Application of component-resolved diagnostics in treatment of severe atopic dermatitis: a case report

Delara Babaie, MD [1]
Shabnam Eskandarzadeh, MD [1]
Rudolf Valenta, MD, PhD [2]
Mehrnaz Mesdaghi, MD, PhD [1*]

1. Department of Allergy and Clinical Immunology, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Division of Immunopathology, Department of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Austria

*Corresponding author:
Mehrnaz Mesdaghi, MD, PhD
Department of Allergy and Clinical Immunology, Mofid Children's Hospital, Shariati St, Tehran, Iran
E-mail: m.mesdaghi@sbmu.ac.ir

Received: 25 September 2021
Accepted: 25 January 2022

Atopic dermatitis (AD) is a chronic allergic inflammation of the skin. Precise identification of the causative allergen is an important step in the successful treatment of patients with moderate to severe AD. Common diagnostic methods in allergy assess the presence or absence of allergen-specific sensitization, but none exhibits a complete clinical correlation. Component-resolved diagnostics (CRD) is a new precise method for identifying the culprit allergen. Here, we report the case of a nine-year-old boy with severe AD. He was polysensitized (based on a skin prick test), with a poor response to routine AD therapeutic measures and food elimination diets. He had experienced recurrent flares while under treatment. Skin biopsy confirmed AD. Systemic therapy with cyclosporine (200 mg per day) was initiated and caused significant symptom relief within eight weeks. However, he had a flare when the dose was decreased to 150 mg daily. The causative allergen was diagnosed based on CRD, and he was successfully treated by allergen immunotherapy. CRD can determine the causative allergen in selected polysensitized patients with AD with poor response to treatment. The application of allergen-specific immunotherapy in AD management is controversial, but highly sensitized patients could benefit from it once the disease-causing allergen is identified.

Keywords: cyclosporine, phototherapy, pityriasis lichenoides, therapeutics

Iran J Dermatol 2023; 26: 95-99

DOI: 10.22034/ijd.2022.305690.1438

INTRODUCTION

Atopic dermatitis (AD) is a chronic, remitting-relapsing inflammatory dermatitis [1]. Epidemiologic studies have shown a prevalence of up to 18% in school-aged children and 7% in adults in the United States [2-4]. As a chronic, relapsing pruritic disease, AD profoundly affects the quality of life of patients and families, which results in clinically relevant anxiety or depression in 21.8% of adults with moderate-to-severe AD [6]. It has a substantial socioeconomic burden, partly because of the lack of an efficient long-term treatment [1,5-7]. The disease has heterogeneous clinical phenotypes, and the role of IgE-mediated sensitization or food allergy is debated [8,9]. It is characterized by complex immune dysregulation, as well as skin barrier abnormalities, and colonization or infection by various microbes [10]. Identifying and avoiding proven allergens is one of the treatment strategies [10].

Common diagnostic methods in allergy assess the presence or absence of allergen-specific sensitization, but none exhibits a complete clinical correlation [11].

Please cite this article as: Babaie D, Eskandarzadeh Sh, Valenta R, Mesdaghi M. Application of component-resolved diagnostics in treatment of severe atopic dermatitis: a case report. Iran J Dermatol. 2023;26(2):95-99. doi: 10.22034/ijd.2022.305690.1438.

In recent years, diagnosis and treatment based on component-resolved diagnostics (CRD) have been successful [12]. CRD, also named molecular allergy diagnosis, is practicing precision medicine in diagnosing and treating allergic disorders. In CRD, a wide array of purified natural or recombinant allergen molecules is used to define the IgE sensitization pattern of the patient and identify the disease-causing allergen(s). It can precisely discriminate true sensitization from cross-reactions. This new diagnostic modality introduces new forms of management by allergen-specific and T cells-targeting or IgE-targeting interventions in a personalized medicine approach [13,14]. Besides its diagnostic accuracy, it is even more valuable in children with AD. The usual allergy diagnosis modality (skin prick test) may not always be feasible in these patients, as it needs healthy skin and is painful, especially when multiple allergens are tested.

