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The Association Between Paranasal Mucous Retention Cysts and Allergic Sensitization

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ABSTRACT

Objective: Although there is no consensus regarding the etiology of paranasal mucous retention cysts (MRCs) in the literature, several studies suggest an allergic etiology. This study aimed to investigate a potential association between paranasal MRCs diagnosed with MRI scans and allergic sensitization in the pediatric population.

Materials and Methods: A total of 4559 MRI scans were retrospectively evaluated for MRC in patients who presented to the pediatric neurology outpatient clinic with headache complaints. Fifty children with MRI findings conclusive for paranasal MRC and 50 children without such findings were included in the study. All study and control patients were invited for atopy/allergy evaluation. Total IgE measurements, blood eosinophil levels, nasal smear and skin prick tests were performed to evaluate the allergic status of the children. In addition, an allergic rhinitis symptom questionnaire was administered.

Results: The mean age was 13.0±2.8 years (median 14 y, range 6-18 y) with a female-to-male ratio of 1.4:1 in the study group. The prevalence of MRC was found to be 1.1% (50 in 4559). The two groups did not differ with regard to the frequency of blood eosinophilia, nasal eosinophilia, serum IgE levels, and allergic rhinitis symptom severity ($p>0.05$). Positive skin test for at least one of the allergens tested was more common in the MRC group than the controls (40% vs. 16%, $p=0.007$). Multivariate analysis identified that a positive skin prick test for at least one allergen was a significant independent predictor of MRC (OR, 4.6; 95% CI 1.2-17.0, $p=0.023$).

Conclusion: Our study showed that paranasal MRCs were significantly more frequent in atopic children compared to controls. Additionally, MRCs were found to be strongly associated with allergic sensitization.

Keywords: Cysts, allergic rhinitis, children, diagnostic tests, signs and symptoms

INTRODUCTION

Mucous retention cysts (MRCs) of the paranasal sinuses are benign lesions mostly located in the maxillary sinus. They are usually found incidentally as dome-shaped opacities originating from the wall or floor of the sinus. In previous studies with MRCs, their appearance has been defined in various imaging studies including panoramic radiographs, Water's view, and computerized tomography (1). However, studies with magnetic resonance imaging (MRI) scans are relatively rare (2). The reported prevalence of paranasal MRC shows great variation, ranging from 1.4% to 35.6% which is suggested to be caused by the utilization of different diagnostic methods (1, 3-13).

There is no consensus over the nomenclature, since various terminologies have been used to address mucous retention cysts: pseudocyst, retention cyst of the maxillary sinus, intramural cyst, antral cyst, serous cyst, mucous cyst and benign maxillary mucous cyst (1, 2).

Various conditions and factors including dental diseases, barotrauma, rhinitis, allergy, inflammation, and chronic rhinosinusitis have been associated with MRCs (1, 9). However, current evidence in terms of allergic

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etiology is controversial. While several studies have found an association with allergic conditions such as seasonal allergy or other allergies, several other studies have not found any association (3, 12-17). Only a small number of studies examined the possible association with allergy, but none had the appropriate methodology on allergic parameters. In addition, none of these studies were performed exclusively in the pediatric age group.

This study aimed to investigate the possible relationship between allergic findings and paranasal MRCs diagnosed with MRI scans in pediatric patients. For this purpose, allergic sensitization findings were evaluated and compared in patients with and without paranasal MRC.

MATERIALS and METHODS

Patients

A total of 4559 school-age children (6 and 18 years), who had presented to the Pediatric Neurology outpatient clinic of Bezmialem Vakif University Faculty of Medicine with headache complaints and had undergone magnetic resonance imaging (MRI) between April 2018-April 2019, were retrospectively screened for study inclusion. MRC was detected in 50 children by an MRI scan and all were included as the patient group in the study. The control group was selected from patients who presented to the neurology clinic with headache complaints, who did not have a chronic disease or additional neurological disease, and who did not have MRC in their MR images. Patients were invited to our outpatient clinic for atopy evaluation and were asked to stop using their allergy medication (if any) one week before their visit.

Ethics and Foundation

Research and Publication Ethics were complied with and the study protocol was approved by the Bezmialem Vakif University Ethics Committee for Clinical Trials (date, 28.02.2018; no, 5/31). All patients and parents provided informed consent prior to study enrollment. The study was conducted with financial support from the Bezmialem Vakıf University Scientific Research and Projects Unit (Date: 01.03.2018).

Evaluation of Atopy

A 3 ml blood sample was obtained from each patient for complete blood count and total IgE measurement. Total IgE levels were measured with the Immulate 2000 (Siemens) device which employed a chemiluminescence method. Complete blood counts were performed with the Sysmex XT2000i (Roche) device. An eosinophil count of ≥500/μL was defined as eosinophilia and IgE levels exceeding 100 IU/mL were considered to be high (18-20).

