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LETTER TO THE EDITOR

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Local allergic rhinitis: considerations

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ABSTRACT

The term "local allergic rhinitis" has gained popularity as a clinical entity in recent years. Despite the apparent contradiction in the definitions of "nasal" and "local," we offer insights based on our extensive experience in the field. Local allergic rhinitis has been recognized and treated for many years, so it is not a new discovery. The nasal provocation test, which was introduced in the 1980s, was critical in identifying allergic rhinitis cases with suggestive symptoms but negative allergy tests. Our reflections aim to contribute to a precise terminological decision that is consistent with various points of view.

Key words: local allergic rhinitis; rhinitis; naso-sinus pathologies.

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We present our perspective on this topic, discussing our clinical experience and referencing pertinent scientific literature to foster a terminological decision regarding this clinical entity, considering diverse viewpoints.

From the initial publications by Carmen Rondón and collaborators [1,2], our contention has not been the existence of this rhinitis type but rather the terminology employed to define it. The term "local allergic rhinitis" (LAR) appears redundant, as rhinitis inherently implies inflammation confined to the nasal cavities or, at most, the paranasal sinuses. Analogously, one might consider designating atopic dermatitis as "local allergic dermatitis," rendering the term "atopic rhinitis" more fitting for what is termed "local allergic rhinitis".

As otorhinolaryngology specialists with a focus on allergy and immunology, influenced by the pioneering work of Prof. Crifò [3] in the 1970s, we acknowledge the existence of this rhinitis type. However, labeling it "local allergic rhinitis" diminishes the immunological role of the nasal mucosa. In our view, atopy is the genetic predisposition to sIgE production; sensitization, with the consequent presence of type 2 helper T cell inflammatory pattern, production of specific IgE and cytokines responsible for clinical symptoms, can occur primarily either at the skin, lower airways or nasal mucosa level. In other words, allergic rhinitis (AR) cannot exist without atopy because atopy is encoded in our genes, but it can exist without systemic atopy markers, i.e., in a localized form. Prof. Crifò [3] contributed significantly to the development and standardization of the nasal provocation test (NPT). Dr. Rondón and collaborators [1] posit that a positive NPT with local production of tryptase, ECP, and specific IgE identifies patients with "local allergic rhinitis," characterized by suggestive nasal symptoms but negative skin tests, PRIST, and RAST. Prof. Crifò's scientific rationale for the NPT emphasizes the nose as a primary site for specific IgE production and IgE-allergen interaction; only later the surplus of IgE and inflammatory mediators, through systemic circulation, will colonize lower airways mucosa and skin. However, verification of this assumption is challenging due to medical ethics precluding the non-treatment of diagnosed nasal allergy patients.

Notably, long-term follow up studies [4] by Rondón-Campo at 5 and 10 years from the local allergic rhinitis diagnosis indicate a similar rate of development of systemic markers of atopy in LAR and controls. Atopy appears confined to the nasal cavities, aligning with the analogy to atopic dermatitis without the need for redundant terms.

The recent proposal to term the clinical picture with positive skin tests and local IgE production "dual allergic rhinitis" [5] adds further complexity to the terminology, potentially complicating therapeutic approaches. For additional insights into the nasal secretions' allergic reaction mediators and specific IgE levels, please refer to the paper published in 2004 by our research group in collaboration with the University of Siena, the Institute of Pediatrics of the University of Perugia, and the Department of Experimental Medicine of the University of L'Aquila [6].

The preceding discussion aims not only to provide a semantic clarification but also to elucidate and emphasize the pathogenetic mechanisms underlying localized sensitization. In this context, the term "local allergic rhinitis" should be regarded as a new endotype of allergic rhinitis, assuming the endotype denotes a specific underlying pathophysiologic mechanism.

Younger readers might be unfamiliar with von Mutius' [7] outdated studies that once supported the multifactorial nature of allergic rhinitis, akin to asthma and atopic dermatitis, influenced by familial (genetic) and environmental factors. Our stance aligns with contemporary research focusing on the immunological barrier function of the upper airways mucosa, analogous to asthma and other inflammatory diseases at the interface between self and non-self [8].

Precision medicine, the future of our profession, relies on deep patient phenotyping, collecting medical history, lifestyle, physical examination, basic laboratory tests, imaging, functional test results, immunology-histology data, and "omics" data. "Multi-omics" refers to high-throughput technology characterizing a set of molecules relevant to a field of biology such as inflammation, oxidative stress, immune reaction, *etc*. It encompasses a variety of "omes": genome, epigenome, transcriptome, proteome, metabolome, microbiome, and exposome.

In essence, a comprehensive understanding of genetics, epigenetic changes, mRNA expression, proteins, enzymes, metabolites, and the microbiome will illuminate the pathophysiological processes leading to both AR and LAR.

At present, hypotheses based on upper airway microbiome studies suggest that a healthy nasal microbiome serves as the primary defense of the upper airways, constituting the outermost layer of the mucosal barrier [9]. Conversely, nasal microbiome dysbiosis has been implicated in the pathophysiology of various airway diseases, including chronic rhinosinusitis (CRS), asthma, AR, bronchitis, the flu, and otitis media [10].

Authors have reported differential microorganisms and perturbed metabolic pathways in AR patients, influencing immune regulation [11]. Understanding the airway microbiota's role may modulate therapeutic strategies for different AR subtypes and elucidate the contrasting prevalence of LAR. In a Spanish rhinitis population, LAR was diagnosed in 25.7% of subjects [2]. Conversely, Eckrich and colleagues [12] questioned the existence of LAR in a German non-selected student population, finding nasal IgE in subjects positive for house dust mite prick tests, but absent exclusive local IgE production.

Hypothesizing that distinct antibiotic usage patterns in Spain and Germany may alter nasal microbiota and impact local immunological processes, these conflicting results underscore the necessity for a "multi-omics" approach in naso-sinus pathologies, given the nasal mucosa's potential and complexity as a barrier between our body and the environment.

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