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Epidemiological analysis of chronic rhinitis in pediatric patients

Elizabeth A. Erwin, M.D.¹, Russell A. Faust, M.D., Ph.D.², Thomas A.E. Platts-Mills, M.D., Ph.D.³, and Larry Borish, M.D.³

¹Center for Innovation in Pediatric Practice, Nationwide Children's Hospital, Columbus, Ohio

²Pediatric Otolaryngology, St. John Health System, Ascension Health Michigan, Novi, Michigan

³Asthma and Allergic Diseases Center, Carter Immunology Center, University of Virginia Health System, Charlottesville, Virginia

Abstract

Background—Nonallergic rhinitis is a poorly understood entity, especially among pediatric patients. Objective: This study identifies clinical features that may distinguish phenotypes of allergic and nonallergic patients and to evaluate the usefulness of current diagnostic modalities.

Methods—We reviewed medical records for 151 pediatric patients with perennial rhinitis, evaluated in a multidisciplinary allergy and otolaryngology clinic. Results obtained by standard history, validated questionnaire (SN-5), epicutaneous allergy testing, acoustic rhinometry, and sinus CT were compared.

Results—Nasal congestion was the most frequent primary presenting complaint (62%). Among subjects having a positive allergy test, associated eye symptoms were more frequent ($p = 0.01$) and responses to the SN-5 allergic domain were higher ($p = 0.02$). Sinus CT scores were similar among allergic and nonallergic subjects (median 7 and 8, respectively) and did not correlate with symptom scores ($p = 0.6$). Among nonallergic subjects, quality of life ratings weakly correlated with sinus CT scores ($r = 0.4$; $p = 0.05$). By rhinometry, absolute mean cross-sectional area was similar among allergic (0.32 cm^2) and nonallergic (0.36 cm^2) subjects and did not correlate with symptom scores ($p = 0.8$ for allergic and $p = 0.6$ for nonallergic subjects). Distinct groups of nonallergic patients including those with prominent conjunctival pruritus ($n = 24$), frequent cold symptoms ($n = 3$), and chronic sinus disease ($n = 2$) were observed.

Conclusion—It is difficult to distinguish allergic and nonallergic rhinitis in patients with perennial disease, but associated eye symptoms and questionnaire responses are predictive of allergy. Acoustic rhinometry and sinus CT suggest that physical obstruction and sinus disease are not related to nasal symptoms including, surprisingly, the sensation of congestion.

Rhinitis is a generic term used to describe a constellation of symptoms including rhinorrhea, posterior pharyngeal drainage, sneezing, and nasal congestion. Predisposing issues that can result in long-term nasal symptoms are believed to include anatomic, neurogenic, and

inflammatory processes.¹ Some of the most commonly cited causes include allergic rhinitis, “nonallergic rhinitis,” infection, and laryngeal pharyngeal reflux disease.² Anatomic concerns such as adenoid hypertrophy, septal deviation, and nasal polyposis are also relevant.

Based on differences in definitions and terminology, the prevalence of “nonallergic” rhinitis is difficult to determine. Estimates suggest that in the United States 31 million patients are affected each year.³ It is increasingly recognized that an even larger proportion of individuals may be affected by nonallergic rhinitis if patients with “mixed” rhinitis, who have both allergic and nonallergic disease components, are included.⁴

“Nonallergic rhinitis” encompasses a heterogeneous group of disorders including rhinitis medicamentosa, hormonal rhinitis, nonallergic rhinitis eosinophilia syndrome (NARES), vasomotor rhinitis, and, more recently, local IgE. One adult study estimated vasomotor rhinitis to be the most prevalent nonallergic problem (61%).⁵ Despite the description of vasomotor rhinitis historically in the medical literature, understanding its disease process remains poor. An imbalance of the sympathetic and parasympathetic nervous system was assumed the cause.⁶ It remains unknown whether this mechanism is valid. Alternatively, whether some or all of these patients, in fact, suffer from a primary inflammatory disease has never been adequately assessed.^{7,8} Similarly, the mechanism or trigger for persistent inflammation in NARES is unknown. It is defined by the presence of eosinophils in nasal secretions in patients with negative skin tests and has been observed in up to 15% of adult patients with rhinitis.⁹ With more widespread use of rhinoscopy and CT scanning, many of these patients have been shown to have chronic hyperplastic eosinophilic sinusitis with or without nasal polyps, so the true prevalence of NARES may be much less. Despite an extensive differential diagnosis for nonallergic rhinitis, no reliable diagnostic tests are available and mechanisms are not well understood.

