasında endoskopik sinüs cerrahisi uygulanan yetmiş-yedi nazal polipozisli hastanın (52 erkek, 25 kadın; yaş ortalaması: 46.99±13.27) verileri incelenmiştir. Yapılan retrospektif değerlendirmede endoskopik skorları, Lund-Mackay bilgisayarlı tomografi skorları, nazal obstrüksiyon semptom değerlendirme skalaları, alerji ve astım varlığı ve kan eozinofil düzeyleri kaydedilmiştir. Bu veriler histopatolojik bulgularla (bazal membran kalınlığı, goblet hücre hiperplazisi, subepitelyal ödem, submukozal gland formasyonu, eozinofilik infiltrasyon, lenfositik infiltrasyon ve polimorfonükleer infiltrasyon) karşılaştırılmıştır.

Bulgular: Bulgular değerlendirildiğinde eozinofil infiltrasyonu ve kan eozinofil düzeyleri arasında istatistiksel açıdan anlamlı bir ilişki saptanmıştır ($p<0.01$). Bunun dışında histopatolojik bulgular ve eşlik eden faktörler arasında herhangi bir anlamlı bağlantı saptanmamıştır.

Sonuç: Çalışmamızın bulgularına bakıldığında nazal poliplerin histopatolojik özellikleri ile hastalığın şiddeti, yaygınlığı veya eşlik eden klinik veya hematolojik parametrelerle anlamlı bir ilişkili bulunmamıştır.

Anahtar sözcükler: Nazal polipozis, histopatoloji, eozinofili, şiddet, korelasyon.

Nasal polyps which are hyperplastic swellings of the nasal mucous membranes are the most common cause of nasal masses located in the nasal cavity. Nasal polyposis (NP) is a multifactorial disease that affects 2–4% of the general

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population.[1,2] Although there are many studies investigating the etiopathogenesis of NP, the exact reason has not been known yet.

A complete evaluation of a patient with NP must include some clinical measures such as severity of nasal obstruction, endoscopic and radiological evaluation as well as presence of allergy and asthma. Although many studies have been conducted about the histopathology of the NP, to the best of our knowledge, none of them has evaluated the relationship between histopathological changes with the allergy, asthma and some other accompanying factors. Since nasal polyps may be associated with many diseases, histological features may vary according to these factors and clinical measures.

In this study, we aimed to investigate histopathological findings in nasal polyps of patients with NP and to investigate the relationship between histopathological features of NP and disease severity as well as the concomitant clinical and hematological factors.

Materials and Methods

The study group consisted of 77 patients with nasal polyposis who underwent endoscopic sinus surgery (ESS) at a tertiary care center between 2007 and 2011. The study protocol was reviewed and approved by the research ethical committee in Fatih Sultan Mehmet Education and Research Hospital.

Nasal polyposis was diagnosed by endoscopic findings and computerized tomography (CT) views. Patients with sinonasal malignancy and antrochoanal polyps were excluded from the study.

Outcome Parameters

Allergy and asthma: Skin prick tests with commercial extracts of the main airborne allergens were performed. Blood eosinophil counts were obtained through routine blood analysis. Patients were consulted to a chest disease specialist for the diagnosis of asthma by means of clinical symptoms, physical findings and pulmonary function tests.

Nasal symptom score: Nasal obstruction was evaluated by Nasal Obstruction Symptom Evaluation (NOSE) scale.[3]

Polyp size: Endoscopic score of polyposis was calculated from 0 to 3 for each nasal cavity: 0, no polyp; 1, mild polyposis limited to middle meatus; 2, moderate polyposis reaching below middle concha; 3, diffuse polyposis (complete involvement of ipsilateral nasal cavity).[4]

Radiological score: Paranasal sinus CT scans were performed routinely in all patients and staging was made according to the Lund-Mackay score system as follows:[5] 0, no opacity; 1, partial opacity; and 2, total opacity for each sinuses. The osteomeatal complex scores 0 for no obstruction or 2 when obstructed. The total score of the system was 24 bilaterally.

