ASTHMA ALLERGY IMMUNOLOGY
ASTIM ALLERJİ İMMÜNOLOJİ

doi: 10.21911/aai.228
Asthma Allergy Immunol 2024;22:78-81

CASE REPORT

Received: 16.02.2023 • Accepted: 05.09.2023
Online Published: 04.12.2023

A Rare Case of Eczema Herpeticum After Subcutaneous Immunotherapy

Fatma Merve TEPETAM[1], Seyma OZDEN[1], Tugce YAKUT[2], Selver Seda MERSIN[3], Cihan ORCEN[4]

[1] Department of Immunology and Allergy, University of Health Sciences Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey
[2] Department of Immunology and Allergy, University of Health Sciences Diyarbakir Gazi Yaşargil Training and Research Hospital, Diyarbakir, Turkey
[3] Department of Immunology and Allergy, Doktor Ersin Aslan Training and Research Hospital, Gaziantep, Turkey
[4] Department of Immunology and Allergy, Derince Training and Research Hospital, Kocaeli, Turkey

Corresponding Author: Seyma Ozden ✉ seymaglhn@hotmail.com

ABSTRACT

Eczema herpeticum (EH), also known as varicelliform eruption of Kaposi, is a herpes simplex virus infection that develops mainly in the setting of pre-existing chronic dermatoses such as atomic dermatitis, ichthyosis, seborrheic dermatitis, Darier's disease, pemphigus foliaceus, mycosis fungoides, and psoriasis, and is most commonly associated with atopic dermatitis.

In this article, we describe an 18-year-old female patient with atopic dermatitis diagnosed with EH after subcutaneous allergen immunotherapy for allergic rhinitis and present this very rare side effect in the light of the current literature.

Keywords: Atopic dermatitis, eczema herpeticum, HSV, immunotherapy

INTRODUCTION

Allergen immunotherapy (AIT) is a treatment method that enables the development of immunotolerance against allergens with the administration of clinically sensitive allergen extract at regular intervals and in increasing doses (1,2). It is a treatment alternative that should be considered in patients who do not have adequate elimination of particularly severe allergies and who do not receive an adequate response despite appropriate medical treatment or who need regular medication for a long time. It consists of two main phases: start-up and maintenance. Indications for allergen immunotherapy are:

- Allergic rhinitis and/or asthma symptoms as a result of natural exposure to inhalant allergen and development of anaphylaxis and/or systemic reaction to bee venom, and demonstration of sensitization to inhalant allergens by skin test and/or the presence of specific IgE in-vitro
- Symptoms cannot be controlled with medical treatment and preventive measures
- Patient refusal of long-term pharmacotherapy
- Side-effects of medicines
- The severity of symptoms affecting the patient's quality of life (3).

Atopic dermatitis (AD) is a chronic, inflammatory skin disease characterized by persistent itching that usually begins in early childhood.

One of the most common viral infections occurring in AD patients is EH, a herpes simplex virus (HSV) skin infection. Although EH is relatively rare, occurring in about 3% of AD patients, this initially local disease may progress to a potentially life-threatening systemic infection. The pathogenesis of EH remains largely unknown

ORCID Fatma Merve Tepedam / 0000-0002-9794-5662, Seyma Ozden / 0000-0002-6646-9894, Tugce Yakut / 0000-0001-8297-1289, Selver Seda Mersin / 0000-0003-1325-3237, Cihan Orcen / 0000-0003-1047-2004

so far (4). Subcutaneous allergen-specific immunotherapy (SCIT) is a disease-modifying therapy in immunoglobulin (IgE)-mediated allergic diseases. Allergen extracts are administered in gradually increasing doses, followed by a maintenance dose at regular intervals for at least 3 years (5). Although local side effects are frequently observed during and after the subcutaneous allergen-specific immunotherapy (SCIT) application, systemic side-effects can also be encountered rarely. We aimed to present a young female patient diagnosed with AD who developed EH after SCIT application in the light of the literature. The patient's consent was obtained and patient information is presented.

