Nasal Endoscopy in Children with Suspected Allergic Rhinitis

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Objective/Hypothesis: Ear, nose, and throat assessment may be frequently requested for children with allergic rhinitis (AR). Nasal endoscopy allows a thorough evaluation of the nose. The aim of the study was to investigate whether there are endoscopic signs predictive for AR diagnosis in a cohort of children with suspected AR.

Study Design: Cohort of observational study.

Methods: There were 176 children (99 males; mean age, 7.5 years) studied. Clinical visit, nasal endoscopy, and skin prick test were performed in all patients. Nasal endoscopic signs were pale turbinates, middle turbinate contact, and inferior turbinate contact. The AR diagnosis was made when nasal symptom history was concordant with sensitization.

Results: AR was diagnosed in 141 children. Inferior and middle turbinate contact were reliable predictive factors for AR (odds ratio 5.38 and 3.42, respectively), whereas pale turbinates did not predict it.

Conclusions: This study suggests that nasal endoscopy may reveal signs predictive for AR diagnosis in children.

Key Words: Nasal obstruction, allergic rhinitis, endoscopy, children.

Level of Evidence: 2b.

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INTRODUCTION

Allergic rhinitis (AR) is a common chronic disorder characterized by typical symptoms, including itchy nose, sneezing, rhinorrhea, and nasal obstruction, sustained by IgE-mediated inflammation. Nasal obstruction may be considered the most relevant AR symptom as it is closely related to allergic inflammation. AR is moreover associated with impaired quality of life and school performance. Patients may also be bothered by sleep disorders, emotional problems, impairment in activity and social functioning; nasal obstruction largely contributes to affect all of these aspects. These reasons explain why, in the Allergic Rhinitis and Its Impact on Asthma guidelines, AR classification is based on quality of life, symptoms’ severity, and duration.

In this regard, nasal obstruction constitutes the most bothersome symptom, and it has been proposed as a key symptom in AR. The clinical relevance of nasal obstruction results from the demonstration that the severity of obstruction is significantly related to clinical, immunological, and functional parameters. Allergic inflammation, mucosal congestion, and increased production of mucus contribute to nasal obstruction. Allergic inflammation induces a swollen mucosa, vasodilation causes engorgement of sinusoidal capacitance vessels, and excess mucus contributes to impairment of nasal airflow. The relationship between nasal obstruction, Th2-dependent inflammation, and airflow limitation has been evidenced both in adults and children suffering from AR.

Children with nasal obstruction should be adequately investigated by pediatricians, as this symptom may promote and worsen other disorders such as rhinosinusitis and asthma. Ear, nose, and throat (ENT) specialists are frequently consulted in this regard. Nasal endoscopy is usually performed during an ENT visit to investigate nasal cavities and visualize all anatomical details. Recently, it has been reported that there was a significant relationship between endoscopic findings and perception of nasal symptoms in children with AR.

For some time, pale turbinates as an expression of mucosal edema have been anecdotally considered a suggestive rhinoscopic sign for AR, therefore most physicians suspect allergy when observing pale turbinate. Turbinate enlargement is also frequently detected during nasal endoscopy in allergic subjects. Some endoscopic findings might contribute to AR diagnosis even though it must be confirmed by the concordance between history and a positive skin prick test.

There is no study that investigated whether there are endoscopic signs that may actually be predictive factors for AR diagnosis. In fact, it may be very useful in common practice to look into a child’s nose and see something that would support a diagnosis of allergy. Therefore, this study was designed to confirm this hypothesis by evaluating a cohort of children with suspected nasal allergy who were visited by an ENT specialist. The aim of this study was to define some endoscopic finding that may be a predictive marker for allergy.

MATERIALS AND METHODS

Patients

This study was performed on 176 children (99 males), ages between 2 and 16 years (mean, 7.5 years; median, 7 years;
standard deviation, 2.9 years), with suspected AR who were consecutively visited by an ENT specialist (F.A. or F.B.).