Endoscopic sinus surgery (ESS) was performed using standard technique under general anesthesia. Patients had received at least 8 weeks of topical nasal corticosteroid sprays in addition to irrigation of the nose with isotonic saline. Systemic glucocorticoid use prior to the ESS was not a standard treatment protocol in our clinic. During ESS, nasal polyp tissue was obtained from each patient and stained with hematoxylin-eosin. In order to avoid bias and to standardize the findings, the specimens obtained previously were evaluated by the same pathologist again. Light microscopy was used for evaluation and scoring of the following histopathological characteristics:[6,7]

Basement membrane thickening: At a magnification of x400, the thickest part of the basement membrane was measured by the ocular micrometer of Olympus CX41 microscope. A score was assigned according to the thickness: <9 µm=0, 10–19 µm=1, 20–29 µm=2, ≥30 µm=3.

Goblet cell hyperplasia: At a magnification of x400, a score was assigned according to the number of goblet cells visible: 0 (<3 cells); 1 (3–10 cells); 2 (11–20 cells); or 3 (>20 cells).

Subepithelial edema: At a magnification of x100, a score was assigned according to the degree of subepithelial edema: 0 (none); 1 (mild); 2 (moderate); or 3 (marked).

Submucous gland formation: At a magnification of x100, a score was assigned according to the number of submucous glands visible in a section: 0 (<3 glands); 1 (3–10 glands) or 2 (>11).

Eosinophil infiltration: At a magnification of x400, the number of eosinophils present within epithelial cells and in the submucosa was scored as: 0 (none); 1 (1–2 eosinophils); 2 (3–10 eosinophils); 3 (>11).

Lymphocyte infiltration: At a magnification of x400, the number of lymphocytes present in the submucosa was scored as: 0 (<20 lymphocytes); 1 (21–50 lymphocytes); 2 (51–80 lymphocytes); 4 (>120 lymphocytes).

Polymorphonuclear lymphocyte (PMNL) infiltration: At a magnification of x400, the number of PMNs present in submucosa was scored as follows: 0 (none); 1 (one or two PMNs); 2 (three to 10 PMNs); 3 (>10 PMNs).

Statistical Analyses

All statistical calculations were performed with NCSS 2007 and PASS 2008 Statistical Software (NCSS, Kaysville, UT, USA). In addition to standard descriptive statistical calculations (mean, median, and standard deviation), the Kruskal-Wallis Test and the one-way ANOVA test was used in the assessment of parameters according to groups. The Student t test and the Mann-Whitney U test were used for the evaluation of differences between two groups. The statistical significance level was established at $p<0.05$ and confidence intervals were 95 percent.

Results

General Features

The mean age of patients was 46.99±13.27 years (range: 17 to 71 years). 32.5% (n=25) of the patients were female subjects whereas 67.5% (n=55) of the patients were male subjects. The range of operation numbers for the patients included in the study varied from 1 to 12 (1.82±1.84). 85.7% (n=66) of these patients had bilateral nasal polyps, 6.5% (n=5) of them had in the right nasal cavity and 7.8% (n=6) of them had only in the left side.

Clinical Features

Allergy and asthma: 32.5% (n=25) of patients had asthma but 67.5% (n=52) of the patients were not asthmatic. Only 9.1% (n=7) of the patients had aspirin intolerance whereas 90.9% (n=70) of them did not have aspirin intolerance. Allergy test was positive for 27.3% (n=21) of patients, but negative for 72.7% (n=56) of them. The blood eosinophil levels ranged from 0 to 1.3 (0.325±0.26) and average blood eosinophil percentages were ranging between 0 and 16 (4.36±3.29).

Nasal symptom score: The NOSE score of the cases was ranging between 5 and 20 (13.06±3.31).

Polyp size: 85.7% (n=66) of the patients had grade 1 polyp, 6.5% (n=5) of them had grade 2 polyp and 7.8% (n=6) had grade 3 polyp according to endoscopic polyp scoring.

Radiologic score: According to the Lund and Mackay CT grading system the CT scores ranged from 4 to 24 (18.64± 5.64).

