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EPIDEMIOLOGICAL STUDY ON NORTH ITALY POPULATION AFFECTED BY ALLERGIC (AR) AND NON ALLERGIC RHINITIS (NAR)

Cristiano Lingua *, Alberto Macchi§, Anna Miglietta°, Claudio La Melia°, Michela Mancini **, Giulia Gramellini°, Flavio Arnone §§, Paola Terranova §, Elena Digilio §, Paola Rosso***

°Libero professionista Verona, §ASST Settelaghi Varese-Università degli Studi dell'Insubria Varese, °°Dept of ENT Ausl Imola,** Libero Professionista Rimini, °°°ASST Grande Ospedale Metropolitano Niguarda Milano, §§ Clinica Univesitaria ORL- Ospedale San Paolo di Milano, *Reparto ORL Ospedale Santa Croce e Carlo Cuneo, ***U.O. ORL Ospedale Civico di Chivasso (TO)

Key Words: NAR, cellular rhinitis, nasal cytology, NARESMA

ABSTRACT

An epidemiologic study on patients with NAR is done by collecting the results of 4529 patients. The prevalence was of 2293 males (50,63%) and 2236 females (49,37%) with a mean age of 38 years old. The overlapping types of rhinitis can definitely explain the therapeutic failure of immunotherapy in some patients despite the fact that they are IgE sensitized, since immunotherapy is useful only for IgE-mediated component. Furthermore the percentages of asthma and polyposis has been shown to be significantly higher than in typical allergic rhinitis, therefore it may be important to clearly identify those patients.

The aetiology of NAR is still largely unknown is still classified as idiopathic or vasomotor rhinitis. This high percentage of idiopathic aetiology is, at least in part, due to the fact that nasal cytology is very rarely performed. Indeed, nasal cytology only allows to recognize and identify the different types of NAR on the basis of the particular inflammatory cell infiltrate but in the future it could become a fundamental diagnostic examination in order to tailor a specific treatment upon every patient.

Introduction

Rhinitis is a very common finding in our daily practice since it affects about 10-20% of world population of all age. There are

two different types of rhinitis defined by the presence or absence of specific serum

IgE. Allergic rhinitis (AR) affects 35% of world population. Non-Allergic Rhinitis

(NAR) is an heterogeneous disease, characterized by nasal hyperreactivity that results in typical symptoms due to irritation, such as rhinorrhea, sneezing, and/or nasal obstruction due to vasodilatation. Diagnosis of NAR is based on persistent symptoms throughout the year after excluding an infection and any anatomical or medical disorder, and evidence of absence of serum specific IgE to relevant aeroallergens and it seems to affect about 25% of all rhinitic patients.

The aim of this study is to define an epidemiologic study of the patients with NAR.

Materials and methods

An epidemiologic study was conducted in the northern regions of Italy on an heterogeneous group of 4529 adult patients that were invited to undergo a cytological examination on their nasal mucosa.

The prevalence was of 2293 males (50,63%) and 2236 females (49,37%) with a mean age of 38 years old.

All patients underwent the nasal mucosa scraping and the sample was sent for cytological examination.

All samples were taken without using any kind of anaesthesia, scraping the Rhino-Probe device on the central portion of the inferior turbinate (area that usually is

characterized by a huge number of nasal cells) and brushing the collected material on a slide. After fixing the slide they were coloured using the May- Grünwald-Giemsa system.

The microscopic observation was done at 400X in order to check the coloring quality and the cells distribution; then at 1000X, in immersion, in order to discriminate between the different types of cells: eosinophils, mastocytes, neutrophils, bacteria and spores; with the aim to calculate their percentages, comparing the number of total leucocytes and analyze the intracellular components ¹.

Results

From the collected data it was seen that among all patients the number of those affected by NAR was largely higher than those affected by AR (1778 vs 835).

24,10% has an increase of eosinophilic cells (NARES), 5,12% show the presence of mastocytes (NARMA), 8,42 .% has an increased number of neutrophils and in 9,87%patients there were both increased mast cells and eosinophils (NARESMA) (Tabella 1) .

The presence of the overlapping of both rhinitis (NAR and AR) was affecting 53 patients, representing only the 1,17% of the examined population.

CYTOLOGICAL EXAM	Number	%
NARMA	233	5,12
NARES	1096	24,10
NARESMA	449	9,87
INFECTION	76	1,69
NARNE	383	8,42
OVERLAPPING	53	1,17
NORMAL	1309	29,18
ALLERGIC	835	18,36
METAPLASIA	56	1,23
SPORE	19	0,42
LYMPHOCYTOSIS	20	0,44
TOTAL	4164 (?)	

Tabella 1. General results on the cytological examination of the nasal discharge

The mean age calculated is 38 years old for all categories, the mean age calculated on the gender type is similar in all analyzed groups, the gender prevalence is 1:1.

	Nares	Narma	Narne	Naresma
Total (M + F)				
Number	1096	233	383	449
Age mean	37,5	39	38,15	38,1
Range	1 - 91	1 - 81	2 - 91	1 - 80
Males				
Number	525	119	182	224
Age mean	37	38	39	37
Range	1 - 91	1 - 81	2 - 91	1 - 80
Females				
Number	571	114	201	225
Age mean	38	39	38	39,42
Range	1 - 91	1 - 79	2 - 74	1 - 78

Tabel 2. Population data partition in relation to the diagnosed rhinitis

Discussion

An everyday observation in clinical practice is the presence of patients with seasonal allergic rhinitis with nasal symptoms also when the exposure to the allergens is totally absent, out of the pollen season. These patients have a sensitivity to not specific stimuli, such as sudden temperature changes, strong smells or smoke.