Inclusion criteria was the presence of nasal symptoms suggestive for AR, such as nasal itching, sneezing, watery rhinorrhea, and nasal obstruction. Exclusion criteria were previous allergy diagnosis and current antiallergic treatment, acute rhinosinusitis in the previous 4 weeks, and chronic rhinosinusitis. The study was approved by the local review board and informed consent was obtained from the parents.

**Study Design**

All children were evaluated by clinical visit, nasal endoscopy, and skin prick test.

**Endoscopy**

Endoscopy was performed with a pediatric rigid endoscope, diameter 2.7 mm, with a 30° angle of vision (Karl Storz 7207; Karl Storz, Tuttlingen, Germany), and with a 300-W cold light source (Storz Xenon Nova; Karl Storz) and a light cable of 1.8 mm length. Endoscopy was video recorded by a microcamera connected to digital recorder set (Karl Storz Tele Pack; Karl Storz). A flexible endoscope (2.7 mm in diameter) was used in restless children and in those with narrow nasal fossa due to anatomical abnormalities. The child was placed in a supine position, with the head bent by about 45°. Cotton wool soaked with anesthetic solution (oxybuprocaine 1%) was placed into the nose for 5 minutes.

The complete details of the procedure were previously described.9 Briefly, the nasal fossa was evaluated in three steps that allowed investigation of the following anatomical structures according to Lang’s description10: 1) the inferior turbinate and its relationship with the inferior meatus, the inferior part of the septum, the aspect of the mucosa and the presence of secretion, and the rhinopharynx; 2) the maxillary line (beginning superiorly at the middle turbinate attachment corresponding at the agger nasi area), the olfactory tract when possible, the middle turbinate and its contacts with septum or uncinate process; and 3) the uncinate process, the middle meatus and the half posterior of the nasal septum, the ethmoidalis bulla and its mucosal contacts, and the sphenoid recess (this step was possible only when the space inside the nasal fossa was adequate, otherwise sometimes after local decongestion).

Three endoscopic parameters were considered: 1) the contact point between the middle turbinate and adjacent structures, such as the uncinate process and septum (Fig. 1); 2) the contact point between the inferior turbinate and inferior meatus (Fig. 2); and 3) the pale medium or inferior turbinate. All of these were considered as either present or absent. The contact point corresponds to a local enlargement of mucosa, often swollen, with a white or pale color of part of the middle or inferior turbinate, and often corresponding to the head. The contact point definition was previously described in detail.11

### Skin Prick Test

Allergy was assessed by the presence of sensitization to the most common classes of aeroallergens by performing a skin prick test. The test was performed as stated by the European Academy of Allergy and Clinical Immunology.12 The allergen
Aspergilli trees, olive trees, cypress, grasses mix, Compositae mix, Parteria judaica, birch, hazel trees, olive trees, cypress, Alternaria tenuis, Cladosporium, and Aspergilli mix). The concentration of allergen extracts was 100 immune reactivity/mL (Stallergenes, Milan, Italy). A histamine solution in distilled water (10 mg/mL) was used as a positive control, and the glycerol-buffer diluent of the allergen preparations was used as a negative control. Each patient was skin tested on the volar surface of the forearm using 1-mm prick lancets (Stallergenes). The skin reaction was recorded after 15 minutes by evaluating the skin response in comparison with the wheal given by the positive and the negative control. A wheal diameter of at least 3 mm was considered a positive reaction.

The AR diagnosis was made if nasal symptom history was concordant with sensitization. A positive skin prick test is the gold standard for defining the presence of an allergy.

**Statistical Analysis**

Mean and standard deviation for continuous covariates and counts, and percentages for categorical characteristics were showed. The skin prick test was categorized as positive when it identified the patient as having an allergy, or negative when it identified an absence of allergy, whereas endoscopic signs were classified as "yes" if the patient had the relative characteristic or "no" if the patient did not show it. A univariate logistic regression was assessed to evaluate any relationship between allergy, defined by positive or negative skin prick test, and the presence of endoscopic signs, such as pale turbinates, middle an inferior turbinate contacts, and demographic characteristics. The results of the skin prick test (positive/negative) were considered as dependent variables. Moreover, factors that were statistically significant in the univariate model were considered in a multivariate logistic model. Odds ratio (OR) and 95% confidence interval (CI) were calculated.