Histopathological Changes

Distribution of histopathological findings was reported in Table 1. Basal membrane thickening, subepithelial edema and intense eosinophil infiltration were demonstrated in the Figs. 1–3. These histopathologic changes were compared with CT and NOSE scores, blood eosinophil level, allergy and asthma conditions one by one (Tables 2–7).

Table 1. Distribution of histopathologic characteristics.

		n
Basal membrane thickness	None	23 (25.8)
	Mild	52 (58.4)
	Moderate	11 (12.4)
	Marked	3 (3.4)
Goblet cell hyperplasia	<3	24 (27.0)
	3 – 10	32 (36.0)
	11 – 20	19 (21.3)
	>20	14 (15.7)
Subepithelial edema	None	1 (1.1)
	Mild	23 (25.8)
	Moderate	51 (57.3)
	Marked	14 (15.7)
Submucosal gland formation	<3	41 (46.1)
	3 – 10	35 (39.3)
	>11	13 (14.6)
Eosinophil infiltration	None	15 (16.9)
	1 – 2	33 (37.1)
	3 – 10	13 (14.6)
	>11	28 (31.5)
Lymphocyte infiltration	<20	21 (23.6)
	21 – 50	42 (47.2)
	51 – 80	7 (7.9)
	81 – 120	14 (15.7)
	>120	5 (5.6)
PMNL infiltration	None	16 (16.9)
	1 – 2	43 (48.3)
	3 – 10	26 (29.2)
	>10	5 (5.6)

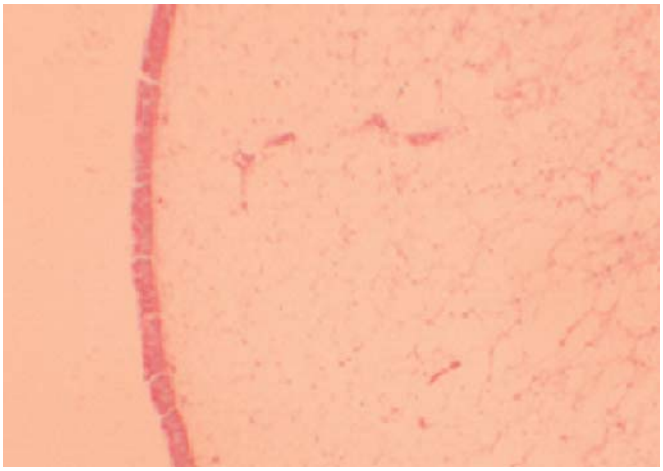

Fig. 1. Marked basal membrane thickening (arrow) (HE x400).

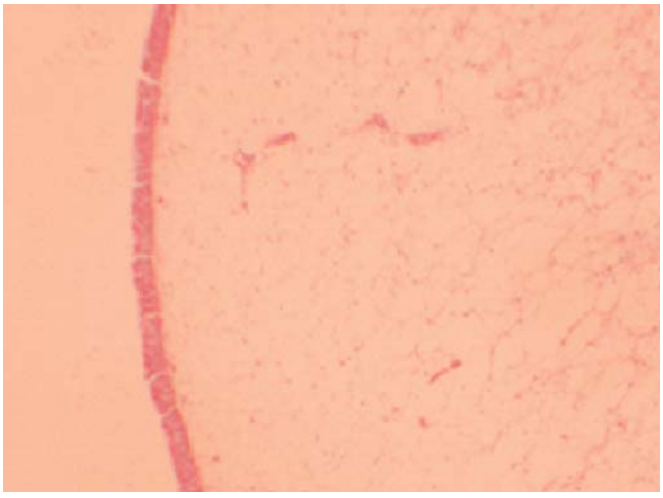

Fig. 2. Supepithelial edema (HE x40).