CASE

An 18-year-old woman had suffered with asthma, allergic rhinitis, and AD since childhood. The patient's asthma was under control with inhaled corticosteroid (ICS) + long-acting beta agonist (LABA). For allergic rhinitis, she was using nasal antihistamine, nasal steroid, and oral levocetirizine + montelukast combination. Despite these treatments, the patient complained of runny nose, nasal itching, frequent sneezing, and burning and watery eyes for at least 5 days a week. These complaints were all seasonal and increased in the spring. The patient's skin prick test (SPT) revealed house dust mites, grass pollen, dog, and rye pollen sensitization. It was decided to start SCIT with grass pollens and house dust mites before the pollen season to the patient who could not achieve complete symptom control with the current medical treatment and did not want to use these medications for a long time. In blood tests performed before SCIT treatment, the hemogram, kidney and liver function tests were within normal limits except for serum total IgE: 1078 IU/mL, specific IgE to D1-ptero: 42.7 KU/L, and D2-farin: 77.1 KU/L with the Pharmacia CAP System™ (Phadia, AB, Uppsala, Sweden). SCITs were initiated at the same time with grass pollens (Allergovit® 006; Allergopharma, Reinbek, Germany), and house dust mites (NovoHelisen Depot 708-725; Allergopharma, Reinbek, Germany) before the pollen season in accordance with the simultaneous cluster dose scheme (Table I, II). On the same day, 0.1 ml of bottle A (1000 TU/ml) for grass pollen and 0.7 ml of bottle 1 (50 TU/ml) for house dust mites were injected at 30-minute intervals. One or two days after the first injection, the patient started to complain of diffuse redness, itching and burning on the full face and especially the cheeks, and white crusted lesions formed on the patient's face within a week (Figure 1). The patient's skin complaints, which were like atopic dermatitis, increased in severity and the lesions were thought to be infected. Both SCITs were stopped. In the serum test, anti-HSV type 1 IgM was found to be positive and IgG was negative. There was no growth in the wound swab culture. The patient was consulted to the dermatology department, and treatment of EH was started with amoxicillin+clavulanic-acid 1000 mg 2*1/day per oral, acyclovir 250 mg 3*1/day intravenous, and acyclovir topical, and completed in 10 days. Simultaneous systemic and tropical treatment was initiated with the recommendation

Table I: NovoHelisen Depot® 708-725 Cluster Dose Scheme.

Week No	Bottle No	Dose (mL)
1	1	0.1 mL
1	1	0.2 mL
1	1	0.4 mL
2	1	0.8 mL
2	2	0.1 mL
2	2	0.2 mL
3	2	0.4 mL
3	2	0.8 mL
4	3	0.1 mL
4	3	0.2 mL
5	3	0.6 mL
6	3	0.8 mL
7	3	1.0 mL
Maintenance	3	1.0 mL

Maintenance Dose Bottle No: 3 1.0 mL at 4-6 week intervals
Doses in the same week are administered at 30 min intervals

Table II: Allergovit® 006 Cluster Dose Scheme

Week No	Bottle No	Dose (mL)
1	A	0.1 mL
2	A	0.2 mL
3	A	0.4 mL
4	A	0.8 mL
5	B	0.15 mL
6	B	0.3 mL
7	B	0.6 mL
9	B	0.6 mL
Maintenance	B	0.6 mL

Maintenance Dose Bottle B 0.6 mL at 4-8 week intervals

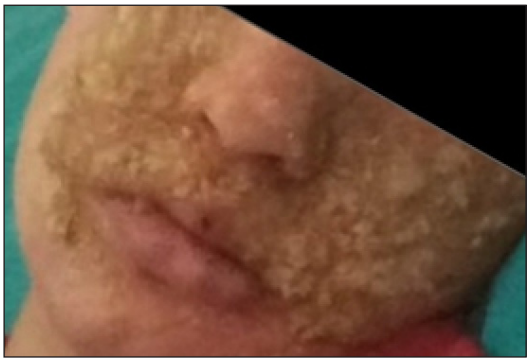

Figure 1: Lesions appearing on the patient's face immediately after SCIT.

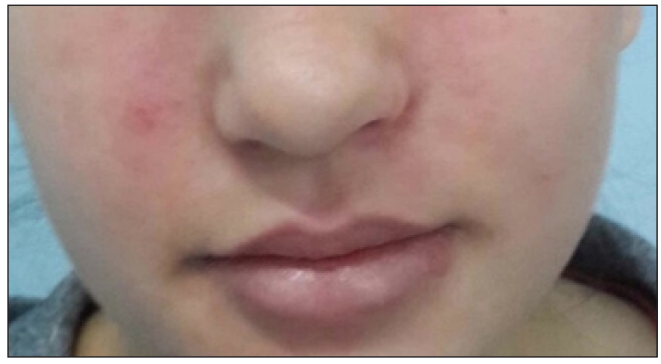

Figure 2: Improvement in the patient's face approximately 1 month after antiviral treatment.

of the dermatology department. The skin lesions gradually regressed during follow-up. The lesions disappeared completely after about a month (Figure 2). The patient, who was very concerned that the lesions were in the facial area and might leave scars during the healing period, did not accept AIT for allergic rhinitis and medical treatment was continued.

DISCUSSION

AD is a chronic relapsing skin disease with a prevalence of 5% to 20% that frequently affects children; it is characterized by erythematous and pruritic rashes and has a complex etiology (6). It is usually associated with high serum total IgE levels and a personal or family history of atopy, including a group of diseases such as eczema, asthma, and allergic rhinitis. EH, also known as Kaposi's varicelliform eruption, is a rare complication that occurs in less than 3% of patients with AD. The most common causes of EH are HSV type 1 and type 2. It has also been shown that Coxsackie virus A16 and the vaccinia virus play a role in the pathogenesis of EH (7). In some patients, it may be disseminated or fatal with visceral involvement. The mortality rate is between 1% and 9% (8). Severe eczema, high serum total IgE levels, and a history of food allergy or asthma are predisposing factors for EH (9). Although the disease can be seen clinically anywhere on the body where epithelial barrier damage is present, it is most commonly localized on the face and neck. The presence of diffuse lesions 2-3 mm in diameter is a clue for the diagnosis. Fever and regional lymphadenopathies may accompany the lesions (10). Similar to the literature, our patient had diffuse lesions on the face, but no fever or lymphadenopathy was observed.