Experts have concluded that “more research is essential and a better understanding of the pathophysiology is needed.”¹ This is certainly true for pediatric patients for whom even less data are available. The purpose of our study was to identify clinical features that may distinguish allergic and nonallergic patients and to evaluate the value of information that can be obtained using current diagnostic testing methods of sinus CT and acoustic rhinometry in pediatric patients.

METHODS

From August 2006 to May 2009, 154 patients referred for evaluation of chronic rhinitis were seen in a multidisciplinary pediatric otolaryngology and allergy clinic at Nationwide Children’s Hospital in Columbus, OH. All patients were evaluated and treated by the same allergist and the same otolaryngologist (E.A.E. and R.A.F., both board certified in their respective specialties). Medical records from these visits were retrospectively reviewed by a single investigator (E.A.E.). A total of 151 patients were included. Three patients who were evaluated in the clinic but did not have allergy testing performed at their visits were not included. This study was approved by the Institutional Review Board at Nationwide Children’s Hospital.

Medical records were reviewed using a predetermined evaluation form. Specific historical details obtained included symptoms of rhinoconjunctivitis, doctor's diagnosis of eczema or asthma, immediate family history of allergic disease, and secondhand smoke exposure. A validated symptom score questionnaire (SN-5) was used to quantify sinus symptoms, nasal obstruction, allergy symptoms, emotional distress, and activity limitations.¹⁰ This tool uses a Likert scale of 0–6 with higher scores suggesting increased burden of symptoms. Overall quality of life was assessed on a scale of 1–9 with 1 indicating the worst possible quality of life and 9 indicating the best possible quality of life.

Standard epicutaneous allergy testing was performed at the initial visit using Sharp-Test Applicators (Panatrex, Placentia, CA). A panel of 38 inhalant allergens (ALK-Abello, Round Rock, TX) with positive (histamine) and negative (glycerol-saline) controls was placed. Results were read at 15 minutes, and a wheal response ≥ 3 mm (in greatest diameter) larger than the negative control was considered positive. Dust-mite, cat, and grass pollen extracts were standardized; the remainder were commercially available, Food and Drug Administration–approved weight/volume extracts.

Forty-seven patients had coronal sinus CT scans performed as part of their clinical evaluation because of suspicion of sinusitis or unexplained persistent nasal symptoms. Mucosal thickening was quantified by using the Lund-Mackay scoring method with a maximum score of 24.¹¹

To obtain additional clinical information in a subgroup of 28 patients with primary complaints of nasal congestion, acoustic rhinometry was performed using a RhinoScan SRE 2100 (Interacoustics, Assens, Denmark).¹² Bilateral minimal cross-sectional areas (MCA) were measured at the nasal valve (MCA1) and the inferior turbinate (MCA2). The right and left values were averaged for a mean onesided value to account for the nasal cycle. The absolute MCA was the lower of the two measurements.¹²

All statistical analyses were performed using SPSS 17.0 (SPSS, Inc., Chicago, IL). Subjects with at least one positive skin test were classified as allergic, and the rest were considered nonallergic. Clinical predictors of allergy taken from the standard history were tested using χ^2 -analyses. Mean symptom and quality-of-life scores from questionnaire responses and absolute MCA from acoustic rhinometry were compared in allergic and nonallergic subjects by using Student's t-test. Group differences in median sinus CT scores were analyzed by using the Mann-Whitney test. The correlation between symptoms and the results of sinus CT scans and acoustic rhinometry were compared by using Spearman rank and Pearson correlation, respectively.