Predictive positive value was calculated as a percentage of patients with positive result at prick test considering the patients with the turbinate’s contact. Furthermore, a receiver operating characteristic curve was obtained, and an area under the curve (AUC) with 95% CI was calculated. A P value <.05 was considered statistically significant. SPSS version 18 (IBM Corp., Armonk, NY) was used for computation.

**RESULTS**

The demographic, clinical, and endoscopic characteristics of patients are reported in Table I.

Pale turbinates were detectable in 70 (39.8%) children, whereas middle turbinate contact was present in 130 (73.9%) children and inferior turbinate contact was present in 160 (90.9%) children. The skin prick test was positive in 142 (80.7%) children.

<table>
<thead>
<tr>
<th>Covariates</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (1-year increment)</td>
<td>1.10 (0.96-1.27)</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (male vs. female)</td>
<td>1.58 (0.75-3.36)</td>
<td>NS</td>
</tr>
<tr>
<td>Inferior turbinate contact (yes vs. no)</td>
<td>5.15 (1.78-14.97)</td>
<td>.003</td>
</tr>
<tr>
<td>Pale turbinates (yes vs. no)</td>
<td>1.08 (0.50-2.30)</td>
<td>NS</td>
</tr>
<tr>
<td>Middle turbinate contact (yes vs. no)</td>
<td>3.32 (1.51-7.27)</td>
<td>.003</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Prick Test</th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior turbinate contact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>8 (23.5)</td>
<td>8 (5.6)</td>
<td>16</td>
</tr>
<tr>
<td>Yes</td>
<td>26 (76.5)</td>
<td>134 (94.4)</td>
<td>160</td>
</tr>
<tr>
<td>Pale turbinate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>14 (41.2)</td>
<td>56 (39.4)</td>
<td>70</td>
</tr>
<tr>
<td>Yes</td>
<td>20 (58.8)</td>
<td>86 (60.6)</td>
<td>106</td>
</tr>
<tr>
<td>Middle turbinate contact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>16 (47.1)</td>
<td>30 (21.1)</td>
<td>46</td>
</tr>
<tr>
<td>Yes</td>
<td>18 (52.9)</td>
<td>112 (78.9)</td>
<td>130</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Nasal symptoms depend on the mucosal inflammation consequent to the causal allergen exposure. Experimental evidence supports a direct relationship between the IgE-mediated reaction and the resulting inflammatory process in AR. Allergen exposure activates mast cells, which consequently release preformed mediators, mainly histamines, leukotrienes, and cytokines that are capable of inducing the recruitment and activation of inflammatory cells, including eosinophils, neutrophils, and Th2 lymphocytes.

Air filtering, warming, and humidifying are the main nasal functions, and all of them depend on the particular characteristics of nasal anatomy and physiology. Turbinates allow for having the maximal...
surface useful to perfectly carry out these functions and create a turbulent airflow optimal for achieving an ideal contact between inspired air and nasal mucosa. In addition, turbinates may regulate the airflow quantity by modifying their size; the typical example is the periodic and continuous nasal cycle. The vascular submucosal system is fundamental for guaranteeing adequate nasal functions. Nasal circulation is composed of four parallel and overlapped networks: arterial-venous anastomosis, cavernous plexus, subepithelial, and periglandular microcirculation. Sympathetic and parasympathetic innervations regulate the blood supply in these different structures. The impact of airflow is also important for understanding vascular phenomena. The head of the inferior and middle turbinate is the first portion that frontally impacts with inspired airflow, thus it is particularly exposed to allergens and represents the site of local inflammation. Nasal inflammation induces the occurrence of anatomic changes that may be easily observed during endoscopy. The typical endoscopic picture in children with AR is characterized by hypertrophic turbinates with relevant edema of the inferior turbinate head. The edema is usually localized and sectorial, and may be so relevant as to cause a contact between the inferior turbinate and the lateral wall. The sectorial edema may derive from a local, direct, and continuous allergic reaction in the site of impact between inspired airflow, containing allergens, and the head of the middle and inferior turbinate.

