Sequential nasal eosinophil determinations in an allergy practice
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Abstract

INTRODUCTION
Nasal eosinophils are often observed in allergic rhinitis, nasal polyposis, allergic fungal sinusitis, and non-allergic rhinitis with eosinophilia syndrome (NARES). Determinations of nasal eosinophils quantities are performed by most clinical laboratories and are often viewed as an adjunct to diagnosing upper airway inflammatory disease (1). Although increasing nasal eosinophils have been observed during seasonal allergen exposure (2), the role of monitoring nasal eosinophils has not been defined in the context of clinical practice. The purpose of this paper is to describe serial nasal eosinophil quantities in 3 patients treated over time in a single allergy practice and to discuss the relevant recent literature regarding nasal eosinophil quantification techniques and their utility.

CASE REPORT
A 66 year old African American male was seen initially in March 2004 with complaints of a persistent cold lasting 1 month. His primary symptoms were nasal congestion and sneezing. Five years prior, he had similar symptoms and was treated by an otolaryngologist with nasal saline spray after being told that there was no pathology. He denied a history of asthma or seasonal allergies. He had no pets or infestations with roaches or mice. On physical examination there was moderate edema of the inferior turbinates. ImmunocapTM (3) serology revealed positive results for d.farinae, American cockroach, various tree pollens, and common ragweed pollen. Using a RhinoprobeTM to obtain a sample, nasal eosinophil determinations were determined by a commercial laboratory (Quest Diagnostics). Thirteen percent eosinophils, 69% neutrophils, and 18% lymphocytes/mononuclear cells were reported. A CT scan of the sinuses showed chronic sinusitis and right osteomeatal complex obstruction. The patient was treated with triamcinolone nasal spray and instructed on dust mite avoidance measures. Over the following 3 months the patient did not have adequate relief and started to have wheezing. He was treated additionally with azalastine nasal spray, montelukast, and albuterol inhalation. A repeat nasal eosinophil determination showed 8% eosinophils on a sample deemed to have between 10-100 cells per 10 low power fields (Quest Diagnostics). Nine months after his initial visit he still had intermittent nasal symptoms. A repeat nasal eosinophil determination in January 2005 showed 43% nasal eosinophils, with a note that many epithelial cells were observed (Quest Diagnostics). 2 years after his initial visit the patient developed worsening shortness of breath. Wheezing was noted and the FEV1 was 67% of his predicted value. A short course of prednisone, a macrolide antibiotic and fluticasone/salmeterol 500/50 dosed inhalation were prescribed. IgG, IgA and IgM levels were normal. The IgE level was 389 IU/ml. Over the third year of treatment, the patient required further bursts of prednisone and repeat courses of antibiotics. Nasal endoscopy revealed nasal polyposis but the patient declined the recommended sinus surgery. During the fourth year of treatment the patient started omalizumab injections which have been continued now for 3 years, during which time a single burst of prednisone was required. Overall symptomatic improvement was noted by the patient for both respiratory and nasal symptoms.

A 45 year old Caucasian female was seen initially in 2007 for asthma and nasal polyposis for many years duration. She had a history of allergy immunotherapy for 1 year duration. She claimed anosmia. She was taking cetirizine, montelukast, fluticasone/salmeterol 250/50 and albuterol inhalations. On physical examination, there were...
nasal polyps, mucoid nasal secretions, expiratory wheezing, and a hyponasal voice. The FEV1 was 82% of her predicted value. ImmunocapTM serology revealed negative results for all relevant aeroallergens. RhinoprobeTM obtained nasal secretions showed 40 percent eosinophils(Quest Diagnostics). She was treated additionally with azelastine and budesonide nasal sprays. Over the following year, repeated treatments with prednisone and antibiotics were required. A CT scan showed pan-sinusitis. In the beginning of 2009, the patient underwent sinus surgery which included ethmoidectomies, polypectomies, and maxillary antrostomies. Two and three months post-operative, the patient returned with complaints of recurrent wheezing despite inhaled corticosteroid/long acting bronchodilator/leukotriene receptor antagonist therapy. Expiratory wheezing and grayish mucoid secretions were noted in the nasal cavities. The patient was also still using nasal corticosteroid spray treatment. A repeat nasal eosinophil determination showed 8% eosinophils, 90% neutrophils, and 2% lymphocytes. More than 100 cells per 10 low power fields were noted(Quest Diagnostics).

