

## Nasal Cytology as a Biomarker of Inflammatory Respiratory Pathology Type 2: Results of a Cross-Sectional Analysis

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### Abstract

The epidemiological, clinical and phenotypic correlation between asthma and chronic rhinosinusitis (CRS), in particular with nasal polyps (CRSwNP), type 2 inflammatory respiratory pathologies, spread and addressed the research for a biomarker able to identify different phenotypes in asthma and CRSwNP at first, but also monitoring the effect of therapy, giving a right prognostic value in treatment. The nasal cytology has been proposed in this study as the biomarker: 31 patients (diagnosed as "severe or difficult-to-control asthma") were subjected to nasal cytology and were divided, on the basis of rhinocyte observation on the optic microscope in 5 categories: NARES (non-allergic rhinitis with eosinophilia), NARMA (NAR with mastocytosis), NARESMA, NARNE (neutrophils) and some patients had a normal cytology.

In the study have been valued: CRSwNP, ASA hypersensitivity atopia, mycotype specific IgE and staphylococcus toxins, total IgE, current and maximum eosinophilic count, oral corticosteroid treatment (OCS), TC score according with Lund-Mackay; it was evaluate the treatment with biological drugs (immunoclonal antibody).

Patients with type 2 inflammatory respiratory pathology with asthma (severe or difficult-to-control) and CRSwNP associated the nasal cytology can provide a differentiation of patients in phenotype with eosinophilia (NARES), from the one with mastocytosis (NARMA). Blood eosinophilia, atopy, ongoing use of systemic treatment (OCS, biological drugs) do not appear to effect on the cytology panel).

**Keywords:** NARES (Non Allergic Rhinitis with Eosinophilia); Nasal Cytology; NARMA (NAR with mastocytosis); Nasal Polyposis; Asthma; Biomarker

### Background

Type 2 (type 2) inflammatory respiratory pathology is accompanied by a close epidemiological, clinical and endotypical correlation between severe asthma and chronic sinusitis (CRS), in particular with the presence of nasal polyposis (NP). The search for

biomarkers who are able not only to identify more appropriately the different phenotypes of patients with asthma and CRS but also to have a prognostic value and an ability to direct the customization of the treatment is one of the most current objectives to be pursued [1,2].

Nasal cytology is a simple, reproducible and non-invasive method, which can be proposed as a type 2 pathology biomarker, especially in the presence of CRS with and without NP [3]. The use of well-defined diagnostic categories from the point of view of cytological vision for chronic non-allergic rhinitis (NAR) facilitate clinical and pathological framing and identify different clinical-inflammatory phenotypes [4,5].

### Materials and Methods

Thirty one (31) patients diagnosed with severe or difficult-to-control asthma (step 5 or 4 according to GINA) and concomitant CRSwNP were subjected to nasal cytology according to a cross-sectional design. Patients were divided into 5 categories according to the predominance of sampled inflammatory cells [5]: NARES (non-allergic rhinitis with eosinophils), NARESMA (eosino-promastocytic non-allergic rhinitis), NARMA (mastocytic non-allergic rhinitis), NARNE (rhinitis non allergic neutrophil) and NORMAL cellularity. NP, ASA hypersensitivity, atopy, mycophyte-specific IgE for moulds and staphylococcal toxins, total IgE, current and maximum eosinophilic count, oral corticosteroid treatment (OCS), TC

score according to Lund-Mackay and treatment with biological drugs were evaluated.

### Results and Discussion

The population analysed had the following characteristics: NP 84%, ASA hypersensitivity 25.8% and atopy (polysensitization to inhalant allergens) 58%. Moulds allergy was reported in 48% of cases, of which 40% (6/15) monosensitization to *Aspergillus fumigatus*. 61% of patients underwent at least one NP surgery and 90% had started (35%) or was about to start (65%) biological therapy. Cytological analysis was compatible with NARES in 32%, NARMA in 45%, NARESMA or NARNE in 9% (3 subjects) and normal in 13% (4 subjects). Average eosinophilia and total IgE total were  $743 \pm 113$  mm<sup>3</sup> and  $492 \pm 135$  KU/l, respectively, while the average Lund-Mackay CT score was  $14.1 \pm 1.2$ . Among the 2 most represented groups, NARES and NARMA, differed significantly in the CT score (18.3 vs.12.6 p = 0.048) and age (48.4 vs 62.4, p = 0.02), while did not differed in total IgE and eosinophilic values, as well as atopy, fungal sensitization, ASA allergy, ongoing OCS or biological therapy, and number of interventions (Figure 1).

Figure 1

## Conclusion

In a cohort of patients with type 2 inflammatory respiratory pathology with severe or difficult-to-control asthma and associated CRS, the use of nasal cytology is able to differentiate a phenotype of patients with predominantly nasal eosinophilia (NARES), younger and with a significantly more severe nasal CT score compared to patients with a larger mastocyte component (NARMA). Peripheral eosinophilia, atopy or the ongoing use of systemic (OCS or biological) treatment do not appear to affect the cytological picture. Further serious studies that correlate cytology with the different clinical-therapeutic phases of rhino-asthmatic pathology are necessary to define its role as a biomarker.

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