The diagnosis of EH is mainly clinical. However, due to the potential diversity of EH clinical manifestations, physicians confirm their diagnosis using diverse laboratory techniques such as the Tzanck smear, HSV culture, direct immunofluorescence (IF), or polymerase chain reaction (PCR). Nowadays, molecular biological techniques are preferentially chosen because of their ease of use, reliability, and high sensitivity (4). Indeed, PCR is positive in 100% of cases when performed on early lesions, and positivity rates remain higher than 80% on later lesions as well (over 30 days) (11). Because of potential severe complications and fatal outcomes, the diagnosis must be established without delay, upon the first consultation. Treatment should start based on clinical characteristics as soon as the infection is suspected and without waiting for the results of the complementary analyses.

Allergic contact dermatitis, impetigo and histiocytosis, especially varicella zoster, should be considered in the differential diagnosis (12). In the treatment of EH, systemic antiviral and antibacterial therapy should be planned in addition to topical antiviral and antibacterial therapy, depending on the extent of the lesion (13). In our patient, oral amoxicillin + clavulanic-acid and acyclovir and topical acyclovir treatment were used due to the widespread involvement of the face area. The lesions were completely controlled within a month. We experienced that this patient had a diagnosis of AD, which was a predisposing factor for EH, and that eczema herpeticum emerged after SCIT. We think that the presence of AD should be considered in patients who are planned to start AIT against the complications that may occur in the later stages of treatment. Our patient also had a diagnosis of AD before SCIT was started. In this patient, we initiated 2 different SCIT treatments on the same day. Simultaneous initiation of 2

SCIT treatments in a patient with AD may have triggered the development of EH. However, there is no data in the literature on EH after AIT so we wanted to share a very rare case.

Conflict of Interest

No conflict of interest.

Funding

There are no sources of funding to declare.

Authorship Contributions

Concept: **Fatma Merve Tepetam, Seyma Ozden,** Design: **Tugce Yakut, Selver Seda Mersin,** Data collection or processing: **Tugce Yakut, Cihan Orcen,** Analysis or Interpretation: **Fatma Merve Tepetam, Seyma Ozden,** Literature search: **Tugce Yakut, Cihan Orcen,** Writing: **Fatma Merve Tepetam, Seyma Ozden, Tugce Yakut,** Approval: **Selver Seda Mersin, Cihan Orcen.**

Ethical Approval

Informed consent was obtained from the patient who agreed to take part in the study. Ethical approval is not required at our institution to publish an anonymous case report.

REFERENCES

1. Calderon MA, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S. Allergen injection immunotherapy for seasonal allergic rhinitis. Cochrane Database Syst Rev 2007;2007(1):CD001936
2. Norman PS. Immunotherapy: 1999-2004. J Allergy Clin Immunol 2004;113(6):1013-23; quiz 1024.
3. Kalpaklıoğlu AF, Demirel YS. Turkish National Society of Allergy and Clinical Immunology Alerjik Rinit Tanı ve Tedavi Rehberi 2022. Ankara, 2022:124.
4. Damour A, Garcia M, Seneschal J, Lévêque N, Bodet C. Eczema herpeticum: clinical and pathophysiological aspects. Clin Rev Allergy Immunol 2020;59(1):1-18.
5. Baççıoğlu A, Kalpaklıoğlu AF, Poyraz M, Alan Yalım S, Dumanoğlu B, Alpağat G. Characteristics of adverse reactions and compliance in patients who underwent allergen-specific subcutaneous immunotherapy; ten-year real-life data. Asthma Allergy Immunol 2022;20:6-15.
6. Nelson HS. Advances in upper airway diseases and allergen immunotherapy. J Allergy Clin Immunol 2004;113(4):635-42.
7. Kang BC, Johnson J, Morgan C, Chang JL. The role of immunotherapy in cockroach asthma. J Asthma 1988;25(4):205-18.
8. Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I. et al. Allergen immunotherapy: a practice parameter third update. J Allergy Clin Immunol 2011;127(1 Suppl):S1-55.
9. Williams H, Robertson C, Stewart A, Aït-Khaled N, Anabwani G, Anderson R, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. J Allergy Clin Immunol 1999;103(1 Pt 1):125-38.
10. Spergel JM. From atopic dermatitis to asthma: the atopic march. Ann Allergy Asthma Immunol 2010;105(2):99-106; quiz 107-9, 117.
11. Ozcan A, Senol M, Saglam H, Seyhan M, Durmaz R, Aktas E et al. Comparison of the Tzanck test and polymerase chain reaction in the diagnosis of cutaneous herpes simplex and varicella zoster virus infections. Int J Dermatol 2007;46(11):1177-9.
12. Leung DY. Why is eczema herpeticum unexpectedly rare? Antiviral Res. 2013;98(2):153-7.
13. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968. N Engl J Med 1969;281(22):1201-8.