In these patients nasal cytology can be useful if done out of pollen season in order to identify non allergic components. Inflammatory cells in nasal scraping (in absence of air pollens) define non allergic rhinitis (NAR) overlapping the allergic rhinitis.

Three main types of NAR characterized by distinct inflammatory cell infiltrate have

been defined: NARES non-allergic rhinitis with eosinophils' infiltration, NARMA non-allergic rhinitis with mast cells' infiltration initially described by Connell ² , and NARNE non-allergic rhinitis with neutrophils' infiltration, characterized by predominant neutrophilic inflammation without infections. These forms of NAR are characterized by a local inflammation that appears to be the main underlying pathogenetic mechanism. NARES is characterized by a profound nasal eosinophilia (>20% of the cells present in the mucosa), not associated

with allergic disease. NARES may be prevalent in up to one-third of adults, and in severe cases may be associated with non-IgE-mediated asthma, aspirin intolerance and nasal polyps ³. A fourth type of NAR is characterized by the simultaneous infiltration of eosinophils and mast cells: non-allergic rhinitis with eosinophils and mast cells, NARESMA.

The nasal mucosa is characterized by a ciliated pseudo-stratified epithelium which is composed of ciliated mucous-secreting cells, striated and basal. The ciliated cell is the most differentiated element of the nasal mucosa ⁴ and, together with mucous-secreting cells, it represents the first-line defence of the airways (the so-called mucus-ciliated system). The diagnosis of nasal disorders through nasal cytology is based on the consideration that, in healthy subjects, the nasal mucosa is composed by four normal subsets of cells, which commonly characterize the pseudo-stratified epithelium; besides neutrophils, no other cells are detected in healthy individuals. Therefore, on a rhinocytogram, the presence of eosinophils, mast cells, bacteria, spores and fungi has to be considered as a clear sign of nasal pathology.

Nasal cytology was introduced in 1889, when Gollash highlighted the presence of numerous eosinophils in the nasal

secretions of an asthmatic patient and suggested that these cells could be the key elements for the pathogenesis of the disease ⁵. Eyer mann, in 1927, detected the presence of granulocyte eosinophils in the nasal secretions of allergic patients and showed their importance in diagnosing the disease ⁶. Thanks to this discovery, a great value was attributed to the identification of specific cellular subsets related to different nasal pathologies ^{7,8,9}, and this consideration opened the way to the routine use of nasal cytology in the study of allergic and non allergic, infectious and inflammatory rhinitis. Different factors have been responsible for the increased interest for this diagnostic tool and its widespread use: on one hand, the fact that the technique is easy to perform, and, on the other hand, that it is a non-invasive approach. Therefore, this tool may be easily repeated on the same patient, with is essential both in the follow-up of the disease and to monitor the efficacy of medical and surgical interventions. Based on the fact that this method is simple, safe, non-invasive and poorly expensive, it could be routinely used in outpatient clinics at all ages, even in children ¹⁰.

The following steps characterize the cytological technique: sampling, processing (with fixing and staining), and

observation through microscopy. The cytological sampling consists of collecting the nasal mucosa surface cells and it can be performed either through the use of a sterile swab (such as an oro-pharyngeal swab) or a small scraper made of disposable plastic such as the Rhinoprobe (Arlington Scientific, Springville, UT, USA) ^{11,12}. Sampling collection may be even done by scraping the middle portion of the inferior turbinate, where there is an optimal ratio between ciliated and mucous-secreting cells, usually in favour of ciliated cells. Nevertheless, on a routine basis, nasal swab is preferred to scraping, since it is easier and less troublesome, using the latter only when investigating more collaborative patients. The sampling step must be carefully performed through anterior rhinoscopy, using a nasal speculum and good lighting. As mentioned before, it is a minimally invasive method, so that local anaesthesia is usually not required.

When the sampling is obtained, the material is placed on a glass slide, fixed by air drying and stained by May-Grunwald-Giemsa (MGG) method, which allows the detection of all the cellular components of the nasal mucosa, including those cells that are associated to the immune inflammation process (such as neutrophils, eosinophils, lymphocytes and

mast cells), and bacteria, spores and fungi. Staining usually requires about 30 min; nevertheless, new staining systems are currently available (MGG QUICK STAIN Bio-Optica, Milan, Italy), allowing completing such step in less time.

Conclusions

This study showed a very high incidence of NAR among the sample analyzed, representing more than twice the AR group, and this means that there is a huge number of patients affected by an unknown cellular rhinitis, since the nasal cytology is not a commonly used examination. The overlapping types of rhinitis can definitely explain the therapeutic failure of immunotherapy in some patients despite the fact that they are IgE sensitized, since immunotherapy is useful only for IgE-mediated component. Furthermore the percentages of asthma and polyposis has been shown to be significantly higher than in typical allergic rhinitis, therefore it may be important to clearly identify those patients ¹³. The aetiology of NAR is still largely unknown is still classified as idiopathic or vasomotor rhinitis. This high percentage of idiopathic aetiology is, at least in part, due to the fact that nasal cytology is very rarely performed. Indeed, nasal cytology only allows to recognize and identify the

different types of NAR on the basis of the particular inflammatory cell infiltrate but in the future it could become a fundamental diagnostic examination in order to tailor a specific treatment upon every patient.

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