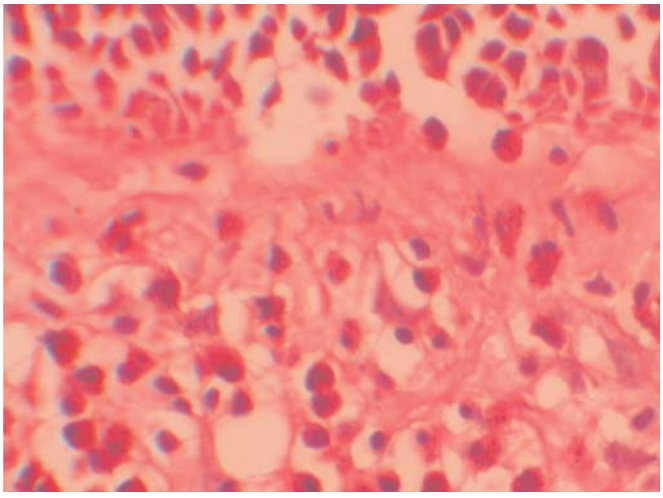

Fig. 3. Intense eosinophil infiltration (HE x400).

The comparison of basal membrane thickness, goblet cell hyperplasia, subepithelial edema, submucosal gland formation, lymphocyte infiltration and PMNL infiltration with BT and NOSE scores, blood eosinophil level, allergy and asthma displayed statistically no significant difference (p>0.05) (Tables 2–7).

The assessment of eosinophil infiltration according to BT and NOSE scores, allergy and asthma also revealed statistically no significant difference (p>0.05). However, when we evaluated tissue eosinophil infiltration with blood eosinophil level, there was a statistically significant difference (p<0.01) (Table 6).

Discussion

In the literature, there are many publications focusing on the degree of symptoms, endoscopic scores, CT findings of disease and presence or absence of allergy and asthma in patients with chronic rhinosinusitis and NP.[2,7,8] However, studies investigating the correlation of these aforementioned issues with histopathology of nasal polyps are scarce. In this study, we investigated main histopathological features of nasal polyp tissues in order to seek any correlations between histopathological features and clinical measures, severity of the disease and co-existent morbidities.

Table 2. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to basal membrane thickening.*

		Basal membrane thickening			p value
		None (n=23) mean±SD	Mild (n=52) mean±SD	Moderate-Marked (n=14) mean±SD	
CT score		17.61±5.66	19.58±5.57	20.07±4.62	0.285
NOSE		12.35±3.20	14.00±3.26	13.43±3.41	0.136
Blood eosinophil‡		0.31±0.29 (0.30)	0.31±0.19 (0.30)	0.38±0.35(0.20)	0.783
		n (%)	n (%)	n (%)	p value†
Allergy	Present	6 (26.1)	14 (26.9)	3 (21.4)	0.916
	Absent	17 (73.9)	38 (73.1)	11 (78.6)	
Asthma	Present	5 (21.7)	12 (23.1)	3 (21.4)	0.987
	Absent	18 (78.3)	40 (76.9)	11 (78.6)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test.

Table 3. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to goblet cell hyperplasia* *(According to goblet cell hyperplasia in <3, 11–20 and >20 groups due to the limited number of findings CT score groups were not assessed).*

		Goblet cell hyperplasia				p value
		<3 (n=24) mean±SD	3–10 (n=32) mean±SD	11–20 (n=19) mean±SD	>20 (n=14) mean±SD	
NOSE		12.46±3.69	14.50±2.99	13.11±3.60	13.43±2.41	0.133
Blood eosinophil‡		0.31±0.27 (0.25)	0.26±0.17 (0.20)	0.44±0.33 (0.30)	0.31±0.21 (0.30)	0.191
		n (%)	n (%)	n (%)	n (%)	p value†
Allergy	Present	5 (20.8)	9 (28.1)	4 (21.1)	5 (35.7)	0.720
	Absent	19 (79.2)	23 (71.9)	15 (78.9)	9 (64.3)	
Asthma	Present	6 (25.0)	6 (18.8)	6 (31.6)	2 (14.3)	0.618
	Absent	18 (75.0)	26 (81.3)	13 (68.4)	12 (85.7)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test.

