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Cell-mediated non-allergic rhinitis in children

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ABSTRACT

Objective: Non-allergic rhinitis is a heterogeneous disease whose etiology is largely unknown. Nasal cytology only allows us to recognize different non-allergic rhinitis forms on the basis of the prevalent inflammatory cell infiltrate: non-allergic rhinitis with eosinophils, with neutrophils, with mast-cells and with both eosinophils and mast-cells. The aim of this study is to define the incidence, clinical features and comorbidity of the different types of cell-mediated non-allergic rhinitis in a pediatric age group.

Methods: One hundred and fourteen non-allergic children with chronic nasal obstruction and associated symptoms (rhinorrhea, sneezing and nasal itchiness) were retrospectively selected. All patients had been submitted to a clinical history, pediatric evaluation, anterior rhinoscopy and fiberoendoscopy, rhinomanometry and nasal cytology.

Results: Non-allergic rhinitis with neutrophils was present in 46 (40.4%) children, non-allergic rhinitis with eosinophils in 53 (46.5%), non-allergic rhinitis with mast-cells in 12 (10.5%) and non-allergic rhinitis with both eosinophils and mast-cells in 3 (2.6%).

Nasal obstruction was prevalent in non-allergic rhinitis with eosinophils and in non-allergic rhinitis with mast-cells patients ($P < 0.001$) whereas rhinorrhea and sneezing only in the form with eosinophils ($P < 0.0001$). Nasal itching on the other hand was prevalent in the form with mast-cells ($P < 0.0003$).

Non-allergic rhinitis with eosinophils group showed a higher probability of asthma ($P < 0.02$) and respiratory sleep disorders ($P < 0.04$).

Conclusions: In the pediatric age group the most frequent forms of non-allergic rhinitis are those with eosinophils or with neutrophils. A diagnosis of non-allergic rhinitis with eosinophils in children presumes more severe symptoms and a higher incidence of pulmonary disease and roncopathy.

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1. Introduction

Rhinitis describes inflammation of the nasal mucosa, clinically defined by several common symptoms such as nasal blockage, nasal discharge, itching and sneezing. There are three types of rhinitis commonly seen in clinical practice: infective, allergic and non-allergic rhinitis (NAR) [1].

NAR is a diagnosis of exclusion characterized by nasal hyper-reactivity and persistent symptoms throughout the year but without allergic sensitization relevant to symptoms and without signs of infection [2].

NAR is a heterogeneous disease whose etiology is largely unknown. In fact for about 75–80% of patients NAR is classified as idiopathic or vasomotor rhinitis. This high percentage of idiopathic

etiology is, at least in part, due to the fact that nasal cytology is very rarely performed. Indeed nasal cytology only allows us to recognize different NAR on the basis of particular inflammatory cell infiltrates: (1) non-allergic rhinitis with eosinophils (NARES) characterized by eosinophil infiltration (Fig. 1); (2) non-allergic rhinitis with neutrophils (NARNE) characterized by neutrophil infiltration (Fig. 2); (3) non-allergic rhinitis with mast-cells (NARMA) infiltrated by mast-cells (Fig. 3); (4) non-allergic rhinitis with eosinophils and mast-cells (NARESMA) characterized by eosinophil and mast-cell infiltration [3].

The importance of identifying allergic and non-allergic subtypes of rhinitis is very important in order to choose an appropriate treatment [4]. Some studies have evidenced the clinical features of the different cell-mediated NAR in adults [3], but there is a relative lack of literature on NAR in children.

The aim of this study is to define the incidence of the different types of cell-mediated NAR in a pediatric age group and to evidence the clinical features, comorbidity and quality of life of each participant.

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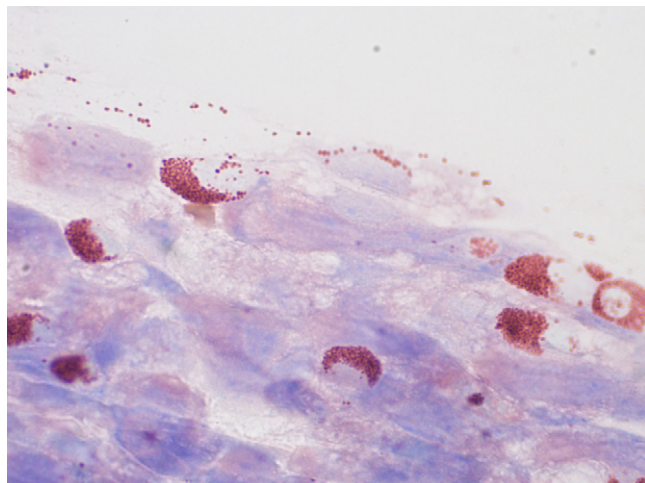


Fig. 1. Rhinocytogram of NARES patient: eosinophils are >20% of nasal mucosa cells (M.G.G. 400×).

