ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Sublingual immunotherapy in the management of local allergic rhinitis in childhood: a case report

Imunoterapia sublingual no tratamento da rinite alérgica local na infância: relato de caso

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ABSTRACT

Local allergic rhinitis (LAR) is a recently defined rhinitis phenotype, and its diagnosis represents a major challenge for both physicians and patients. LAR shows no evidence of systemic sensitization and is therefore often inappropriately classified as non-allergic rhinitis. This rhinitis phenotype shows a nasal T2 allergic inflammatory response and local IgE synthesis, and nasal allergen challenge is considered the gold standard method for its diagnosis. LAR has clinical features similar to those of other rhinitis phenotypes, and due to diagnostic difficulties, it is underdiagnosed in all age groups. The correct phenotypic diagnosis of LAR offers potential benefits for patients not only by enabling the implementation of care to reduce environmental exposure to identified allergens, but mainly by allowing allergen-specific immunotherapy.

Keywords: Allergic rhinitis, dust mite allergy, child, sublingual immunotherapy.

RESUMO

A rinite alérgica local (RAL) é um fenótipo de rinite definido recentemente e seu diagnóstico configura um grande desafio tanto para médicos, como para os seus pacientes. A RAL não apresenta evidências de sensibilização sistêmica e, por essa razão, é frequentemente classificada de forma inadequada como uma rinite não alérgica. Este fenótipo de rinite apresenta resposta inflamatória alérgica T2 nasal e síntese local de IgE específica, sendo que o teste de provocação nasal específico é considerado o método padrão ouro para realizar o seu diagnóstico. A RAL possui características clínicas semelhantes aos outros fenótipos de rinite, e pela dificuldade diagnóstica é subdiagnosticada em todas as faixas etárias. O diagnóstico fenotípico correto da rinite tem potenciais benefícios para os pacientes, não apenas por possibilitar a implementação de cuidados para a redução da exposição ambiental aos alérgenos identificados, mas principalmente por permitir a realização de imunoterapia alérgeno específica.

Descritores: Rinite alérgica, alergia a ácaros, criança, imunoterapia sublingual.

Introduction

Local allergic rhinitis (LAR) is a recently defined rhinitis phenotype whose diagnosis poses a major challenge for both physicians and patients. Because there is no evidence of systemic sensitization in LAR, it is often misclassified as non-allergic rhinitis. It presents with a nasal type 2 allergic inflammatory response and local synthesis of specific IgE.[1] A specific nasal allergen challenge is considered the gold standard diagnostic method.[2,3] The clinical characteristics of LAR are similar to other rhinitis phenotypes[1] and, due to diagnostic difficulty, it is underdiagnosed in all age groups. In adults, it is estimated that up to 50% of rhinitis patients without systemic sensitization could be diagnosed with LAR .[4] In children, a recent systematic

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review[5] found great variability in the prevalence of LAR, being higher in Western countries (22.3% to 83.3%) than Eastern countries (3.7% to 16.6%). In Brazil, the incidence of LAR among children and adolescents has been estimated at 40% in a tertiary allergy and immunology service among patients with rhinitis and without systemic sensitization.[6]

The correct phenotypic diagnosis of rhinitis can benefit patients, not only by enabling care implementation through reducing environmental exposure to identified allergens, but by allowing allergen-specific immunotherapy.

Case description

This case report describes a 14-year-old female patient with sporadic rhinitis symptoms that began at approximately 2 years of age and were associated with weather changes. At 8 years of age, the symptoms became more frequent, and treatment with a topical nasal corticosteroid (budesonide) and oral antihistamines was initiated.

At 11 years of age, due to persistent symptoms, the patient was referred to a tertiary allergy and immunology service. During the etiological investigation, she showed no positive response to systemic sensitization tests (ie, an immediate hypersensitivity skin test and specific serum IgE measurement) for the following allergens: *Dermatophagoides pteronyssinus*, *Blomia tropicalis*, *Blattella germanica*, *Periplaneta americana*, dog epithelium, cat epithelium, and a mix of fungi. An endoscopic evaluation of the upper airway (nasofibroscopy) ruled out other local diseases that could explain or contribute to the lack of therapeutic response.

During the first months of follow-up, despite treatment with a combination of leukotriene receptor antagonists and corticosteroids + nasal antihistamine (fluticasone + nasal azelastine), the symptoms and frequent need for oral antihistamines persisted, including a nasal symptom score of 6 (on a scale of 0 to 12), which indicated uncontrolled severe rhinitis.

