

Allergen immunotherapy in the polyallergic adolescent

Alergen imunoterapija u polialergičnog adolescenta

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Summary

Allergen immunotherapy is the only disease-modifying treatment option for allergic rhinitis, with adherence being its major limitation. We report a case of an adolescent with rhinitis, proven allergy to multiple non-homologous pollens, and troublesome symptoms despite maximal symptomatic therapy during the late spring and early summer months. Allergen immunotherapy to the most clinically relevant allergen was initiated under the supervision of a pediatrician. Shortly before her second year of treatment, she transferred to adult care and maintained a high degree of adherence and a favourable response to immunotherapy. In conclusion, allergen immunotherapy is effective in polyallergic adolescents with good adherence.

Key words: allergen immunotherapy, rhinitis, adolescents, therapy adherence

Sažetak

Alergenska imunoterapija je jedina terapijska opcija alergijskog rinitisa koja modificira tijek bolesti, a glavno ograničenje je terapijska adherencija. U ovom radu prikazujemo slučaj adolescentice s rinitisom i dokazanom alergijom na višestruke nehomologne peludi sa simptomima koji su joj ometali svakodnevni život unatoč maksimalnoj simptomatskoj terapiji tijekom kasnog proljeća i ranog ljeta. Alergenska imunoterapija na klinički najrelevantniji alergeni započeta je pod nadzorom pedijatra, a neposredno prije druge godine liječenja bolesnica je prešla u skrb interniste. Unatoč prelasku u adultnu skrb, održana je adherencija liječenja i pratio se povoljan odgovor na imunoterapiju. Zaključno, alergenska imunoterapija je učinkovita u polialergičnih adolescenata s dobrom terapijskom adherencijom.

Ključne riječi: alergenska imunoterapija, rinitis, adolescenti, adherencija za terapiju

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Background

Allergic rhinitis is the most prevalent immunological disorder¹, which impairs people's quality of life² and imposes considerable economic expenses.³ The British Society of Allergy and Clinical Immunology (BSACI) guidelines advocate a progressive approach to pharmacotherapy dependent on the severity of the disease.⁴ Patients with moderate-severe persistent allergic rhinitis who do not respond to maximal symptomatic treatment

should be considered for allergen immunotherapy.^{4,5}

Unfortunately, compliance with allergen immunotherapy, particularly sublingual immunotherapy, is challenging across all age groups.⁶ Adherence to therapy is particularly problematic in adolescents and young adults (AYA), a subgroup of patients aged 11 to 25 who have been recognised to lack self-management skills⁷, resulting in poor compliance.⁸ The pandemic of COVID-19 (Coronavirus disease 2019) has only exacerbated the problem. A recent European Academy of Allergy

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and Clinical Allergy (EAACI) survey revealed widespread undertreatment with allergen immunotherapy across all age categories since the pandemic began, owing to limited healthcare resources.⁹ This case report aims to present successful allergen immunotherapy with good adherence to therapy in a polyallergic AYA during a pandemic.

Case presentation

An adolescent Caucasian female patient presented to her paediatrician with symptoms consistent with late spring rhinitis (with the highest peak of symptoms in May and June), including itching, sneezing, nasal obstruction and discharge. The symptoms persisted for more than four days per week and more than four weeks, impairing sleep and daily activities as measured by a Visual Analogue Scale (VAS) rating of more than 5. According to Allergic Rhinitis and its Impact on Asthma (ARIA) criteria, rhinitis was classified as moderate-severe persistent.^{10,11}

She experienced similar symptoms in early spring and early autumn, but with duration shorter than four days a week, and four consecutive weeks, with no impairment of sleep, daily activities, or school, and a VAS score under 5, which ARIA classifies as mild intermittent rhinitis.^{10,11}

The patient reported no lower respiratory tract disease symptoms or pollen food syndrome. She had mild atopic dermatitis as an infant, which was resolved by her second year of life. She attended high school and shared an apartment with her family that was well-ventilated and free of moulds and pets. The family history was positive for atopy. The patient was an exceptionally self-confident clarinet player. Unfortunately, her clarinet performance was significantly hindered by her rhinitis symptoms, which made her upset. Otherwise, she had no psychological or other medical issues.