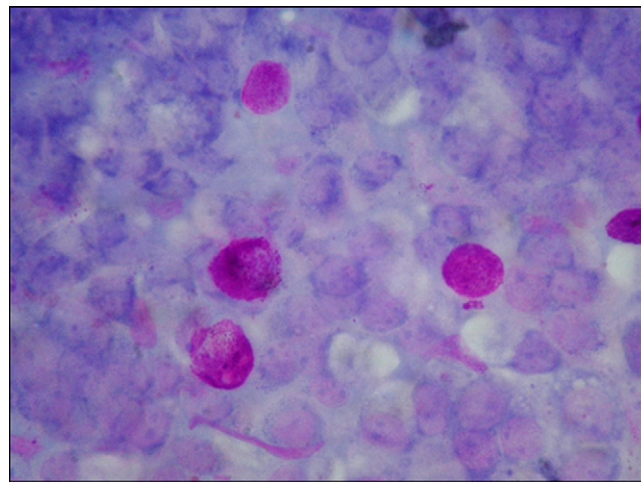


Fig. 3. Rhinocytogram of NARMA patient: predominant mast-cells infiltration (M.G.G. 400×).

2. Materials and methods

From January 2008 to January 2011 all pediatric patients with symptoms of chronic nasal obstruction and symptoms most likely associated with this disorder (rhinorrhea, sneezing and nasal itchiness) were retrospectively selected among the patients of the rhino-allergologic ambulatory of the Department of Otorhinolaryngology of the University of Foggia.

The children had been submitted to:

- *Clinical history*: nasal symptoms were evaluated using an examiner-guided questionnaire investigating the severity of the nasal obstruction, the sneezing, the rhinorrhea, and the nasal itchiness; The presence of snoring and respiratory sleep disorders (referred by parents) was also investigated as well as the impact of the nasal disease on their scholastic education (identified with the days the child was absent from school).
- *Anterior rhinoscopy and fiberendoscopy*: assessment of the nasal cavity and adenoid hypertrophy graded according to the endoscopic Cassano classification (I degree: adenoids occupying 1–25% of the rhinopharyngeal cavity; II degree: adenoids occupying 26–50% of the rhinopharyngeal cavity; III degree: adenoids occupying 51–75% of the rhinopharyngeal cavity; IV

degree: adenoids occupying 75–100% of the rhinopharyngeal cavity) [5];

- *Skin prick allergy test*: to identify allergic subjects;
- Active anterior rhinomanometry performed with a rhinomanometer (Atmos 300, Atmos, Milan, Italy); total nasal resistance baseline at 150 Pa was taken as the reference value;
- *Nasal cytology*: performed by scraping the middle part of the inferior turbinate with a Rhino-Probe. The sample was stratified on a slide, fixed with methanol for 4 min and colored using the May–Grunwald Giemsa staining method. Microscopic observation was performed at 400× magnification to check coloration quality and cell distribution, and at 1000× magnification in immersion to discriminate different cell types and to study the intracellular components. NARES was diagnosed if nasal eosinophils were >20% of total cells recovered on a slide, including both inflammatory and epithelial cells (Fig. 1); NARMA was diagnosed if nasal mast cells were >10% of total cells (Fig. 3). NARNE if neutrophils were >50% of total cells (Fig. 2) and NARESMA when concurrent nasal eosinophils were >20% and mast cells were >10% of nasal cells.
- *Pediatric evaluation*: to identify the presence of bronchial asthma using clinical and spirometric data.



Fig. 2. Rhinocytogram of NARNE patient: neutrophils are predominant without infections (M.G.G. 400×).