Thus, the etiological investigation was continued by performing a multiple specific nasal allergen challenge with *Dermatophagoides pteronyssinus* and *Blomia tropicalis* (FDA ALLERGENIC Brazil, 5000 UBE/ml) according to a previously validated protocol for children and adolescents.[6] This test consists of sequentially increasing concentrations of the allergens (bilateral nasal spray) in 15-minute intervals during the same visit. The results were monitored subjectively by a symptom questionnaire and objectively by acoustic rhinometry (Figure 1).

The nasal allergen challenge results were negative for *Dermatophagoides pteronyssinus* and positive for *Blomia tropicalis* at a concentration of 1:100, which was documented through acoustic rhinometry by a 32% volume reduction in the first 5 cm of the nasal cavity (V5)(Figure 2A).

After LAR was confirmed, sublingual immunotherapy for *Blomia tropicalis* (IPI ASAC Pharma, Brazil) was initiated. Nasal symptoms were partially reduced after the fourth month of treatment (nasal symptom score = 4) and progressed to adequate control beginning in the ninth month of sublingual immunotherapy (nasal symptom score = 3), allowing a gradual reduction in medication, including topical nasal corticosteroids; oral antihistamines were used only as needed.

After 18 months of sublingual immunotherapy, the patient remained in the maintenance phase with controlled nasal symptoms (nasal symptom score = 3), only occasionally using oral antihistamine. At this point, new multiple nasal allergen challenges were performed with *Dermatophagoides pteronyssinus* and *Blomia tropicalis*, both of which were negative (Figure 2B).

Discussion

The present case highlights not only the difficulties in diagnosing LAR, but also the potential benefits of doing so. It also illustrates that LAR severity does not differ from other rhinitis phenotypes, as has been demonstrated by other authors.[7] Correct diagnosis of this phenotype is important, since without proper diagnosis, specific allergen immunotherapy cannot be administered, limiting the therapeutic arsenal for individualized treatment.

Sublingual immunotherapy containing *Blomia tropicalis* is an important tool for children and adolescents with LAR. In adults with LAR, subcutaneous allergen immunotherapy has shown good results.[8,9] Two recent meta-analyses[8,9] have investigated the efficacy and safety of subcutaneous allergen immunotherapy for adults with LAR. Both suggested that immunotherapy has a significant effect on symptom improvement, reduces medication consumption, increases serum-specific IgG4 after 2 years of treatment, and results in increased