Skin Prick Test

Standard activity and concentration allergen solutions of ALK and Allergo companies were used for the prick test. Skin prick tests with a panel of common aeroallergens including house dust mites, grass pollens, weed pollens, tree pollens, and animal epithelium were used to evaluate atopy. Histamine was used as positive and saline solution as negative control. The observation of a wheal diameter ≥3mm larger than the negative control was defined to demonstrate a positive skin reaction against the tested allergen. A positive skin reaction against at least one of the tested allergens was defined as atopy (21).

Nasal Smear

To obtain a nasal smear, the patients were asked to blow their nasal secretions from both nasal passages onto a slide. The secretions were smeared over the slide, dried at room temperature; and then left in May Grünwald solution (Biooptica, Milan, Italy) for 10 minutes and rinsed with tap water. Slides were covered with Giemsa solution (Biooptica, Milan, Italy), left for 20 minutes, and rinsed with tap water. They were dried in a low temperature (37-50 °C) drying stove. Dried slides were examined with a standard light microscope and the cells were counted. More than 1 eosinophil in 20 counted cells was defined as nasal eosinophilia (22).

Evaluation of Allergic Rhinitis Symptoms

According to the Allergic Rhinitis and Its Impact on Asthma (ARIA) classification system, which was introduced in 2001 and is based on the duration and severity of symptoms and their impact on the quality of life (QoL), allergic rhinitis (AR) is divided into classes based on the intermittent and persistent pattern of symptoms (23). Intermittent AR is defined as symptoms that occur 4 or fewer days per week or last less than 4 consecutive weeks; whereas persistent AR (PER) occurs more than 4 days per week or lasts longer than 4 consecutive weeks. Symptoms of intermittent AR or PER may be mild or moderate to severe based on their impact on QoL and symptom severity. Mild AR characteristically does not affect daily, leisure, or sport activities, does not have an

impact on work or school attendance, does not disturb sleep, and causes only minor symptoms. Moderate-to-severe rhinitis is characterized by impairment of at least one of these parameters (24).

The AR symptom scoring system was also used for the evaluation of disease (25). Patients and/or parents were questioned for the presence of daytime nasal and ocular symptoms, which include nasal blockage, runny nose, nasal itching, sneezing, ocular itching, ocular redness, watery eyes, and periocular swelling. In addition, nighttime symptoms, which included nasal blockage, difficulty in falling asleep, and night time awakening were also questioned. Based on the patient history, these 11 symptoms were scored on a scale from 0 to 3 points: 0: asymptomatic, 1: mild symptoms, 2: moderate symptoms, and 3: severe symptoms. Average symptom scores were calculated, rounded to the closest integer, and the patients were categorized as experiencing no allergic rhinitis symptoms (0), mild symptoms (1), moderate symptoms (2), or severe symptoms (3).

Statistical Analysis

IBM SPSS Statistics version 20.0 software (SPSS Inc., Chicago, IL) was used for data analyses. Descriptive data are presented in number (percentage), mean ± standard deviation and median (range), when and where appropriate. The Kolmogorov-Smirnov test and graphical methods were used to test the normality of distribution of continuous variables. Depending on the normality of distribution, continuous variables were compared using the Student's t-test or the Mann-Whitney U test. Categorical variables were compared using Pearson's chi-square test or Fisher's Exact test. The logistic regression model was used to identify significant independent predictors of MRC presence. A p value <0.05 was considered to indicate statistical significance.

RESULTS

The mean age of the patients enrolled in this study was 13.0 ± 2.8 years (median 14 y, range 6-18 y) with a female-to-male ratio of 1.4:1. Prevalence of MRC was 1.1% (50 in 4559) among the patients screened for this study. In patients with MRC, the most common localization of MRC was the maxillary sinus (n=45, 90%), followed by the sphenoid sinus (n=3, 6%), and the nasopharynx (n=2, 4%). There was no association between the localization of MRC and allergic rhinitis. Table I shows the emographical characteristics and the allergic status of the patient and control groups. The percentage of older patients (age >14 years) was higher in the patient group compared to

Table I. Demographic characteristics and allergic status of the two groups.