RESULTS

A total of 151 patients were studied, and they are described in Table 1. The median age at the first visit was 7.8 years (range, 1.6–20.6 years). There were 97 male subjects (64%) and 54 female subjects (36%). The most common presenting complaint was nasal congestion (62%). Seventy subjects (46%) were classified as allergic and 81 (54%) were classified as nonallergic.

Allergy was defined by having at least one positive epicutaneous test to an inhalant allergen. The most common allergic sensitivities were grass (26%), dust mites (25%), and tree pollen (21%; Fig. 1). Among the allergic subjects, 28 (40%) had only one measurable allergic sensitivity, and for 12 subjects a single seasonal allergen was identified. Comparison of clinical characteristics suggested that subjects with allergy were younger than subjects without allergy (median age, 7.2 and 9.0 years, respectively; $p = 0.007$; Table 2). Subjects with allergy were also more likely to have conjunctival symptoms (itchy, watery, red, or swollen eyes) when compared with those without allergy (52 and 26% respectively; $p = 0.001$). Of note, nasal pruritus or rubbing the nose was reported as an associated symptom in a small number of allergic ($n = 5$) and nonallergic subjects ($n = 5$).

By using the SN-5 to quantify symptoms, the mean overall symptom score was 2.6 (95% CI, 2.4, 2.8). The mean quality of life score was 6.2 (95% CI, 5.8, 6.6). In general, the most significant symptom reported was nasal obstruction (mean, 3.6; 95% CI, 3.3, 3.9) followed by “sinusitis” symptoms (mean, 3.4; 95% CI, 3.1, 3.5). These scores were compared between the allergic and nonallergic subjects (Table 3). There was no difference in the total symptom score for each allergic group (2.7) and nonallergic group (2.5; $p = 0.6$). Separate comparison of responses for each questionnaire domain confirmed that scores for allergy symptoms (sneezing, itchy nose/eyes, need to rub nose/eyes, or watery eyes) were higher for allergic subjects (3.1 compared with 2.4 for nonallergic subjects; $p = 0.02$). Mean quality-of-life scores were similar between allergic and nonallergic subjects (6.2 and 6.3, respectively; $p = 0.8$).

For all subjects who had a coronal sinus CT scan, the median score was 7. Sinus CT scores did not correlate with overall nasal symptom scores ($p = 0.7$). Furthermore, sinus CT scores did not correlate with symptom scores in any individual domain of the SN-5 including the assessment of symptoms of sinus infection (*i.e.*, nasal discharge, postnasal drip, headache, or facial pain; Table 4). Sinus CT scores were similar in nonallergic subjects compared with allergic subjects (median, 8 and 7, respectively; $p = 0.8$; Fig. 2). When symptoms in allergic and nonallergic subjects were separately compared with sinus CT scores, there were no symptoms that could be used to predict the presence (or severity) of sinus disease (Table 4). Only quality-of-life ratings weakly correlated with sinus CT scores in nonallergic subjects ($r = 0.4$; $p = 0.05$). Interestingly, sinus CT scores were not higher among subjects with asthma compared with those without asthma (median, 7 and 5.5, respectively; $p = 1$). Among subjects having repeat sinus CT because their “sinusitis” symptoms had not improved (five allergic and four nonallergic subjects), the median score decreased from 10 to 2 ($p = 0.1$; Fig. 3).

Acoustic rhinometry was performed in 28 patients who ranged from 4.3 to 16.7 years of age. The overall mean absolute MCA was 0.34. There was no difference in mean absolute MCA between allergic ($n = 15$) and nonallergic ($n = 13$) subjects (mean, 0.32 and 0.36, respectively; $p = 0.4$; Fig. 4). Furthermore, absolute MCA did not correlate with symptom scores for allergic ($p = 0.8$) or nonallergic ($p = 0.6$) subjects.

Further examination of the nonallergic subjects revealed several distinct groups that deserve further study. When primary presenting problems were analyzed among nonallergic

subjects, it was notable that the complaint of drainage (5/5) was strictly nonallergic. Furthermore, presentation with frequent “colds” was slightly more likely to be nonallergic (3/5), and the two allergic with this complaint had only a single, likely irrelevant, allergic sensitivity (grass and cat without home exposure, respectively). When questionnaire responses were analyzed, there were 24 nonallergic subjects who had associated eye symptoms. They had higher questionnaire scores for “allergy symptoms” than other nonallergic subjects ($p = 0.006$). Two nonallergic subjects showed persistent sinus disease on at least two sinus CT scans.