Investigation

The patient presented with mildly wet eyes, allergy shine, nasal blockage, and anterior rhinoscopy revealed a pale hypertrophic nasal mucosa and inferior turbinates with a clear nasal discharge.

Allergy test results, a complete blood count, C-Reactive Protein, immunoglobulin profile, and cytologic examination of the upper respiratory tract are listed in Table 1. The test results showed the sensitisation to grass, trees, ragweed, and cats. Because there was no correlation between symptoms

and cat exposure, the allergy test results to cat dander were interpreted as merely indicative of sensitivity rather than a clinically significant allergy. Pollen allergies were clinically significant, with grass pollen causing the most troublesome symptoms. Nasal allergen challenges to prove the allergies to pollens and exclude allergy to cat dander were not performed. Pulmonary function tests were in reference values with the negative bronchodilatory test, and fractional exhaled nitric oxide was 26 ppb. Other tests recommended by BSACI guidelines⁴ were not performed because there was no clinical need based on the patient's history and examination findings.

Differential diagnosis

Rhinitis is defined as the presence of at least two of the following symptoms: itching/sneezing, nasal discharge, and obstruction for more than one hour on most days.¹² The aetiology of rhinitis can be allergic, non-allergic, infectious, or a combination of these.⁴

Allergic rhinitis in regions with a four-season climate, can be classified as seasonal caused by a variety of outdoor allergens (particularly pollens) and perennial caused by year-round indoor allergens (dust mites, moulds, cockroaches, and animal dander).¹⁰ Furthermore, local allergic rhinitis, a subtype of allergic rhinitis, is defined by the absence of a positive skin prick test and specific immunoglobulin E in the presence of a positive nasal allergen challenge.¹³

Non-allergic rhinitis can be idiopathic, eosinophilic, autonomic, drug, hormonal or food-induced and atrophic rhinitis or part of a systemic disorder.⁴

Our patient was diagnosed with seasonal allergic rhinitis to grass, tree, and ragweed based on the history and clinical findings.

Treatment

The patient was treated with an oral antihistamine, intranasal corticosteroid spray, and allergy avoidance according to BSACI guidelines⁴, but symptoms remained moderate-severe persistent throughout the late spring, with a VAS greater than 5. Step-up with an intranasal spray containing a combination of corticosteroid and antihistamine was trialled with partially successful, but VAS remained greater than 5.

The patient was under the care of a paediatrician in a secondary care hospital for two years. Conversation with her and her parents were held to evaluate her self-care and disease management abilities. The official evaluation suggested by the

Table 1. Results of initial diagnostic tests.
 Tablica 1. Rezultati inicijalnih dijagnostičkih ispitivanja

Skin prick test (mm) <i>Kožni prick test</i>		IgE in serum (kIU L ⁻¹) specific to <i>IgE u serumu (kIU L⁻¹) specifičan na</i>		Blood count <i>Krvna slika</i>	
Positive control <i>Pozitivna kontrola</i>	6.0	Cat dander <i>Epitel mačke</i>	1.21	White blood count (×10 ⁹ L ⁻¹) <i>Bijela krvna slika</i>	6.4
Negative control <i>Negativna kontrola</i>	0.0	Dactylis glomerata	>100.0	Eosinophils (Dunger)	150.0
Grass pollen <i>Pelud trava</i>	15.0	Betula verrucosa	3.16	Haemoglobin (g L ⁻¹)	131.0
Tree pollen <i>Peluda stabala</i>	6.0	Corylus avellana	0.67	Platelets (×10 ⁹ L ⁻¹)	293.0
Ambrosia Ragweed Artemisiifolia pollen <i>Pelud artemisiifolia</i>	7.0	Ambrosia artemisiifolia	5.47	Mean corpuscular volume (fL) <i>Srednji korpuskularni volumen</i>	90.2
House dust mite <i>Kućna grinja</i>	0.0	Cockroach <i>Žohar</i>	0.0	Mean corpuscular hemoglobin (pg) <i>Srednji korpuskularni hemoglobin</i>	30.2
Immunoglobulin profile (gL ⁻¹) <i>Profil imunoglobina</i>		Cytology (%) <i>Citologija</i>		Biochemistry (mg L ⁻¹) <i>Biokemija</i>	
IgA	1.8	Sputum eosinophil proportion <i>Udio eozinofila u sputumu</i>	5.0	C-Reactive Protein <i>C-reaktivni protein</i>	
IgM	1.9	Nasal brush eosinophil proportion <i>Udio eozinofila u brisu nosa četkicom</i>	15.0		
IgG	13.5				

