

LOCAL ALLERGIC RHINITIS – A NEW PHENOTYPE OF ALLERGIC RHINITIS

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ABSTRACT

Local allergic rhinitis is a new phenotype of rhinitis. The purpose of this review is to discuss the aetiopathophysiology and clinical picture that underlies this form of rhinitis that is typically associated with non-atopic non-allergic rhinitis subjects.

INTRODUCTION

Allergic rhinitis is an IgE-mediated inflammatory response of the nasal mucosa after allergen exposure characterised by symptoms that include nasal obstruction, rhinorrhoea, itching and sneezing. The diagnosis is based on a thorough history, clinical examination, and positive skin-prick testing (SPT) or serum specific IgE (sIgE) antibodies to aero-allergens.

In non-allergic rhinitis (NAR), an allergic cause has been ruled out after negative SPT and the absence of sIgE antibodies to aeroallergens. Many subjects previously diagnosed with NAR, when challenged, developed typical local nasal allergic symptoms, with production of sIgE.^{1,2} It is hypothesised that allergic T-helper cell type 2 (Th2) disease pathways could be present in the nasal mucosa of patients with 'non-allergic rhinitis', despite the absence of systemic atopic responses. The term *local allergic rhinitis* has been proposed to describe this concept of localised allergic responses in the absence of systemic atopy.³⁻⁵

LOCAL IgE RESPONSES IN NASAL MUCOSAL SURFACES

Huggins and Borstoff,⁶ in 1975, showed that subjects with clinical histories suggestive of house-dust mite allergy, when challenged nasally with *Dermatophagoides pteronyssinus*, developed typical nasal symptoms and sIgE in nasal secretions, despite having negative SPT and sIgE ('local entropy paradigm'). Subsequent studies on patients with idiopathic rhinitis showed that a large proportion of these subjects shared a localised Th2, IgE-mediated cellular immunopathogenesis similar to allergic rhinitis subjects. Nasal biopsy studies show increased numbers of IgE cells, eosinophils, mast cells and T cells in both idiopathic rhinitis and allergic rhinitis groups when compared to healthy controls.⁷⁻⁹ Sensi *et al.*¹⁰ proposed that systemic IgE-levels in subjects with allergic rhinitis result from surplus nasal mucosa-produced IgE from B-lymphocytes that enter the systemic circulation.

DIAGNOSIS OF LOCAL ALLERGIC DISEASE IN NON-ATOPIC PATIENTS

As sensitised non-atopic patients express the same allergic-type physiological responses to nasal provocation as subjects with allergic rhinitis, the diagnosis is **clinical** and not difficult to make.

The **history** includes complaints of intermittent (seasonal) or constant (perennial) nasal itching, sneezing, discharge and blockage of varying degrees. On examination, **anterior** and **posterior rhinoscopy** show congested ('boggy'), blue-grey inferior and middle turbinates with increased vascularity and excessive watery secretions. In longstanding cases, mucosal disease can be visualised endoscopically in the middle meatus of the nose.

Nasal **provocation testing** and **rhinometry** in sensitised non-atopic individuals express identical allergic-type physiological responses to those of allergic rhinitis patients, characterised by nasal itching, sneezing, discharge and blockage with impaired airflow as measured objectively.^{11,12} **Diagnostic measurement of local sIgE** and other mediators of tissue inflammation (interleukin-1 β (IL-1 β), IL-8, tumour necrosis factor (TNF), eosinophil cationic protein (ECP) and tryptase) is reported to be more sensitive than serological detection, provided appropriate sampling methods are followed to avoid false-negative results due to dilutional effects.¹³ Newer polyurethane foam sampling techniques have been shown to be superior to nasal lavage, as no dilution of inflammatory proteins took place.¹⁴ **Flow cytometry studies** of nasal lavage after allergen challenge in sensitised non-atopic patients showed active involvement of eosinophils and basophils, and CD4+ and B-lymphocyte profiling pointed to a localised CD4+ Th2-IgE-mediated cellular immunopathogenesis.¹ **Immunohistochemical studies** by Powe *et al.*¹⁵ on patients with idiopathic rhinitis showed increased numbers of mast cells and eosinophils, underscoring the importance of these effector cells in the pathophysiology of non-allergic idiopathic rhinitis.

THERAPEUTIC MANAGEMENT OF LOCAL ALLERGY IN NON-ATOPIC PATIENTS

Local treatment of the nose, the target organ, makes common sense. Topical corticosteroids are effective, generally safe and address all of the four main symptoms of allergic rhinitis as well as NAR (congestion, rhinorrhoea, sneezing, post-nasal discharge).¹⁶ **Antihistamines** work in a percentage of NAR patients as they suppress symptoms arising from IgE-dependent as well as IgE-independent mast-cell activation.¹⁶ As IgE could be an independent sensitiser of mast cells and basophils, monoclonal anti-IgE antibodies can be of value to address nasal and resultant bronchial hyperresponsiveness.¹⁷

LONG-TERM FUTURE PROSPECTS

It is generally accepted that there is a definite relationship between local mucosal IgE-production with expression of allergic disease in atopic subjects. There is however no consensus regarding the underlying aetiopathophysiology of local mucosal allergic responses in non-atopic 'non-allergic' rhinitis patients and further studies in this regard will have to be done. Rondón *et al.*¹⁸ showed that 24% of patients with NAR underwent *de novo* sensitisation to aero-allergens as demonstrated by SPT and/or sIgE and concluded that

local allergic rhinitis (entopy) may evolve into systemic allergy (atopy).

CONCLUSIONS

The term entopy describes a local mucosal allergic type response in non-atopics and this new entity shares clinical symptoms, nasal production of IgE, and a Th2 nasal inflammatory pattern with classic allergic rhinitis. This entity furthermore supports the idea that localised allergy and atopy can occur independently and that this response could also apply to other mucosal sites, as well as the skin.

Declaration of conflict of interest

The author declares no conflict of interest.

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