

Original Article

Clinical Characteristics Associated with Conjunctival Inflammation in Allergic Rhinoconjunctivitis

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What is already known about this topic? Conjunctivitis is frequently associated with allergic rhinitis, but cytological studies in patients with both diseases are scarce.

What does this article add to our knowledge? This study analyzed nasal/conjunctival cytology in patients with allergic rhinoconjunctivitis. Male sex and eye itching scores of 3 or more (on a 0-10 scale) were the best predictors for the presence of conjunctival inflammation.

How does this study affect current management guidelines? A large majority of patients with symptoms of allergic rhinoconjunctivitis had no detectable conjunctival inflammation. This could have implications for the use of local anti-inflammatory treatments.

BACKGROUND: Allergic rhinitis affects up to 30% of the general population worldwide and is increasing in prevalence. Among several comorbidities, conjunctivitis is probably the most common and occurs so frequently with allergic rhinitis that the term allergic rhinoconjunctivitis (ARC) has been coined.

OBJECTIVES: The cytological characteristics of conjunctival inflammation in patients with ARC were assessed and then correlated to clinical characteristics.

METHODS: Fifty-one patients with clinically diagnosed ARC (23 men; 32.4 ± 13.5 years old) underwent a detailed clinical history and standard diagnostic allergy workup as well as nasal and conjunctival scraping for cytological analysis. Patients were subdivided into 3 groups on the basis of cytological phenotype: (1) nasal and conjunctival inflammation, (2) nasal inflammation only, and (3) no mucosal inflammation.

RESULTS: Group 1 patients reported significantly higher eye itching scores (5.8 ± 2.9 on a 0-10 scale) than did patients in group 2 (3.8 ± 2.8; $P = .06$) or 3 (2.6 ± 2.9; $P = .018$) and were mostly men (81.8%). Male sex (odds ratio, 8.4; $P = .005$) and

eye itching (odds ratio, 1.3; $P = .019$) significantly correlated with conjunctival inflammation. The odds of exhibiting conjunctival inflammation, at multivariate analysis, increased 13-fold for men and 1.5-fold for each point on the eye itching scale. A cutoff value of 3 or more for eye itching effectively identified patients with conjunctival inflammation.

CONCLUSIONS: Our study demonstrates that some clinical manifestations of ARC correlate well with conjunctival inflammation. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;■:■-■)

Key words: Nasal cytology; Conjunctival cytology; Scraping; Allergic rhinoconjunctivitis

Allergic rhinitis (AR) is a current worldwide health problem. Its prevalence ranges between 5% and 35%¹ within the general population, and this prevalence continues to increase.² The typical nasal symptoms of AR, including itching, rhinorrhea, sneezing, and nasal obstruction, are often accompanied by symptoms in the eye (ie, lacrimation, eye itching, conjunctival hyperemia).³ Some surveys have reported that up to 90% of the patients with AR also suffer from conjunctivitis.⁴⁻⁶ Thus, along with asthma, conjunctivitis represents the most common comorbidity associated with AR; indeed, the term allergic rhinoconjunctivitis (ARC) is commonly used. From a pathophysiological point of view, the diagnosis and management of this association relies on the immunopathological correlation between nasal and conjunctival mucosa, which are directly connected by nasolacrimal ducts^{7,8} and share common allergic inflammation.

The objectives of the present study were to assess the real occurrence of conjunctival inflammation in ARC on the basis of cytological analysis and to establish whether any correlations existed between conjunctival inflammation and clinical manifestations, including symptoms. To address these objectives, we compared the clinical characteristics of patients with ARC with

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Conflict of interest: The authors declare that they have no relevant conflicts of interest.

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Abbreviations used

AR- Allergic rhinitis
ARC- Allergic rhinoconjunctivitis
OR- Odds ratio
SPT- Skin prick test

the presence or absence of nasal and/or conjunctival inflammation determined by cytology. The results of our study identified clinical correlates of conjunctival inflammation, which could have implications for better treatment strategy.

METHODS**Overall design**

Consecutive adult patients suffering from clinically diagnosed ARC were studied by the standard diagnostic workup plus nasal and conjunctival cytology. The study was conducted among outpatients referred to the Rhinoallergy Unit at the University of Bari (Bari, Italy) between April 2013 and March 2014. All patients provided informed consent, and the study was approved by the local Ethical Committee.

Patients and diagnosis

ARC was diagnosed on a clinical basis (eye and nose signs/symptoms) plus at least 1 positive skin prick test (SPT) result. The concordance between SPT results and exposure pattern (eg, pollen count) was also taken into account. The severity and duration of AR were graded according to current Allergic Rhinitis and its Impact on Asthma criteria.³ Patients taking oral/topical antihistamines, topical steroids, or decongestants within the previous 2 weeks were excluded, as well as patients with vernal keratoconjunctivitis or autoimmune diseases. A detailed clinical history was collected, including sex, age, occupation, sports activity, residence (urban/rural), family history for allergic diseases (asthma/rhinitis), suspected or proven aspirin hypersensitivity, and atopic dermatitis in infancy. Symptoms were graded on a 0 to 10 scale for each conjunctival symptom (tearing, red eye, itching, photophobia, burning, and gritty eye) as well as for the 4 nasal symptoms (itching, rhinorrhea, sneezing, and nasal obstruction).