Only children with rhinitis symptoms, negative prick tests, and prevalence of a cytotype identifying a diagnosis of non-allergic cell-mediated rhinitis were included in the study. This was in order to highlight the prevalence of the different sub classifications of the disease (NARNE, NARMA, NARES and NARESMA), their comorbidity (bronchial asthma and respiratory problems during sleep) and the impact of each form on the quality of life of the pediatric patients (using as a quantitative parameter their absence from school caused by the disease).

Exclusion criteria were represented by the presence of other allergic diseases (urticaria, angioedema, atopic dermatitis, conjunctivitis, etc.) or systemic (dysmetabolism) and particular pharmacological therapies, which could bias the study (antihistamines, corticosteroids, etc.). Patients were also excluded from the study if a high level of bacteria was present together with neutrophils, which could therefore confuse a NARNE diagnosis with a simple bacterial infective rhinitis.

The study was approved by the Institutional Review Board of the Department of Otorhinolaryngology of the University of Foggia (Italy).

Table 1

Symptoms in the four cytological groups.

	Nasal obstruction			Rhinorrhea	Sneezing	Itching
	Mild	Moderate	Severe			
NARNE (<i>n</i> = 46)	17 (36.9%)	21 (45.7%)	8 (17.4%)	27 (58.7%)	9 (19.5%)	3 (6.5%)
NARES (<i>n</i> = 53)	2 (3.8%)	36 (67.9%)	15 (28.3%)	52 (98.1%)	48 (90.5%)	15 (28.3%)
NARMA (<i>n</i> = 12)	–	8 (66.7%)	4 (33.3%)	7 (58.3%)	8 (66.7%)	7 (58.3%)
NARESMA (<i>n</i> = 3)	1 (33.3%)	2 (66.7%)	–	2 (66.7%)	2 (66.7%)	2 (66.7%)

3. Statistical analysis

Qualitative data (presence of nasal symptoms, asthma and OSAS) were analyzed by the Pearson chi-square test (for *df* = 1 the chi-square value reported is the Yates chi-square, corrected for continuity) or Fisher's exact test.

A Bonferroni correction was applied to obtain *P*-values adjusted for multiple comparisons.

Days of absence from school were analyzed statistically by parametric tests; the analysis of variance (ANOVA) was used to assess heterogeneity between groups, and the Holm's *t* test was used for multiple comparisons. All tests were two-tailed, and the level of significance was set at 0.05.

The data were analyzed by MedCalc 12.2.1.0 (for Windows) and R 2.11.1 (for Linux) statistical softwares on a Debian 6 Operating System.

4. Results

The study group was therefore made up of 114 patients (68 males and 46 females) between 5 and 15 years of age (average age: 9.3) affected by cell mediated non-allergic rhinitis.

Based on the results of the nasal cytological exam participants were divided into 4 groups:

- 1) NARNE was present in 46 (40.4%) children.
- 2) NARES in 53 (46.5%).
- 3) NARMA in 12 (10.5%).
- 4) NARESMA in 3 (2.6%).

The distribution of symptoms and severity of nasal obstruction in each cytological group is reported in Table 1.

Adenoid hypertrophy grading is shown in Table 2.

The rhinomanometry showed average values of total resistance at 150 Pa of 2.11 (standard deviation: 0.55) in NARNE, 2.14 (standard deviation: 0.78) in NARES, 2.44 (standard deviation: 0.58) in NARMA, 2.56 (standard deviation: 0.78) in NARESMA.

Bronchial asthma was present in 7 (15.2%) patients with NARNE, in 21 (39.6%) with NARES, in 2 (16.7%) with NARMA and 1 (33.3%) with NARESMA (Fig. 4).

Sleep respiratory disorders were reported in 12 (26.1%) of the children with NARNE, in 24 (45.3%) with NARES, and 1 (8.3%) with NARMA and none with NARESMA (Fig. 5).

The rhinopathy led to, on average, 30.3 absent days from school (standard deviation: 10.61) for the group with NARNE, 37.5 (standard deviation: 15.5) for the group with NARES, 23.9

(standard deviation: 14.27) for the group with NARMA and 20 (standard deviations: 0) for the group with NARESMA (Fig. 6).

Due to the exiguity of the sample of the group of patients with NARESMA it was not possible to carry out a statistical analysis.