Goblet cells can be found in different densities on the same type of epithelium. Air flow, different epithelial thickness, age and growth rate of polyps, infections and allergies may give rise to such differences in density.[9] Ardehali et al.[7] founded that not only goblet cell hyperplasia but also basement membrane thickening are chronic inflammatory reactions and these characteristics were more obvious in patients with polypoid sinusitis and asthma. Nevertheless, it was reported that goblet cell density is not statistically different in people with allergy.[9] Similar to this report, we did not come across any remarkable difference in terms of goblet cell hyperplasia and allergy. In addition, there was statistically no significant correlation between goblet cell hyperplasia and endoscopic or radiological extent of the disease, symptom scores and asthma. Alterations in the thickness of the basement membrane were insignificant and did not display any association with these accompanying factors.

When compared with nasal mucosa, capillary permeability was higher in the submucosa of polyp tissue reminding the formation of excessive submucosal edema. There are few vessels in submucosa of polyps indicating a slow reabsorption of the edema fluid. Another important factor in the occurrence of edema is the passive and slow lymphatic flow.[10] In our study, the subepithelial edema was not associated with the extent of the disease.

Table 4. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to subepithelial edema.*

		Subepithelial edema			p value
		Mild (n=24) mean±SD	Moderate (n=51) mean±SD	Marked (n=14) mean±SD	
BT score		18.58±4.80	19.61±5.68	18.43±6.02	**0.657**
NOSE		12.83±3.51	14.06±3.19	12.50±3.15	**0.157**
Blood eosinophil‡		0.34±0.23 (0.30)	0.30±0.24 (0.30)	0.34±0.31 (0.25)	**0.731**
		n (%)	n (%)	n (%)	p value†
Allergy	Present	6 (25.0)	14 (27.5)	3 (21.4)	0.896
	Absent	18 (75.0)	37 (72.5)	11 (78.6)	
Asthma	Present	5 (20.8)	10 (19.6)	5 (35.7)	0.430
	Absent	19 (79.2)	41 (80.4)	9 (64.3)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test.

Table 5. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to submucosal gland formation.*

		Submucosal gland formation			p value
		<3 (n=41) mean±SD	3–10 (n=35) mean±SD	>11 (n=13) mean±SD	
CT score		18.83±6.12	19.66±4.61	18.77±5.79	0.782
NOSE		13.90±3.48	13.29±3.01	12.69±3.59	0.471
Blood eosinophil‡		0.28±0.18 (0.30)	0.34±0.24 (0.30)	0.41±0.40 (0.20)	0.625
		n (%)	n (%)	n (%)	p value†
Allergy	Present	8 (19.5)	10 (28.6)	5 (38.5)	0.355
	Absent	33 (80.5)	25 (71.4)	8 (61.5)	
Asthma	Present	9 (22.0)	9 (25.7)	2 (15.4)	0.744
	Absent	32 (78.0)	26 (74.3)	11 (84.6)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test.

The cellular component of nasal polyps consisted of eosinophils, neutrophils, lymphocytes, plasma cells, macrophages, and mast cells. The density of these cells varies between polyps, and even in different parts of the same polyp and this is in accordance with the dynamic process of polyps.[9,11]

In recent years, owing to the proofs on the release of inflammatory mediators and cellular features, a better insight has been possible on the pathogenesis of NP. Eosinophils are the most frequently studied cells among the cellular elements of nasal polyps. Currently, in addition to NP patients, eosinophils are understood to be the main actor of mucosal inflammation in chronic rhinosinusitis. Therefore, eosinophils have drawn all the attention with the vast majority of histological and immunohistochemical studies focusing on these cells.[11]

Several studies have put forward the correlation between the severity of the disease and tissue eosinophilia. In a study conducted on 223 Japanese patients with chronic rhinosinusitis, mucosal eosinophilia was found in 59.6% of the cases, and mucosal eosinophilia showed to result in higher incidence of recurrence of polyps.[12] In another study, tissue eosinophilia was found to correlate significantly with clinical staging and tends to be higher in

Table 6. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to eosinophil infiltration.*