EAACI guidelines through a questionnaire (such as “ready, steady, go”) was not carried out.⁷

She was offered by her paediatrician a trial of allergy immunotherapy to grass, the allergen that caused her the most distressing symptoms, because she was highly motivated and compliant with the therapy but only had partial success with the standard treatment.

The patient chose pre seasonal sublingual immunotherapy drops for three sequential years because of availability on the market, short therapy duration, and reduced healthcare visits.

Allergen immunotherapy consisted of titration and maintenance phase, and two vials with different concentrations of allergens. One vial contained 10IR/ml (one pressure = 1 IR), and the other one contained 300IR/ml (one pressure = 30 IR) of allergen. After the first dose of titration phase was administered in the secondary care hospital under the supervision of a paediatrician with no immediate adverse effects, the second dose and all subsequent

doses were administered at home. During this phase of treatment, she developed symptoms of itchy ears and small bumps under the tongue half an hour after sublingual immunotherapy, which were treated with oral antihistamines. On day 12, she reached the maintenance phase, which consisted of four pressures of the second vial (300 IR/ml). She responded well to allergen immunotherapy, with a symptom reduction greater than 50% during the first late spring season.

Follow-up

The second year of allergen immunotherapy was complicated by the pandemic and the need to transfer to an adult physician because the patient had turned eighteen. The transfer was accomplished by email conversation between the patient, paediatrician and adult physician. Additionally, the transition report written by the paediatrician, allowed the adult physician to continue treatment with minimal in-person contact. The first dose of the

second year of allergen immunotherapy was administered under the supervision of an adult physician in our secondary care hospital at the first in-person visit. She performed pre-and post-treatment peak flow measurements and was

discharged to home therapy after a half-hour.

The third year of therapy began in early January 2022. Responses to different therapy options measured by VAS are shown in Figure 1.