The efficacy of allergen immunotherapy (AIT) in AD has been suggested in numerous articles, although the topic is still highly controversial [15]. Caraballo *et al.* showed that AD patients treated with AIT had significantly improved SCORAD (SCORing Atopic Dermatitis) scores and reduced overall oral steroid use for exacerbations than those treated with topical steroids/tacrolimus [16]. Similar results with a dose-dependent decline in SCORAD and a decrease in topic corticosteroid use have been shown after one year of AIT therapy in HDM-sensitized patients [17].

The most recent guideline from the American Academy of Dermatology concludes that available data do not support AIT application in the treatment of AD, while the Joint Task Force advises clinicians to consider AIT in selected patients with aeroallergen sensitivities [18]. In its recent guideline, the European Academy of Dermatology agrees with the Joint Task Force that a subset of highly sensitized patients with house dust mite, birch, or grass pollen sensitization and symptom exacerbation may benefit from AIT [19].

Here, we report a case of difficult-to-treat AD, where the causative allergen was identified by CRD and was treated by specific allergen immunotherapy.

CASE REPORT

We report a 9-year-old boy with severe AD who visited the allergy clinic of Mofid Children's Hospital, Tehran, Iran, in 2017. He had generalized xerosis, pruritus, and ulcerative eczematous plaques on his neck, limbs, and back (Figure 1a,b). He was born by normal vaginal delivery to a farmer's family and was breastfed for 15 months. The boy did not have a history of prior allergies, though his father had allergic rhinitis. At the age of 6 months, he began to develop some xerosis and erythema on his face. The skin was itchy, and the parents could not find any relation between the consumption of a specific food item and the worsening of the lesions. The dry, itchy skin improved with emollients.

At the age of 4 years, he developed other plaques on his antecubital areas, neck, back, hands, and legs, with generalized xerosis. He was diagnosed with AD and initially treated successfully with emollients and short courses of topical corticosteroids. Since the age of 5, the disease worsened, and he experienced a severe exacerbation of AD with disseminated dryness, redness, itching, and ulcerative skin plaques

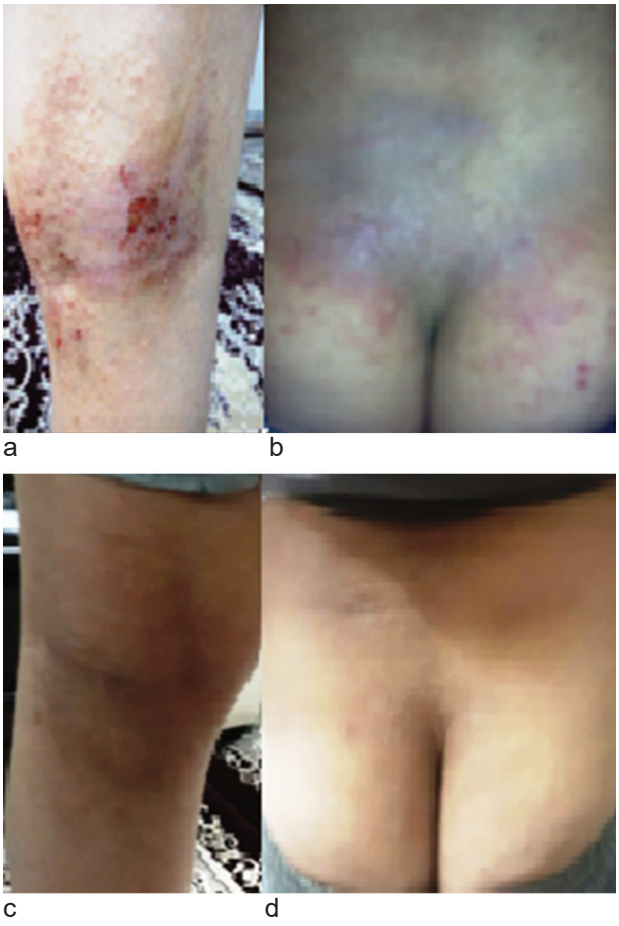

Figure 1. a and b: patient's skin (knee and buttocks) before subcutaneous immunotherapy; and c and d: patient's skin (knee and buttocks) after subcutaneous immunotherapy

when referred to our clinic. On his first visit, the SCORAD index was 81.6.