	MRC absent n=50	MRC present n=50	p
Demographic features			
Age, years (mean±SD)	12.5 ± 3.0	13.5 ± 2.5	0.113
Age >14y, median (%)	13 (26.0)	22 (44.0)	**0.046**
Gender, female, n (%)	29 (58.0)	29 (58.0)	0.580
Body mass index, kg/m^2, (mean±SD)	20.4 ± 3.7	20.2 ± 3.2	0.893
Allergy parameters, n (%)			
Eosinophilia (blood), (≥500 cells/μL)	4 (8.0)	10 (20.0)	0.074
Eosinophilia (nasal)	7 (14.0)	6 (12.0)	0.500
High IgE, (>100 IU/mL)	8 (16.0)	13 (26.0)	0.163
Allergic Rhinitis Symptom Score			
0 (none)	27 (54.0)	21 (42.0)	0.490
1 (mild)	12 (24.0)	19 (38.0)	
2 (moderate)	6 (12.0)	5 (10.0)	
3 (severe)	5 (10.0)	5 (10.0)	
Skin test positivity*	8 (16.0)	20 (40.0)	**0.007**

MRC: Mucous retention cyst. Unless otherwise stated, data presented in frequency (percent). *Against at least one common aeroallergen.

controls (44% vs. 26%, p=0.046). The two groups were similar with regard to BMI values (Table I).

Regarding allergy parameters, patients with MRC and controls were similar in terms of blood and nasal eosinophil counts, serum IgE levels, and severity of allergic rhinitis symptoms (Table I). However, positive skin prick test for at least one of the allergens tested (sensitization) was more common among patients when compared to controls (40% vs. 16%, p=0.007). Multivariate analysis of allergic factors also identified positivity for at least one allergen as a significant independent predictor of MRC (OR, 4.6; 95% CI 1.2-17.0, p=0.023). Table II summarizes multivariate analysis results.

Table III shows the distribution of positive skin prick tests for specific common aeroallergen. Among allergic factors, positive skin prick tests for house mite allergen (36% vs. 12%, p=0.005) and all pollens (24% vs. 8%, p=0.027) were more common in MRC patients compared to controls. MRC patients and controls were similar in terms of the frequency of test positivity for other allergens. In the patient group, there were 13 patients with AR symptoms and a positive skin prick test while 4 subjects were positive in the control group.

Allergic rhinitis had been previously diagnosed in 21 (42%) patients with MRC. Among these, 13 had received treatment for allergic rhinitis prior to this study, and only

Table II. Multivariate analysis of allergic factors that may potentially predict mucous retention cysts.

Factors	Odds ratio (95% CI)	p
Eosinophilia (blood) (≥500 cells/μL)	2.1 (0.5-9.8)	0.337
Eosinophilia (nasal)	0.4 (0.1-1.6)	0.191
High IgE levels, (>100 IU/mL)	0.8 (0.2-2.8)	0.676
Allergic Rhinitis Symptom Score		
0 (none)		ref
1 (mild)	1.5 (0.6-4.0)	0.414
2 (moderate)	0.8 (0.2-3.4)	0.740
3 (severe)	0.7 (0.1-3.4)	0.639
Skin test positivity*	4.6 (1.2-17.0)	0.023

*Against at least one common aeroallergen.

Table III. Distribution of positive skin prick test results to specific common allergens in the groups.

	All subjects n=100	Subjects without MRC n=50	Subjects with MRC n=50	p
Positive skin prick test*	28 (28.0%)	8 (16.0%)	20 (40.0%)	**0.007**
House mite	24 (24.0%)	6 (12.0%)	18 (36.0%)	**0.005**
Cat epithelium	4 (4.0%)	1 (2.0%)	3 (6.0%)	0.309
Wheat pollen	4 (4.0%)	1 (2.0%)	3 (6.0%)	0.309
Weed mixture	8 (8.0%)	2 (4.0%)	6 (12.0%)	0.134
Olive tree	1 (1.0%)	0 (0.0%)	1 (2.0%)	0.500
Cockroach	1 (1.0%)	0 (0.0%)	1 (2.0%)	0.500
Parietaria officinalis	2 (2.0%)	1 (2.0%)	1 (2.0%)	0.753
Tree pollen mix	1 (1.0%)	0 (0.0%)	1 (2.0%)	0.500
All pollens[1]	16 (16.0%)	4 (8.0%)	12 (24.0%)	**0.027**

MRC: mucous retention cyst. Positive for at least one of the aeroallergens tested. Data presented in frequency (percent). The allergens against which at least one patient showed a positive response were listed.

[1]: All pollens included wheat pollen, weed mixture, olive tree, parietaria officinalis and tree pollen mix.

5 had been attending their scheduled visits regularly. Furthermore, 10 patients were diagnosed with allergic rhinitis during this study. Twenty-four of the patients with allergic rhinitis described intermittent symptoms, while 7 of them reported persistent symptoms. Of those who were diagnosed with allergic rhinitis during our study, only one had persistent symptoms. In the MRC group, 5 patients had asthma, 1 patient had atopic dermatitis, 2 patients had asthma and atopic dermatitis, and 1 patient had urticaria.