Statistical analysis of symptoms revealed a difference between the various groups: nasal obstruction was prevalent in NARES and NARMA patients ($P < 0.001$) while rhinorrhea only in NARES ($P < 0.0001$ with a standardized residual of +1.66). In addition sneezing mostly affected NARES patients ($P < 0.0001$; standardized residual: +3.02), whereas it was uncommon in NARNE patients (standardized residual: −3.47). Nasal itching was instead prevalent in NARMA ($P < 0.0003$; standardized residual: +2.61) but was uncommon among NARNE patients (standardized residual: −2.29).

Confronting the various groups for bronchial asthma, a significant statistical difference emerged between the NARNE, NARES and NARMA groups ($P = 0.017$). According to the procedure for multiple comparisons in 2×2 contingency tables, the NARES group showed a higher probability of asthma compared to the NARNE and NARMA groups ($P < 0.02$; standardized residual: +1.63).

Regarding the respiratory sleep disorders a significant statistical difference was shown between the four groups ($P < 0.01$). The NARES group presented a higher probability of being affected by respiratory sleep disorders ($P < 0.04$; standardized residual: +1.39) as opposed to the NARMA and NARNE groups. In particular in the NARMA group these disorders were uncommon (standardized residual: −1.5).

Confronting the absent days from school using analysis of variance (ANOVA) and the Holm's *t* test it emerges that there were not significant differences between the NARMA and NARNE group ($P = 0.112$) and that the NARES group presented a higher number of absences compared to the NARMA and NARNE groups ($P < 0.03$).

5. Discussion

Allergy tests in vivo (skin prick test) and in vitro (RAST) are extremely useful in the differential diagnosis between allergic rhinitis and NAR.

Such a distinction is fundamental since the former can make use of specific immunotherapy and the avoidance of the incriminating allergen whilst the latter presents a much longer course [6].

However, non-allergic forms cannot be considered a unique nosological entity since this term includes all the forms of chronic rhinitis in the absence of an allergic sensibility including atrophic,

Table 2

Adenoid hypertrophy grading in the four cytological groups.

	Grade I	Grade II	Grade III	Grade IV	Total
NARNE	–	25 (54.4%)	13 (28.2%)	8 (17.4%)	46 (100%)
NARES	–	4 (7.6%)	34 (64.1%)	15 (28.3%)	53 (100%)
NARMA	–	8 (66.7%)	4 (33.3%)	–	12 (100%)
NARESMA	–	1 (33.3%)	2 (66.7%)	–	3 (100%)

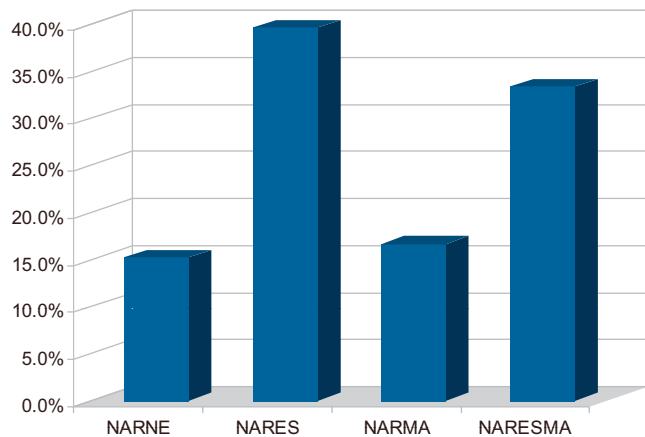


Fig. 4. Prevalence of asthma in the four cytological groups. Fisher's exact test was used to compare the groups: NARES group presented a higher probability of asthma compared to NARNE and NARMA groups ($P < 0.02$).

hormonal, and medical, and a noteworthy amount of so-called idiopathic rhinitis, of which the cause is unknown.

With the coming of nasal cytology the idiopathic forms have found a nosological collocation, for it became evident that patients with a negative prick test result presented a prevalence of a cytotype which influenced the clinical picture, the prognosis and the comorbidity [3]. While the British Society for Allergy and Clinical Immunology of 2010 only placed NARES in its guidelines under the rare forms of non-allergic rhinitis [1], the guidelines of the Italian ARIA 2011 project (www.progetto-aria.it) clearly report a cytological classification of NAR.