Allergic sensitization was assessed by SPT⁹ using a standard panel of commercial extracts (Stallergenes, Milan, Italy) including house dust mites, grass mix, parietaria, olive, cypress, compositae mix, alternaria, cat/dog dander, Cladosporium, and Aspergillum. ImmunoCAP radioallergen sorbent test was also used as second-level assay when SPT was not feasible or was in disagreement with clinical history (ThermoFisher Scientific, Uppsala, Sweden). Nasal endoscopy was carried out by using a 3.4-mm diameter Vision-Sciences ENT-2000 flexible fibroscope (Vision-Sciences, Inc, Orangeburg, NY) to assess the presence of major alterations such as septal deviation, polyposis, turbinate hypertrophy, or exudation from the ostiomeatal complex.

Cytology

Nasal scraping was performed on the middle third of the inferior turbinate, and conjunctival scraping was performed on the inferior palpebral lid. A Rhino-Probe (Arlington Scientific, Inc, Springfield, Utah) was used without applying local anesthetics. Samples were smeared on a glass slide, air dried, and then stained with May-Grünwald-Giemsa (Carlo Erba Reagents, Milan, Italy). Results were read by a Nikon E600 (Nikon, Ontario, Canada) microscope at a 1000 \times magnification. Fifty fields per sample were evaluated to

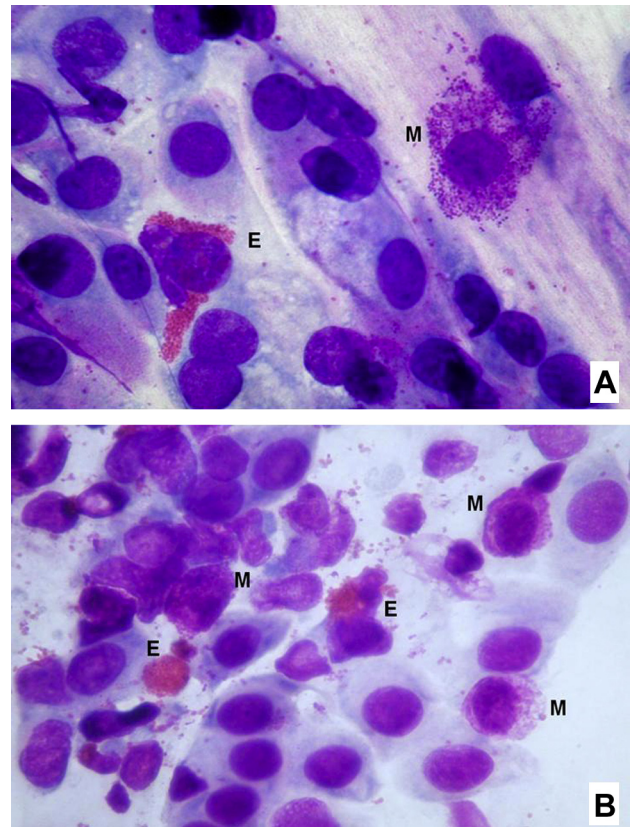


FIGURE 1. Cytology of patients with ARC. All samples were stained with May-Grünwald-Giemsa. Nasal (A) and conjunctival (B) cytology with the presence of eosinophils (E) and mast cells (M). Original magnification: 1000 \times , oil immersion.

identify and quantify cell types. Inflammation was defined by the presence of neutrophils, eosinophils, and mast cells. A semi-quantitative scoring method was used to determine differential counts in both nasal and conjunctival scrapings.^{8,10-12}

Statistical analysis

Within groups, continuous variables were expressed as the mean \pm SD and categorical variables were expressed as a percentage. The ARC patient population was subdivided into the following groups for analysis: (1) presence of nasal and conjunctival inflammation, (2) presence of nasal inflammation only, and (3) absence of nasal and conjunctival inflammation. These groups were compared with each other for age, sex, residency, sports activity, and clinical characteristics. These same parameters were evaluated among the groups using a *t* test. The χ^2 test was used for dichotomous parameters. The ANOVA test was also applied when appropriate. Differences achieving a 2-tailed value of $P < .05$ were considered statistically significant. Symmetry analysis (standard error of skewness) demonstrated that data could be considered as normally distributed. A stem and leaf plot was also constructed.

Univariate and multivariate analysis (binomial logistic regression) was carried out separately for age, sex, and conjunctival symptoms using eye cytology as a dependent variable. After the best predictors were identified by univariate analysis, a binomial logistic regression was performed using conjunctival cytology as the dependent variable and eye itching (range, 0-10) and sex as independent variables.

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