In the control group, 12 children were previously diagnosed with allergic rhinitis, and all had received treatment prior to enrolling to the study while 8 of them had attended regular visits for their treatment. Thirteen children in the control group were diagnosed with allergic rhinitis during this study. Twenty children had intermittent and 5 had persistent symptoms. Among those who were diagnosed with allergic rhinitis during the study, 11 had intermittent and 2 had persistent symptoms. In the control group, 3 children had asthma, 1 child had atopic dermatitis, and 3 children had urticaria.

DISCUSSION

This study examined a potential association between several allergy parameters including serum IgE levels, blood eosinophilia, nasal smear, and self-reported allergic rhinitis symptoms and paranasal MRC. To the best of our knowledge, this is the first study of its kind performed in a pediatric population. Our results showed that the frequency of allergic sensitization, as measured by skin prick test, was increased among children with paranasal MRC. Our findings suggest that allergic sensitization may contribute to the development of MRC in the pediatric age group.

Only a small number of studies have investigated potential allergic etiology for MRC in the literature. However, the earliest findings on allergic origin of paranasal mucous cysts date back to 1956. In a report by Van Alyea, an allergic origin was proposed for non-secretory maxillary cysts, but not for secretory cysts, without supporting evidence (26). The reported incidence of MRC shows great variation in previous studies (1). Although an accurate method (MRI) has been utilized and all paranasal sinus MRCs were included -not limited to the maxillary sinuses- in this study, the MRC incidence was found as 1.1%, which is lower than previously reported values. The results may have been lower because the current study focused on the pediatric population. On the other hand, a higher incidence of MRC was found in older children in our study. These findings suggest that this pathology develops at a relatively older age. In addition, most of the MRCs were found in the maxillary sinus in our study. This finding was consistent with previous studies (2, 27).

A study from 2013 reported a 7% prevalence of maxillary sinus MRC using panoramic radiographs and found associations between seasonal allergy and smoking, as well as a higher incidence among men compared to women (13). In another study by Casamassimo and Lilly (3), 73 patients with maxillary mucosal cysts were examined and almost half of them reported some type of allergy, including drug allergy (18%), pollen allergy (23%), and food/metal/dust allergy (4%). Similarly, Gothberg et al. (14) and Halstead (15) found a history of allergy in a substantial proportion of their patients with mucosal cysts. In another study, Nemati et al. (11) examined 800 digital panoramic radiographs for maxillary mucosal retention cysts, and reported the frequency as 4%. This study found an increased incidence in males and during spring. Although the study had no direct evidence supporting allergic etiology, the authors claimed a possible association due to the determination of higher incidence in the spring season.

There are also studies that have not found an association between mucosal cysts and allergy. In a recent study, Niknami et al. (12) reviewed 710 panoramic radiographs and 90 cone-beam computed tomography scans of adults in the search of mucous retention pseudocysts in the maxillary sinus and their association with various parameters including age, gender, season, smoking, allergy, asthma, chronic sinusitis, nasal polyps, mucosal thickening, and post-nasal drip. Cysts were found in 2.4% of the patients. Smoking and postnasal-drip were associated with increased frequency of pseudocyst, and the highest frequencies were observed in the spring and summer. However, this study did not find a significant association between cysts and seasonal allergy or asthma. Similarly, in a large study on 5021 patients examining the prevalence of mucosal abnormalities of the maxillary sinus, it was found that 7% of patients had mucosal antral cysts and the incidence was unassociated with self-reported asthma, environmental allergy, hay fever, or other allergic rhinitis (17). Berg et al.(16), studied the pathogenesis of intramural maxillary cysts in 27 patients (mostly adult) and proposed an inflammatory etiology rather than an allergic

etiology, based on their findings of normal IgE levels and the lack of eosinophilia in histological examination of the cysts. In addition, only one patient had a history of allergic or hyperreactive rhinitis in their study.

The main limitation of our study is its retrospective nature, which precludes the direct examination of potential associations between allergic episodes and the development of cysts. The number of patients with sensitization to a specific aeroallergen was low, and the numbers were also too low to compare. This was another limitation. However, the relationship between positive skin test and MRC frequency, in our opinion, provides an explanation to the allergic associations that have been previously suggested.

In conclusion, our findings in this study suggest a possible allergic etiology for the development of paranasal MRCs as their frequency was significantly higher among sensitized children. This study examined a potential association between several allergy parameters including serum IgE levels, blood eosinophilia, nasal smear, and self-reported allergic rhinitis symptoms and paranasal MRC. To the best of our knowledge, this is the first study of its kind performed in a pediatric population. Our results showed that the frequency of allergic sensitization, as determined by skin prick test, was increased among children with paranasal MRC. Our findings suggest that allergic sensitization may contribute to the development of MRC in the pediatric age group.

In our opinion, further studies should be conducted on the incidence, progression, etiology and the management of mucous retention cysts in the pediatric age group, with particular focus on allergic findings.

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