We can therefore distinguish 4 forms of cell-mediated NAR:

- NARES is the most widely known and can be associated with the most severe forms of non-allergic asthma, aspirin intolerance and nasal polyposis.
- NARMA.
- NARNE is a form with prevalence of neutrophil infiltration in the absence of infections. The etiology is multifactorial and is usually associated with cystic fibrosis, pollution, cigarette smoke, etc.
- NARESMA is the (fourth) form with a greater severity of symptoms and co-morbidity [3].

The characteristics of these forms have frequently been studied in the adult population but the prevalence and the clinical characteristics have never been studied in pediatric patients.

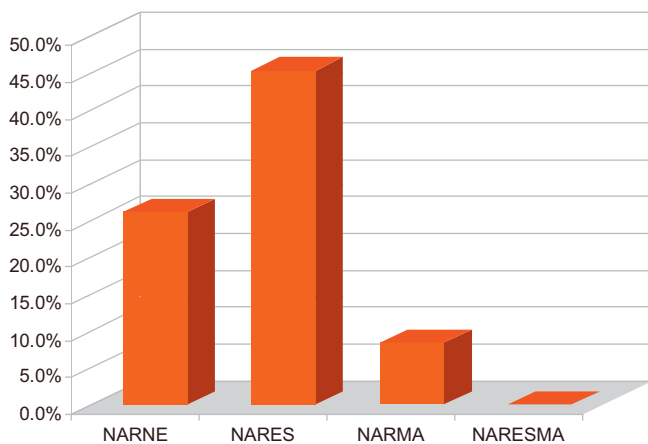


Fig. 5. Prevalence of OSAS in the four cytological groups. Fisher's exact test was used to compare the groups: NARES group presents a higher probability of being affected by respiratory sleep disorders ($P < 0.04$).

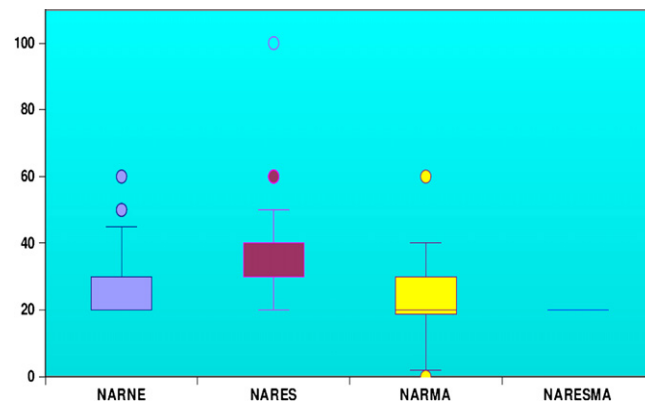


Fig. 6. Days of school absence were compared in the four groups by Holm's t test: NARES groups presented a higher number of absences compared to the NARMA and NARNE groups ($P < 0.03$).

In our study nasal obstruction appeared to be subjectively more important in the NARES and NARMA ($P < 0.001$) forms (in which moderate and severe degrees prevail) compared to the NARNE and NARESMA forms (where severe forms are present in only a very low percentage) even if the rhinomanometric resistances results are very similar (Table 1).

Such data can be connected to the adenoid hypertrophy, present in the highest degrees (III and IV) in 92.4% of the NARES children compared to 45.6% in the NARNE children, even though it is present in lower percentages in the NARMA groups (33.3% and only of III degree) in which all patients present a moderate or severe obstruction (Table 2).

Rhinorrhea is another symptom that is different in the various cytological subpopulations with an almost constant presence in the NARES patients (98.1%) and in percentages slightly higher than 50% in the other forms (Table 1) with a statistically significant difference ($P < 0.0001$; standardized residual: +1.66).

Moreover our study shows that children with NARES, NARMA and NARESMA present a high percentage of sneezing (90.5%, 66.7% and 66.6%, respectively) and nasal itchiness (28.3%, 58.3% and 66.6%, respectively) compared to the NARNE group in which the symptoms appeared in negligible percentages (19.5% for sneezing and 6.5% for nasal itchiness) (Table 1).

A recent study by Vichyanond compares the symptoms and the comorbidity in a group of allergic children and a group of non-allergic children reporting a higher incidence of sneezing and nasal itchiness in the first group and sleep disorders and sinusitis in the second [7]. However, this study does not show a distinction between the various cellular subclasses of NAR.