AR is a very common disorder in childhood; however, the nasal symptoms are not pathognomonic, and it may be associated with other conditions, mainly infectious rhinosinusitis. Thus, the clinical picture may be complex and a differential diagnosis should be performed. Therefore, pediatricians should frequently consult ENT specialists for a thorough assessment of children with suspected AR by nasal endoscopy. Turbinate enlargement is commonly observed during nasal endoscopy in allergic subjects. Also, pale turbinates are considered by most physicians as a sign suggestive of AR, even though no study has confirmed this hypothesis.

This study addressed this issue of considering a cohort of children with suspected AR evaluated by ENT specialists for better definition of the nasal pathology. The findings show that the localized edema of turbinates, detected by the contact, was very frequent, mainly concerning the inferior turbinate (about 90% of patients). The multivariate analysis showed that the presence of turbinate’s contact may be considered a reliable predictive factor for AR diagnosis. On the contrary, pale turbinates were less commonly observed (about 60%), and overall they were not predictive for AR. Therefore, the presence of the turbinate’s contact is very common and is predictive for AR, whereas pale turbinates are less relevant.

About 20% of children with suspected AR were negative on skin prick test even though there was both a clinical and endoscopic suspect. Nasal mucosa represents the first impact of aeroallergens with the organism. In fact, allergen-specific immunoglobulin-E (IgE) binds with inhaled allergens and the inflammatory cascade starts. As there may be elevated intranasal IgE levels in some patients, it has been demonstrated that intranasal IgE is locally synthesized rather than transported to nasal tissues. The nasal mucosa may contain all of the elements necessary for producing Ig (including IL-4, IL-13, and CD40) and Ig heavy chain classswitching, and they are inducible after allergen exposure. Follow-up exposure to grass pollen, inferior turbinate tissues in allergic patients were found to contain an increase in IL-4 RNA and germline c gene exons, which are spliced out during Ig class-switching gene recombination. An experimental study reported that IgE production occurs first in the target organ induced by allergen exposure, and it is later followed by a systemic response. The relevance of local allergic reaction could be the possible explanation of the sectorial edema that induces the occurrence of the turbinate’s contact. Further studies should explore this issue.

Future attention to the phenomenon of local IgE production within the nose will likely be directed toward the clinical relevance of this finding, including diagnostic and therapeutic options for allergy testing and immunotherapy. Searching nasal IgE can aid in allergy diagnosis when traditional systemic testing fails in patients with suggestive history of AR. Therefore, local phenomena, including immunological, anatomic, and clinical changes, should be carefully investigated, as they could precede systemic IgE detection. Therefore, this study might propose an intriguing hypothesis, such as the endoscopic feature associated with clinical symptoms could precede the classical AR diagnosis based on detection of systemic IgE. This concept may be consistent with the term entopy, which was proposed some years ago for defining a localized allergic reaction in the target organs without systemic IgE. In addition, the entropy theory could also explain the findings of this study concerning the turbinate’s contact. In other words, localized edema might depend on a local allergic reaction...
that in some children occurs with a negative skin prick test.

Another relevant aspect to be considered is that other nasal mucosal conditions differ from contact points for several reasons. Infective or irritative rhinitis is characterized by diffuse mucosal inflammation or edema that is often symmetric, a nasal cycle with spontaneous reciprocal changes in nasal patency caused by decongestion, and congestion of cavernous tissues of the nasal mucosa, and it is monolateral without pathological findings.20

From a clinical point of view, subjects with symptoms and endoscopic signs suggestive of AR and with no specific IgE should be carefully followed up. In this regard, a study is ongoing. On the other hand, this study has some limitations; local immunological parameters were not evaluated, nasal cytology was not performed, and nasal airflow was not considered.

CONCLUSION

This study suggests that the turbinate’s contact may be predictive for AR diagnosis, and children with signs but negative IgE should be carefully followed.

BIBLIOGRAPHY