A 43 year old African American male was seen initially in the Spring of 2001 for chronic rhinorrhea and nasal congestion and recurrent sinusitis treatments. He had a history of childhood asthma and tonsillectomy. He had no pets or infestations with roaches or mice. The physical examination revealed some moderate edema of the nasal mucosa. ImmunocapTM serology revealed positive results for cat dander and oak/birch tree pollens. Ash tree pollen was negative. In January 2008, the patient was again treated for acute sinusitis. At that time RhinoprobeTM obtained nasal secretions, showed 16 percent eosinophils. 76% neutrophils, and 8% lymphocytes. 10 to 100 cells per 10 low power fields were noted(Quest Diagnostics).

**DISCUSSION**

Nasal eosinophil determinations have been performed for years in clinical allergy practice. This methodology is quick, inexpensive, and requires only simple laboratory equipment(4). More recently other techniques to quantify eosinophil presence in upper airway allergic disease have been developed. Methods to increase mucosal cell collection have included use of saline lavage(5) and hypertonic saline nebulization(6). Unlike nasal mucosa scrapings, these collection techniques usually involve a substantial volume of fluid collection from the patient, and also require some sort of post-collection sample processing with mucolytics. Although Wright-Giemsa stains are typically used to identify eosinophils on spray fixative treated slides, some investigators have used eosinophil cationic protein expression as a marker of eosinophils(7). This expression is typically detected by immunohistochemical staining. Nasal cytology also provides an opportunity to examine nasal epithelial cells(8,9). Using ICAM-1 immunohistochemical staining, some investigators have shown correlations between eosinophil numbers and ICAM-1 expression on epithelial cells(10), suggesting that adhesion molecule expression in mucosal epithelial cells relates to eosinophil infiltration/accumulation in allergic nasal disease.

The standard determination of nasal eosinophil is usually performed by a laboratory technician. The eosinophils are expressed as a percentage of all leukocytes observed. Epithelial cells may be the predominant cell type, when Rhinoprobe scrapings are obtained(as opposed to cotton swab samples). Most clinical laboratories do not comment on epithelial cell numbers or use these cells as the denominator in quantifying eosinophil percentages. Some laboratories also report how abundant leukocytes are in the preparation, as was the case with some of the sample reports.
in the 3 patients described. In these case reports, the commercial laboratory reported leukocyte ranges as the number of leukocytes observed in 10 low power fields. Obviously, a sample with few leukocytes could represent a poorly obtained specimen. Some slides have dense cellularity due to specimens that have not been adequately spread out. Reproducibility is a concern in quantifying eosinophil numbers. Most studies suggest that determination of eosinophil percentages is more reproducible than determining eosinophil numbers, thus affirming the traditional reporting of nasal eosinophils as a percentage(6).

Investigators have shown that nasal eosinophils can be decreased by treatment modalities(7). Persistent out of season nasal eosinophilia has been used as evidence to classify patients as having atypical or mixed form of rhinitis(11). In 2 of the patients described in this report, both allergic and non-allergic features were present. Out of season nasal eosinophil counts in these 2 patients were elevated pointing towards the presence of a mixed form of rhinitis. The third case report had an evolution of increasing tree pollen sensitivity over the time, in combination of features of NARES. This patient had episodes that clinically appeared to be consistent with acute sinusitis, but had repeatedly normal radiographic examinations. Although NARES is often characterized as being highly corticosteroid responsive(12), the second patient did not have sustained clinical improvement on nasal corticosteroid sprays. All of these patients showed some nasal eosinophil count elevations despite the use of nasal and/or oral corticosteroids. Although this could have been due to unreported non-compliance, there is also the possibility of corticosteroid resistance that has been reported in asthmatics(13). Preliminary benefits in using monoclonal anti-IL5 in severe asthmatics who have sputum eosinophilia despite oral corticosteroid treatment(14) point towards a possible role for cytokine specific treatment in certain rhinosinusitis patients who have persistent nasal eosinophilia. Should this cytokine approach be applied to rhinosinusitis, this old tried and true clinical laboratory evaluation may have renewed importance.

References
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