Studies of the adult and adolescent population have shown a high prevalence of nasal symptoms in allergic patients compared to non-allergic patients [8,9]. The comparison of the NARES and NARMA groups with the allergic patients results in some contrasting conclusions caused by the high percentage of rhinorrhea, sneezing and nasal itchiness in the two subclasses.

Regarding the comorbidity, the various subclasses present different results. In fact bronchial asthma is present in higher percentages in the NARES and NARESMA groups even though it is possible to notice a significant statistical difference only in the NARES group compared to the other groups ($P < 0.02$) (Fig. 4). Therefore, the concept of similar comorbidity for asthma in children with allergic rhinitis and non-allergic rhinitis proved by different authors [7,10] would need to be re-examined comparing just NARES patients to allergic ones.

Even respiratory sleep disorders are prevalent in the NARES group with a significant statistical difference compared to the

other groups ($P < 0.04$) (Fig. 5). Therefore the higher percentages of respiratory sleep disorders in non-allergic children found in Vichyanonds' study [7] is most likely related to the prevalent percentage of NARES children, for in the NARMA group this disorder was practically absent.

The major severity of the symptoms and comorbidity has consequences on the quality of life causing a high number of absences from school. For these reason NARES patients have shown a higher number of school absences related to their diseases with a significant statistical difference compared to the other groups ($P < 0.03$) (Fig. 6).

If we analyze the percentage of children in the various cytological subgroups, it is evident that the majority of non-allergic children presents NARES (46.5%) and NARNE (40.6%) whereas the other two forms are present in a substantially lower percentage (10.5% per NARMA and 2.6% for NARESMA). Such results clearly contrast the data reported by Gelardi et al. in an adult population of 176 patients in which NARES and NARESMA appeared prevalent (29.5% and 28.4%, respectively) but with percentages close to the other two groups (21.6% NARMA and 20.4% NARNE). NARES and NARESMA also reported the worst quality of life and were more frequently associated with nasal polyposis whereas only NARESMA determined major respiratory sleep disorders and bronchial asthma [3]. In children, the NARESMA forms presented with extreme rarity and with fewer major symptoms compared to NARES.

We can, therefore, hypothesize that mastocyte forms have a more belated development determining a major release of mediators (mostly histamine and leukotrienes) which, causing vasodilatation, increase nasal permeability and nervous stimulation and are at the base of the more severe symptoms and the comorbidity of NARMA and NARESMA in adults. In fact Gonzalez de Olano et al. in a study based on the prevalence of allergies and mastocytosis in Spain report the presence of non-allergic nasal mastocytosis (in the article NARMA and NARESMA were not defined) in only 1 out of 7 children with rhinitis (14.28%) in contrast to 24 out of 51 adults (47%) [11].

The presence of eosinophils would induce a more severe inflammation, responsible for the severity of the symptoms as well as being the principle cell in nasal polyps [12]. Such a disease, frequently seen in adults with NARES and NARESMA [3], does not appear in our population, most likely because its development requires more years of rhinopathy.

The role of the eosinophils was underlined by Chawes who found a nasal inflammation caused by eosinophils in a pediatric age group, especially in children with allergic rhinitis [13]. Our study showed that even non-allergic subjects can present a high percentage of eosinophilic inflammation leading to a rhinopathic form (NARES) characterized by more accentuated symptoms and comorbidity.

The presence of NARNE forms in a high percentage of the pediatric population not affected by cystic fibrosis or antrochoanal polyps could be explained by the increase of air pollution, or, as hypothesized by Berger, the presence of gastro-esophageal reflux. This disease is being seen more frequently and can be accompanied by a non-allergic rhinitis with the presence of neutrophils [14].

6. Conclusion

Non-allergic rhinitis can be supported by various cellular populations that influence the gravity of the symptoms and the

comorbidity. In the pediatric age the most frequent forms of non-allergic rhinitis are non-allergic rhinitis with eosinophils (NARES) or with neutrophils (NARNE) whereas the mastocyte forms are rare (NARMA and NARESMA). The cytological diagnosis of the various forms have a fundamental importance especially under the prognostic point of view, for a NARES diagnosis in the pediatric age presumes more severe symptoms and higher incidence of pulmonary disease and associated roncomopathy.