DISCUSSION

Although rhinitis has not been considered a severe disease in the past, this seems to conflict with data showing that patients will present for frequent physician visits, undergo extensive diagnostic testing, take at least one daily medication, and/or have surgery all in an attempt to correct their nasal symptoms. Recent studies suggest that rhinitis may present a greater burden than previously recognized.¹³ The full burden is more apparent when issues relating to quality of life (*i.e.*, sleep, concentration, and/or missed work) are considered.¹⁴ Parents of pediatric patients with chronic, recurrent rhinosinusitis have reported more school and play limitations due to physical health factors and more bodily pain for their children compared with those having asthma and juvenile rheumatoid arthritis.¹⁵ Furthermore, the now established relationship between rhinitis—both allergic and nonallergic—and lower airway symptoms also makes chronic rhinitis more relevant. We have studied a pediatric cohort presenting for subspecialty evaluation secondary to symptoms of perennial rhinitis. Our results emphasize that by using currently available clinical testing (*i.e.*, standard history, sinus CT, and acoustic rhinometry), it is difficult to distinguish allergic and nonallergic rhinitis disease processes in patients with perennial disease and that there remains a large proportion of patients for whom the cause of symptoms is not clear.

We measured at least one allergic sensitivity in 46% of our patients. Worldwide variation in the prevalence of allergic sensitizations and in the most frequently implicated allergen has been reported.¹⁶ Our results are consistent with the prevalence of allergic sensitization among the general population in a variety of areas studied.^{17–19} This is remarkable because our subjects were selected for symptoms of rhinitis, and it would be expected that the prevalence of allergic sensitivity would be higher than the 54% reported in the general population.¹⁸ Causality between allergic sensitization and symptoms is difficult to prove especially with regard to perennial rhinitis.¹⁶ Although all of our subjects complained of rhinitis throughout the year, 40% had only one positive allergy test. In some cases ($n = 12$), this was a single sensitivity to a seasonal allergen. These subjects most easily meet the definition of “mixed” rhinitis or combined allergic and nonallergic disease processes, because a single seasonal allergic sensitivity would not explain perennial symptoms. However, there were also patients who had several pollen allergies (seasonal allergic rhinitis) who are also likely to have a component of nonallergic symptoms. Finally, there is no way to exclude nonallergic causes as a more relevant component of symptoms when compared with allergic sensitivities, despite the finding of positive skin tests. This group with mixed rhinitis may be identified by having positive allergy tests but lack of classic allergic symptoms (*i.e.*, sneezing, nasal pruritus, or eye symptoms). Thus, in the evaluation

of perennial rhinitis, skin testing alone can not establish that allergies are the underlying mechanism causing symptoms.

The relationship between rhinitis and sinusitis has been difficult to reconcile.^{20,21} The lay community and many physicians diagnose sinusitis based on symptoms of headache, facial pressure, nasal congestion, and nasal drainage. By contrast, specific studies of patients presenting with self- or physician-diagnosed “sinus” headache suggest that migraines, not sinusitis, are more frequently associated with these symptoms.²² Furthermore, tissue examination of the sinuses and nasal tissue in patients with chronic sinusitis reveals distinct differences in the presence of some inflammatory cell types.^{23,24} In our study, mucosal inflammation in the sinuses identified by CT scan was found in both allergic and nonallergic subjects when compared with normal children.²⁵ There was no difference in the degree of symptoms reported by either subject group and no relationship between symptoms and sinus CT scores even in this group of patients having suspicious symptoms. Our findings support the view that sinus disease is not related to nasal symptoms and may be found as a complication or in association with both allergic and nonallergic rhinitis. We identified two patients in our small group of patients with repeat coronal sinus CT who had persistent sinus disease. It is possible that a small, distinct group of pediatric patients has rhinosinusitis. However rhinitis and sinusitis should be considered two different disease states. Interestingly, among our patients, asthma was not related to the presence or severity of sinus disease in contrast to what is reported in adults.^{26–30} Thus, CT scan (or rhinoscopy) must be used to identify patients with sinus disease and the role of chronic inflammation is not clear.