We initially prescribed a daily bleach bath, moisturizing agents, topical steroids, and systemic antibiotics, in addition to antihistamines. His condition was controlled, and his SCORAD index decreased significantly.

In the laboratory examinations, the total IgE was 590 UI/ml, and 650 eosinophils/µL were detected in the peripheral blood. The skin prick test (SPT) for a complete panel of food and aeroallergens (extracts from Greer, USA) revealed polysensitization to food and aeroallergens (Table 1). Food elimination was started based on the SPT results and their correlation with his regular foods. Despite strict food avoidance, he had no improvement in his flares, and he was suffering from recurrent relapses.

Since the current treatment appeared insufficient and the condition was poorly controlled, a dermatology consult was requested, and a skin biopsy confirmed the diagnosis of AD. Due to poor response to steroids and recurrent flare-ups, systemic therapy with cyclosporine (200 mg daily) was started. After four weeks, moderate control of AD symptoms was achieved. Significant symptom relief was achieved by continuing cyclosporine for eight weeks, but when the dose was decreased to 150 mg daily, the disease flared.

Since the allergen extract-based testing was inconclusive and avoidance based on SPT results was unsuccessful, a molecular allergy diagnosis was made using the ImmunoCAP ISAC chip technology (Thermofisher, Uppsala, Sweden). The results showed that the patient was mainly sensitized to *Alternaria alternata* (Alt a1 specific IgE:10.97 kU/L), and no significant food sensitization was reported. He could clearly recall suffering from exacerbations after farm work, even when he wouldn't work directly on the farm and just stayed in the livestock area. Since sensitization to *A. alternata* was the only sensitization clinically relevant to the patient's condition, we explained the risks and benefits of AIT and the controversial results of AIT in AD to the patient and his parents and made a shared decision to start subcutaneous allergen immunotherapy (SCIT) with *A. alternata* (Greer, USA).

Table 1. Skin prick test results

	Wheal in mm	Flare in mm
Histamine	5	8
Negative control	0	0
Wheat	3	5
Egg white	3	3
Peanut	2	3
Sesame	3	4
Alternaria	3	3
Cladosporium	3	5

We used a medium allergen dose maintenance vial (0.75 mL 1:20 w/v *A. alternata* based on Greer). SCIT was started. During the buildup phase, cyclosporine treatment was stopped. His skin was in optimal condition. During the maintenance phase (injections every four weeks), he experienced severe episodes of flare, so we changed the SCIT protocol to high-dose allergen immunotherapy (1 mL 1:20w/v *A. alternata* based on Greer). We discontinued cyclosporine slowly and accomplished the buildup phase. He continued the maintenance phase for 3.5 years. During this period, he was visited regularly, and the skin was evaluated for the severity and location of involvement. He followed regular skin care for AD patients and experienced six mild to moderate exacerbations during AIT, which were optimally controlled by topical steroids (Elecon®); one episode needed an antibiotic in addition (Figure 1c,d).

We recently visited the boy after eight months of discontinuing AIT. His skin was clear, though he experienced xerosis occasionally, which responded to the regular application of moisturizing agents.

DISCUSSION

In this case report, we describe a patient with severe intractable AD in whom initial treatments had failed. AD is a chronic and relapsing form of skin inflammation driven by a combination of penetrating allergens (impaired skin barrier), abnormal T cell subpopulations, and inflammatory cells such as eosinophils, mast cells, and dendritic cells [15]. A comprehensive approach is necessary when managing severe AD, addressing not only the disease's complex pathophysiology and systemic nature but also its profound impacts on patients' and caregivers' quality of life [20].