These patients need, therefore, to undergo careful therapy for rhinitis to avoid the development of nasal polyps, a frequent complication found in adult patients with NARES. These patients are usually affected by asthmatic symptoms and therefore would also need to be monitored by a pediatric broncho-pulmonologist.

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Conflict of interest statement

No author has any personal or financial relationship with other people or organization that could inappropriately influence the work.

References

- [1] E. Angier, J. Willington, G. Scadding, S. Holmes, S. Walker, British Society for Allergy & Clinical Immunology (BSACI) Standards of Care Committee, Management of allergic and non-allergic rhinitis: a primary care summary of the BSACI guideline, *Prim. Care Respir. J.* 19 (2010) 217–222.
- [2] J. Bousquet, W. Fokkens, P. Burney, S.R. Durham, C. Bachert, C.A. Akdis, et al., Important research questions in allergy and related diseases: non-allergic rhinitis: a GA2LEN paper, *Allergy* 63 (2008) 842–853.
- [3] M. Gelardi, A. Maselli del Giudice, M.L. Fiorella, R. Fiorella, C. Russo, P. Soleti, et al., Non-allergic rhinitis with eosinophils and mast cells constitutes a new severe nasal disorder, *Int. J. Immunopathol. Pharmacol.* 21 (2008) 325–331.
- [4] M. Nassef, G. Shapiro, T.B. Casale, Respiratory and Allergic Disease Foundation, Identifying and managing rhinitis and its subtypes: allergic and nonallergic components – a consensus report and materials from the Respiratory and Allergic Disease Foundation, *Curr. Med. Res. Opin.* 22 (2006) 2541–2548.
- [5] P. Cassano, M. Gelardi, M. Cassano, M.L. Fiorella, R. Fiorella, Adenoid tissue rhinopharyngeal obstruction grading based on fiberoendoscopic findings: a novel approach to therapeutic management, *Int. J. Pediatr. Otorhinolaryngol.* 67 (2003) 1303–1309.
- [6] G.K. Scadding, Non-allergic rhinitis: diagnosis and management, *Curr. Opin. Allergy Clin. Immunol.* 1 (2001) 15–20.
- [7] P. Vichyanond, C. Suratannon, P. Lertbunnaphong, O. Jirapongsananuruk, N. Visitsunthorn, Clinical characteristics of children with non-allergic rhinitis vs with allergic rhinitis, *Asian Pac. J. Allergy Immunol.* 28 (2010) 270–274.
- [8] C. Bachert, P. van Cauwenberge, J. Olbrecht, J. van Schoor, Prevalence, classification and perception of allergic and nonallergic rhinitis in Belgium, *Allergy* 61 (2006) 693–698.
- [9] E. Mølgaard, S.F. Thomsen, T. Lund, L. Pedersen, H. Nolte, V. Backer, Differences between allergic and nonallergic rhinitis in a large sample of adolescents and adults, *Allergy* 62 (2007) 1033–1037.
- [10] B.L. Chawes, K. Bønnelykke, E. Kreiner-Møller, H. Bisgaard, Children with allergic and nonallergic rhinitis have a similar risk of asthma, *J. Allergy Clin. Immunol.* 126 (2010) 567–573.
- [11] D. González de Olano, B. de la Hoz Caballer, R. Núñez López, L. Sánchez Muñoz, M. Cuevas Agustín, M.C. Diéguez, et al., Prevalence of allergy and anaphylactic symptoms in 210 adult and pediatric patients with mastocytosis in Spain: a study of the Spanish network on mastocytosis (REMA), *Clin. Exp. Allergy* 37 (2007) 1547–1555.
- [12] G. Ciprandi, A. Vizzaccaro, I. Cirillo, M. Tosca, A. Massolo, G. Passalacqua, Nasal eosinophils display the best correlation with symptoms, pulmonary function and inflammation in allergic rhinitis, *Int. Arch. Allergy Immunol.* 136 (2005) 266–272.
- [13] B.L. Chawes, E. Kreiner-Møller, H. Bisgaard, Objective assessments of allergic and nonallergic rhinitis in young children, *Allergy* 64 (2009) 1547–1553.
- [14] W.E. Berger, J.E. Schonfeld, Nonallergic rhinitis in children, *Curr. Allergy Asthma Rep.* 7 (2007) 112–116.