Our results emphasize the value of having a validated questionnaire. By using historical details, only the presence of conjunctival symptoms was predictive for allergy. The SN-5 domain for allergy symptoms including sneezing, itchy nose, need to rub nose/eyes, or watery eyes was also related to having a positive allergy test. Currently, there is no standard accepted questionnaire to assess rhinitis symptoms. Recent evaluation of the rhinitis control assessment test, a six-item patient completed tool, has shown consistency and validity in adults with seasonal and perennial allergic rhinitis.³¹ However, it has not been tested in patients with nonallergic rhinitis. It contains several questions about sneezing and watery eyes that may not be helpful for the nonallergic patient. The SNOT-22 has been validated in adults who have had sinus surgery secondary to nasal polyposis or chronic rhinosinusitis.³² General weaknesses of current questionnaires include the lack of information on pediatric patients and separate focus on allergic and nonallergic patients. To complicate the situation further, the ability of children to evaluate their own symptoms has been questioned.³³

The sensation of nasal congestion, which was by far the most frequent presenting complaint, was not consistent with measurable nasal obstruction in our study. Our results for absolute MCA (0.34 cm² overall) were not different from the means reported in children without colds measured outside the pollen season (0.36 cm²).¹² Interestingly, acoustic rhinometry revealed slightly higher absolute MCA among nonallergic patients. This is consistent with reports from other investigators showing no difference in MCA between patients with nonallergic rhinitis and controls.³⁴ There are several possible explanations for this finding. It is possible that nasal congestion may be episodic and thus undetectable at times of testing. Alternatively, nasal airflow turbulence may be more relevant to the perception of

congestion. Nasal resistance is dependent on airway radius as well as length, pressure, viscosity, and density. Typically, expiratory flow has more turbulence, and if present, a sensation of obstruction would be the result.

Our study suggests several possible phenotypes of nonallergic pediatric patients that deserve further study. We observed a few subjects who had persistent evidence of sinus disease. Among adults, the diagnosis of rhinosinusitis is used to describe these patients.^{35,36} The nonallergic subjects with associated eye symptoms may be individuals with local allergy. This nasal response has also been described using the term “entropy.”^{37,38} These patients do not have positive allergy tests, but they do have measurable specific IgE in nasal lavage fluid and in some cases positive allergen provocation testing.^{37–39} We also observed a distinct group of patients who complained of “frequent colds.” These patients may have local Staphylococcal infection with a superantigen response.^{40,41}

One of the limitations of our study is its retrospective design. However, the patients included in our study were all seen in the same clinic and were evaluated by the same two practitioners, so we expect that the records were consistent. Another limitation is the absence of a “gold standard” to distinguish allergic and nonallergic patients. Because our patients presented with chronic nasal symptoms, we were as inclusive as possible to maximize our sensitivity in identification of allergic patients. However, people with positive skin tests do not necessarily have symptoms on exposure, which is consistent with our observation that many of our “allergic” children had irrelevant exposure histories and symptom complexes that were more typical of the nonallergic rhinitis cohort. Although allergen challenges can be used to confirm reactivity, this test is not realistic in the clinical care setting.

In conclusion, our study suggests that even with additional clinical testing it is difficult to distinguish allergic and nonallergic rhinitis. With the overall lack of distinct features such as mutually exclusive symptoms and measurable differences in nasal obstruction, it is currently difficult to classify patients with perennial disease. For pediatric patients with chronic rhinitis, we need more information about phenotypes such as local allergy, rhinosinusitis, and Staphylococcal superantigen responses.

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Figure 1.

Epicutaneous skin testing was used to determine prevalence of specific inhalant sensitivities among pediatric patients presenting with primary complaint of chronic rhinitis. *Tree pollens tested include oak, birch, elm, sycamore, hickory, maple, and ash. #Grass pollens tested include timothy, June, and Bermuda. The frequency of cases with a single positive skin test to each allergen is shown in gray.