Until recently, the management of AD consisted of adequate skin hydration, topical ointments, and avoiding triggers including allergens (if known) and emotional stressors [21]. The role of allergen

sensitization in AD pathogenesis needs to be fully elucidated. In some sensitized patients, exposure to food or aeroallergens exacerbates AD symptoms [17]. Although AD patients tend to have higher levels of total serum IgE, their food sensitizations are not usually associated with symptoms upon ingestion [22,23]. This is consistent with our patient, in whom eliminating wheat, egg white, peanut, and sesame based on SPT results did not help manage AD.

Molecular analysis of allergen sensitization patterns may enhance the clinical utility of immunoglobulin E antibody-based allergy diagnostics [9]. Pure natural and recombinant allergen molecules and panels of synthetic peptides have been used for this purpose. In this case, we used CRD to find the most relevant allergen. In CRD, the only positive specific IgE was reported against *A. alternata,* clinically correlated with the patient's history of exacerbations after farm work or staying in the livestock area. AIT for patients with AD is a debating issue and the evidence on its application is controversial, therefore; most recommendations rely on the clinician's judgment.

We discussed the risks and benefits of AIT with the patient and his parents, which resulted in initiating *Alternaria* AIT. After completing the AIT course, his AD showed a dramatic improvement and cyclosporine was discontinued and flares were controlled with regular skin care and topical Elocon®. Ridolo *et al.* recommended that sensitization to aeroallergens must be proven with the skin prick test and/or IgE assay, exposure to aeroallergens must induce AD flare-ups, and the physician must choose a standardized product for AIT [24]. Our management strategy was effective in this sensitized patient with severe AD who was unresponsive to other treatments. It reduced medical requirements and the SCORAD score in this patient. Trials have suggested that desensitization to specific allergens may improve AD [11]. CRD can promptly and accurately determine the causative allergen (if it exists); in the aforementioned conditions [24], it can be conducive to planning treatment for selected polysensitized patients with refractory disease.

CONCLUSION

Considering conflicting evidence for AIT's efficacy and utility, it is currently unclear whether AIT would be an appropriate option for patients with AD. The clinician should consider AIT for patients whose disease has not responded to other treatments, and it should be discussed with the patient to improve treatment literacy and long-term compliance. Selecting allergens should be precise, especially in polysensitized patients, with CRD showing exceptional promise in this regard.

Ethical consideration

AIT was done as an appropriate treatment modality for the patient. The process of AIT, its risks and benefits, and the success rate were explained by the staff physician to the patient and his parents, and they provided written informed consent.

List of abbreviations

AD: Atopic Dermatitis
CRD: Component Resolved Diagnostics
SCORAD: SCORing Atopic Dermatitis

Acknowledgement

None.

Authors contribution

Delara Babaie, Shabnam Eskandarzadeh and Mehrnaz Mesdaghi contributed to the case report conception and design. Mehrnaz Mesdaghi drafted the manuscript. Rudolf Valenta did component resolved diagnosis. All authors critically reviewed the previous version and approved the final manuscript.

Funding source

The article was not supported financially by any institute or person.

Consent statement: The patient's parents signed a publication consent form.

Conflict of interest: None declared.

REFERENCES

1. Eichenfield LF, Ahluwalia J, Waldman A, et al. Current guidelines for the evaluation and management of atopic dermatitis–a comparison of the joint task force practice parameter and American academy of dermatology guidelines. Alergol Polska-Polish J Allergol. 2017;4(4):158-68.
2. Shaw TE, Currie GP, Koudelka CW, et al. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. J Invest Dermatol. 2011;131:67-73.

3. Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. J Allergy Clin Immunol 2013;132:1132-8.
4. Hua T, Silverberg JI. Atopic dermatitis in US adults—epidemiology, association with marital status and atopy. Ann Allergy Asthma Immunol. 2018;121:622-4.
5. Whiteley J, Emir B, Seitzman R, et al. The burden of atopic dermatitis in US adults: results from the 2013 National Health and Wellness Survey. Curr Med Res Opin. 2016;32(10):1645-51.
6. Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): insights from a phase 2b clinical trial of dupilumab in adults. J Am Acad Dermatol. 2016;74(3):491-8.
7. Bieber T, Straeter B. Off-label prescriptions for atopic dermatitis in Europe. Allergy. 2015;70(1):6-11.
8. Werfel T, Allam J-P, Biedermann T, et al. Cellular and molecular immunologic mechanisms in patients with atopic dermatitis. J Allergy Clin Immunol. 2016;138(2):336-49.
9. Canonica G, Ansotegui I, Pawankar R, et al. A WAO-ARIA-GA (2) LEN consensus document on molecular-based allergy diagnostics. Rev Fr Allerg. 2015;55(2):83-99.
10. Brar KK, Nicol NH, Boguniewicz M. Strategies for successful management of severe atopic dermatitis. J Allergy Clin Immunol Pract. 2019;7:1-16.
11. Des Roches A, Paradis L, Menardo J-L, et al. Immunotherapy with a standardized dermatophagoides pteronyssinus extract. VI. Specific immunotherapy prevents the onset of new sensitizations in children. J Allergy Clin Immunol. 1997;99(4):450-3.
12. Fedenko E, Elisyutina O, Shtyrbul O, et al. Microarray-based IgE serology improves management of severe atopic dermatitis in two children. Pediatr Allergy Immunol. 2016;27(6):645-9.
13. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, et al. EAACI molecular allergology user's guide. Pediatr Allergy Immunol. 2016;27:1-250.
14. Campana R, Dzoro S, Mittermann I, et al. Molecular aspects of allergens in atopic dermatitis. Curr Opin Allergy Clin Immunol. 2017;17(4):269.
15. Patrick Rizk, Mario Rodenas, Anna De Benedetto. Allergen immunotherapy and atopic dermatitis: the good, the bad, and the unknown. Curr Allergy Asthma Rep. 2019; 19: 57.
16. Sánchez Caraballo JM, Cardona VR. Clinical and immunological changes of immunotherapy in patients with atopic dermatitis: randomized controlled trial. ISRN Allergy. 2012; 2012:183983.
17. Werfel T, Breuer K, Rueff F, et al. Usefulness of specific immunotherapy in patients with atopic dermatitis and allergic sensitization to house dust mites: a multi-centre, randomized, dose–response study. Allergy. 2006;61(2):202–5.
18. Fichenfield LF, Ahluwalia J, Waldman A, et al. Current guidelines for the evaluation and management of atopic dermatitis–a comparison of the joint task force practice parameter and American academy of dermatology guidelines. Alergol Polska-Polish J Allergol. 2017;4(4):158–68.
19. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. J Eur Acad Dermatol Venereol. 2018;32(6):850–78.
20. Brunner PM, Silverberg JI, Guttman-Yassky E, et al. Increasing comorbidities suggest that atopic dermatitis is a systemic disorder. J Invest Dermatol. 2017; 137:18-25.
21. Hanifin JM, Tofte SJ. Update on therapy of atopic dermatitis. J Allergy Clin Immunol. 1999;104(3): S123–S5.
22. Frischmeyer-Guerrerio PA, Rasooly M, Gu WJ, et al. IgE testing can predict food allergy status in patients with moderate to severe atopic dermatitis. Ann Allergy Asthma Immunol. 2019;122(4):393.
23. Fleischer DM, Bock SA, Spears GC, et al. Oral food challenges in children with a diagnosis of food allergy. J Pediatr. 2011;158(4):578-83.
24. Ridolo E, Martignago I, Riario-Sforza GG, et al. Allergen immunotherapy in atopic dermatitis. Expert Rev Clin Immunol. 2018;14(1):61–8.