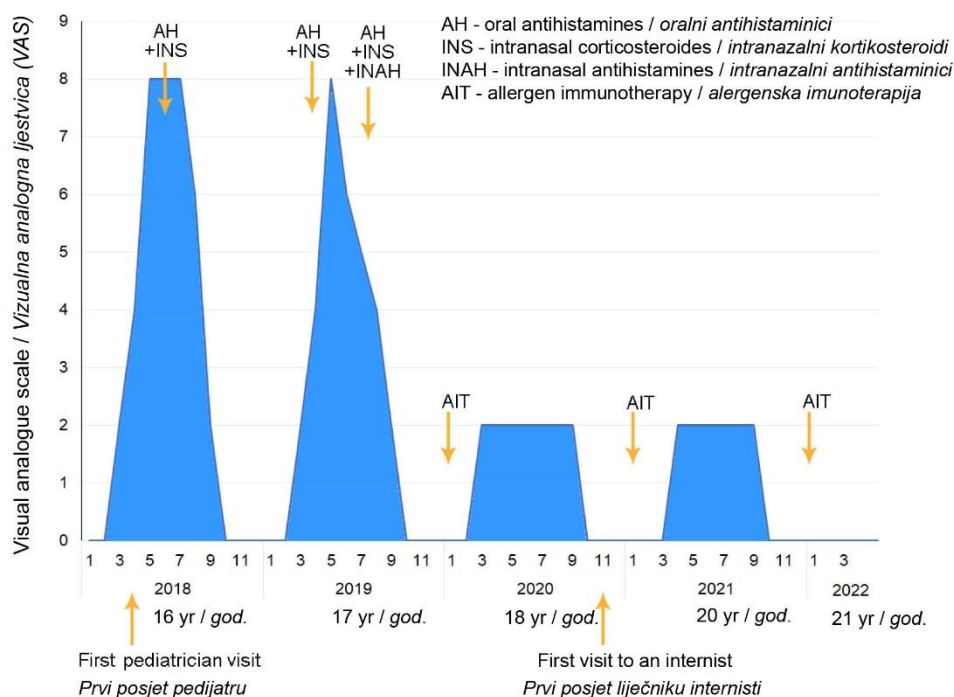


Figure 1. Timeline of therapeutic intervention and outcomes on symptoms of allergic rhinitis as measured by visual analogue scale (VAS).

Slika 1. Vremenski raspored terapijske intervencije i ishoda simptoma alergijskog rinitisa mjereno vizualnom analognom ljestvicom (VAS).

Discussion

Allergen immunotherapy, the administration of high doses of allergens in steadily increasing amounts, is the only disease-modifying treatment of allergic rhinitis. As a result of receiving immunotherapy at high doses, the dendritic cells in the body create cytokines that alter the immune response from Th2 to Th1 and trigger Tregs proliferation and the creation of IgA, IgG, and IgG4 blocking antibodies in Breg cells.¹⁴ Allergen immunotherapy can be administered sublingually or subcutaneously. According to EAACI Guidelines on Allergen Immunotherapy, both monoallergic and polyallergic patients can be treated.^{5,15} Despite the current guidelines, unfortunately, many allergists are still reluctant to administer allergen immunotherapy to polyallergic patients. However, allergen

immunotherapy can be highly successful if the most clinically relevant allergen is used for treatment.¹⁶ Sublingual immunotherapy is safe and effective for patients with allergic rhinitis caused by grass pollen with no reported deaths and local reactions that can be treated with oral H1-antihistamines.^{4, 17-19} The type of allergen immunotherapy used in this patient was carefully selected based on the patient's history, and it was extremely effective.

However, adolescents such as our patient may be incapable of self-management, resulting in insufficient treatment adherence and other adverse outcomes.²⁰ Additionally, as adolescents reach the age of eighteen, they are compelled to move from paediatric to adult medical care resulting in feelings of loss and fear of the unknown²¹, as well as missed appointments and inadequate management of allergic diseases.²² Due to that, EAACI developed guidelines for the effective transition of AYA in

2020, outlining the importance of initiating transfer preparation early enough for the patient to be emotionally prepared.⁷

Transitioning entails acquiring accurate knowledge about the condition in order to avoid exacerbations and sustain disease control through multi-systemic approach, patient activation measures, transition readiness assessment tools (e.g. ready, steady, go questionnaires) and regular meetings between paediatric and adult health care providers.⁷

However, due to the Covid pandemic restrictions on in-person health care management, strict adherence to EAACI guidelines on effective AYA transition was not possible in this instance. Nevertheless, an online interaction between patient, paediatrician and adult physician revealed that the patient was mature and strongly motivated for treatment. Despite the multiple challenges associated with such a young age and pandemic, adherence was outstanding in our case, most likely due to the patient motivation and treatment efficacy and simplicity. This case demonstrates that allergen immunotherapy to single allergen is effective in polyallergic patients even during pandemic-related constrains in health care services in adolescents infamous for their lack of adherence.

Conclusions

- Allergen immunotherapy is the only disease-modifying treatment of allergic rhinitis.
- Allergen immunotherapy using a single allergen is successful in polyallergic patients.
- Adolescents can have good adherence to allergen immunotherapy.
- Sublingual immunotherapy is a good option for allergen immunotherapy during a pandemic.
- Online communication during the pandemic was very useful for patient management and transitioning patients from paediatric to adult care

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