Figure 2.

Sinus CT scores are shown for allergic and nonallergic subjects. A coexisting diagnosis of asthma is indicated by filled circles, and subjects without asthma are shown with open circles. Horizontal lines indicate the median score for each subject group.

Figure 3.
Scores are shown for first and second coronal sinus CT (numbers 1 and 2, respectively).
Filled circles represent allergic subjects, and open circles represent nonallergic subjects.

Figure 4.

Absolute mean cross-sectional area (MCA) for nonallergic and allergic subjects is presented. Those with a primary complaint of congestion are shown with a filled circle; an open circle is used for subjects with any other symptom. Means for each group are shown with horizontal lines.

Table 1

Characteristics of pediatric subjects evaluated for chronic rhinitis

Characteristic	No.
Age at first visit, median (range)	7.8 yr (1.6–20.6 yr)
Sex	
Male, <i>n</i> (%)	97(64)
Female, <i>n</i> (%)	54 (36)
Other allergic diagnoses	
Eczema	34(23)
Asthma	51 (34)
Primary problem at presentation	
Congestion	94 (62)
Rhinorrhea	28 (18)
Epistaxis	7(4.6)
Snoring	7(4.6)
Drainage	6 (4.0)
Frequent “colds”	5 (3.3)
Other*	5 (3.3)
Epicutaneous allergy testing	
Positive	70 (46)
Negative	81 (54)

* Other includes headache (three subjects), sneezing (one subject), and enlarged tonsils (one subject).

Table 2

Comparison of clinical features of allergic and nonallergic subjects

	Allergic (n = 70)	Nonallergic (n = 81)	p Value*
Age [#] (yr; median)	7.2	9.0	0.007
Gender (male; n)	47	49	0.5
Conjunctivitis (%)	52	26	0.01
Nasal pruritus (%)	7.1	6.1	1
Eczema (%)	20	25	0.5
Asthma (%)	43	30	0.09
Family history [§] (%)	61	49	0.09
Tobacco exposure [¶] (%)	40	33	0.4

* Mann-Whitney test was used to compare ages between the groups. The rest of the comparisons were made using χ^2 -testing.

[#] Age at the time of original presentation for allergy testing.

[§] Positive family history for allergic disease(s) in parent or sibling. Family history was unknown for two patients who were adopted.

[¶] Secondhand tobacco exposure as measured by report of smoking by at least one custodial parent.

Table 3

Symptom scores* obtained by administering SN-5 questionnaires to allergic and nonallergic subjects

	Sinus Symptoms	Nasal Obstruction	Allergy Symptoms	Emotional Distress	Activity Limitations	Total	QOL
Allergic	3.5 (3.1, 3.9)	3.6 (3.1, 4.1)	3.1 (2.7, 3.5)	2.2 (1.8, 2.6)	1.1 (0.8, 1.4)	2.7 (2.4, 3.0)	6.2 (5.6, 6.8)
Nonallergic	3.3 (2.8, 3.8)	3.5 (3.0, 4.0)	2.4 (1.5, 2.5)	2.0 (1.5, 2.5)	1.4 (1.0, 1.8)	2.5 (2.1, 2.8)	6.3 (5.7, 6.9)
<i>p</i> Value [#]	0.5	0.6	0.02	0.7	0.2	0.6	0.8

* Questionnaire responses are given as mean (95% confidence interval).

[#] Statistical comparisons were made using Student's *t* test. QOL = quality of life.

Table 4

Relationships between symptom scores and sinus CT scores*

Symptoms	Subjects		
	All	Allergic	Nonallergic
Overall score	0.6	0.9	0.4
Sinus symptoms	0.8	0.4	0.5
Obstructive	0.7	0.5	0.8
Allergy symptoms	0.2	0.4	0.4
Emotional distress	0.2	0.6	0.2
Limitations	0.2	0.5	0.2
Quality of life	0.1	0.6	0.05

* Results are given as Spearman rank correlation p value.