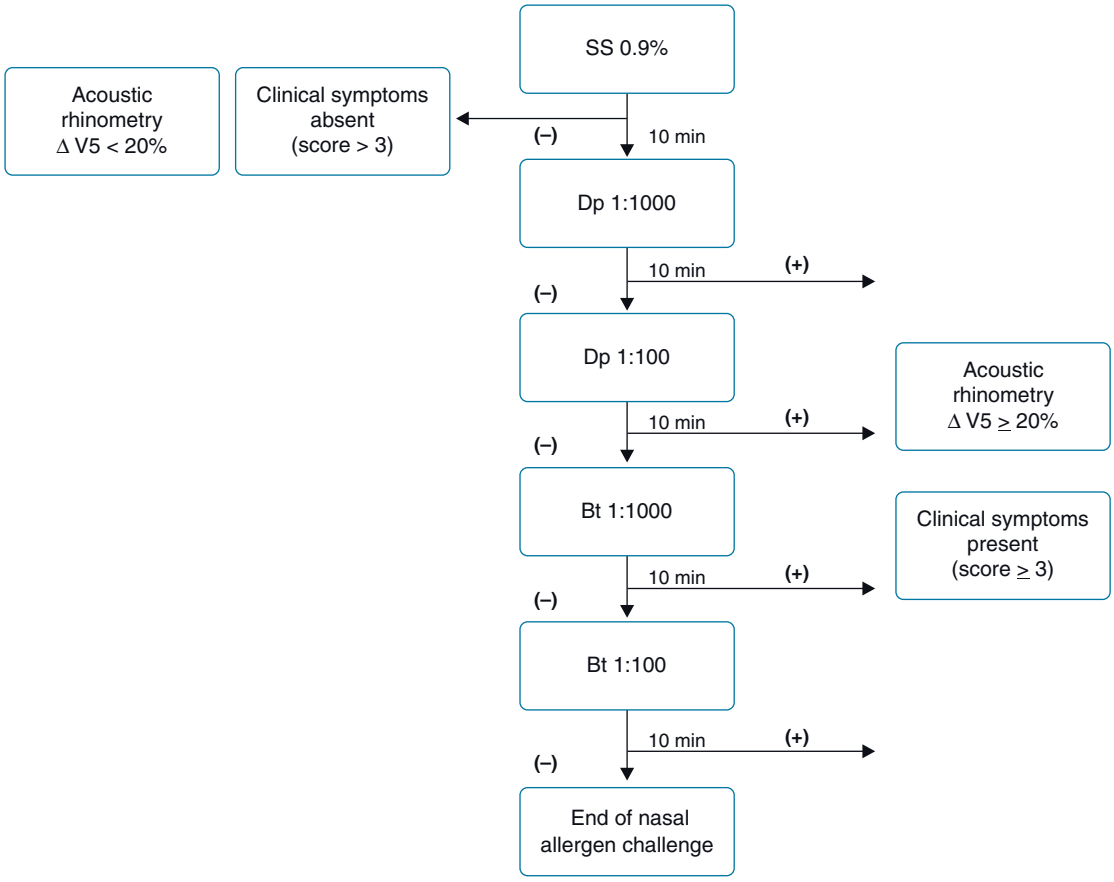

Figure 1
Flowchart for multiple specific nasal allergen challenge with *Dermatophagoides pteronyssinus* (5000 UBE/mL) and *Blomia tropicalis* (5000 UBE/mL) in children and adolescents[6]
SS: saline solution; V5: volume reduction in the first 5 cm of the nasal cavity.

tolerance to the allergen after subcutaneous allergen immunotherapy.[9] Another meta-analysis[8] found a trend towards greater benefit in patients with seasonal LAR compared to those with perennial symptoms. No study in these meta-analyses determined long-term response after treatment. It is noteworthy that in these meta-analyses, the efficacy of sublingual immunotherapy for LAR could not be determined due to a lack of data.

In the exclusively pediatric range, few studies are available on LAR, and there are no reports in the literature on therapeutic response to subcutaneous allergen immunotherapy or sublingual immunotherapy.

In this case, sublingual immunotherapy with *Blomia tropicalis* not only had a good clinical response, as demonstrated by decreased symptom scores and medication consumption, but also resulted in greater tolerance to the allergen during treatment, as shown by the negative multiple nasal allergen challenge results after 18 months of treatment.

New studies in adults and children should be conducted on the short-term benefits of sublingual immunotherapy and subcutaneous allergen immunotherapy, as well as their long-term benefits after 3 years of immunotherapy to determine persistent response and definitive impact on quality of life.

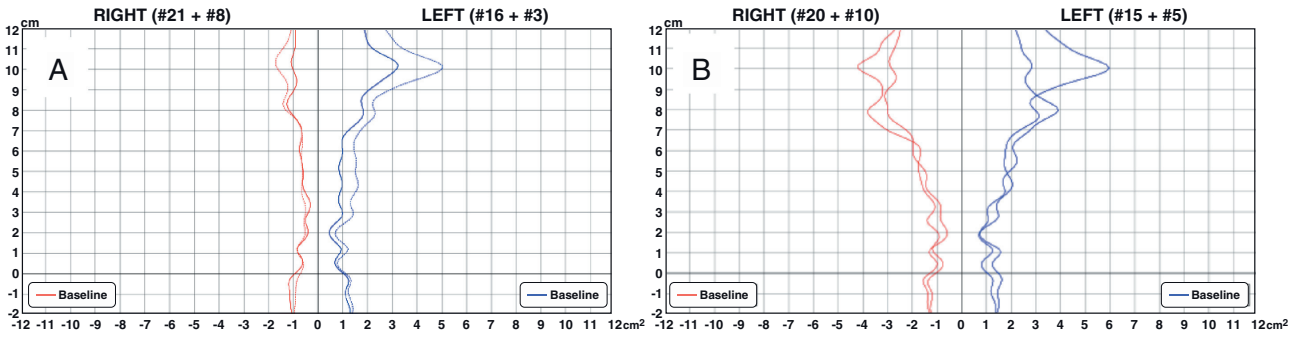

Figure 2

(A) Multiple specific nasal allergen challenge with *Dermatophagoides pteronyssinus* and *Blomia tropicalis*, demonstrating a 32% decrease in volume reduction in the first 5 cm of the nasal cavity (V5) at a *Blomia tropicalis* concentration of 1:100; **(B)** Multiple specific nasal allergen challenge with *Dermatophagoides pteronyssinus* and *Blomia tropicalis* after 18 months of sublingual immunotherapy, demonstrating a 6% decrease in V5 at the end of the test

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