		Eosinophil infiltration				p value
		<2 (n=15) mean±SD	3–10 (n=33) mean±SD	11–30 (n=13) mean±SD	>30 (n=28) mean±SD	
CT score		17.87±6.77	17.64±5.81	20.69±3.88	20.89±4.40	0.063
NOSE		13.13±3.38	13.21±3.66	14.00±3.22	13.75±2.99	0.833
Blood eosinophil‡		0.33±0.35 (0.20)	0.23±0.16 (0.20)	0.41±0.21 (0.40)	0.38±0.26 (0.30)	0.004**
		n (%)	n (%)	n (%)	n (%)	p value†
Allergy	Present	4 (26.7)	5 (15.2)	2 (15.4)	9 (32.1)	0.385)
	Absent	11 (73.3)	28 (84.8)	11 (84.6)	19 (67.9)	
Asthma	Present	5 (33.3)	6 (18.2)	3 (23.1)	9 (32.1)	0.550
	Absent	10 (66.7)	27 (81.8)	10 (76.9)	19 (67.9)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test,**p<0.01.

Table 7. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to lymphocyte infiltration.*

		Lymphocyte infiltration			p value
		<20 (n=21) mean±SD	21–50 (n=42) mean±SD	>51 (n=26) mean±SD	
CT score		18.57±5.32	18.95±5.61	19.92±5.52	0.673
NOSE		12.81±3.53	13.29±3.09	13.48±3.31	0.250
Blood eosinophil‡		0.26±0.17 (0.30)	0.33±0.27 (0.20)	0.32±0.25 (0.30)	0.398
		n (%)	n (%)	n (%)	p value†
Allergy	Present	4 (19.0)	12 (28.6)	7 (26.9)	0.710
	Absent	17 (81.0)	30 (71.4)	19(73.1)	
Asthma	Present	4 (19.0)	11 (26.2)	5 (19.2)	0.729
	Absent	17 (81.0)	31 (73.8)	21 (80.8)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test.

patients with ASA triad.[13] Shen et al.[14] observed allergy in 56% of subjects and they showed that radiological and endoscopical scores were significantly higher in the allergic group. Although a positive relationship between atopy and tissue eosinophilia of nasal polyps has been introduced,[15] there are controversial studies demonstrating that atopy does not have a significant effect on eosinophilic infiltration of nasal polyps.[16,17] Similarly, we did not come across a significant difference in terms of histopathological parameters between allergic and nonallergic patients. Also there was no correlation between tissue eosinophilia and asthma, allergy, endoscopic and radiologic extent of the disease and symptom scores. The only remarkable finding was that there was a statistically significant correlation between tissue and blood eosinophilia.

Conclusion

In conclusion, statistically no significant difference was found between the histopathological changes and CT & NOSE scores, blood eosinophil levels, allergy and asthma conditions in nasal polyposis patients. The only remarkable finding was that there was a significant correlation between tissue eosinophil infiltration and blood eosinophil levels. Therefore, we suggest that histopathological struc-

Table 8. Evaluation of CT and NOSE scores, blood eosinophil level, allergy and asthma according to PMNL infiltration.*

		PMNL infiltration			p value
		None mean±SD	1–2 mean±SD	>3 mean±SD	
CT score		16.80±5.85	19.84±4.27	19.32±0.56	0.178
NOSE		12.47±3.25	13.81±2.69	13.52±4.04	0.401
Blood eosinophil‡		0.26±0.19 (0.20)	0.33±0.23 (0.30)	0.34±0.30 (0.30)	0.695
		n (%)	n (%)	n (%)	p value†
Allergy	Present	3 (20.0)	11 (25.6)	9 (29.0)	0.805
	Absent	12 (80.0)	32 (74.4)	22 (71.0)	
Asthma	Present	2 (13.3)	11 (25.6)	7 (22.6)	0.619
	Absent	13 (86.7)	32 (74.4)	24 (77.4)	

*One-way ANOVA; †Chi square test; ‡Kruskal-Wallis test.

tures of nasal polyps seem not to be associated with the severity or extent of the disease as well as co-existing morbidities such as asthma and allergic rhinitis.

Conflict of Interest: No conflicts declared.

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