Received: 8 January 2020 | Revised: 16 July 2020 | Accepted: 26 July 2020

DOI: 10.1111/dth.14147

THERAPEUTIC HOTLINE: SHORT PAPER

DERMATOLOGIC THERAPY WILEY

Dyshidrotic eczema and seborrheic dermatitis-like eczematous eruption following intravenous immunoglobulin therapy

Zennure Takci[1] | Gulcin Guler Simsek[2] | Hatice Uzuner[3] | Atiye Akbayrak[1] | Havva Yıldız Seckin[1] | Ayse Serap Karadag[4]

[1]Department of Dermatology, Faculty of Medicine, Gaziosmanpasa University, Tokat, Turkey

[2]Department of Pathology, Kecioren Research and Training Hospital, Ankara, Turkey

[3]Department of Pathology, Samsun Research and Training Hospital, Samsun, Turkey

[4]Department of Dermatology, Medical Faculty, Istanbul Medeniyet University, Göztepe Research and Training Hospital, Istanbul, Turkey

Correspondence
Associated Professor Zennure Takci, Department of Dermatology, Faculty of Medicine, Gaziosmanpasa University, Tokat 60100, Turkey.
Email: drzennure80@yahoo.com

Abstract

Intravenous immunoglobulin (IVIg) is increasingly used for the treatment of inflammatory and autoimmune diseases. Although skin reactions to IVIg therapy are usually minor, rare, and not life-threatening, dermatologists need to recognize the nature of these adverse reactions. We describe a 33-year-old man suffering from demyelinating polyneuropathy who developed dyshidrotic eczema on the palms and flaky grayish-white scales on an erythematous base on his face after the administration of IVIg.

KEYWORDS

dyshidrotic eczema, intravenous immunoglobulin, seborrheic dermatitis-like eczematous eruption, skin reaction

1 | INTRODUCTION

Intravenous immunoglobulin (IVIg) is a blood product consisting of mostly IgG antibodies used on- and off-label for the treatment of many immune-mediated neurologic, hematologic, and dermatologic disorders.[1] Adverse reactions to IVIg therapy are usually minor such as mild-to-moderate headache, fever, chills, fatigue, nausea, arthralgias, myalgias, and chest discomfort. Severe complications such as hemolytic anemia, thrombosis, acute renal failure, aseptic meningitis, and anaphylactic shock were rarely reported.[2] Furthermore, 0.4% to 6% of patients treated with IVIg may display cutaneous adverse effects.[3] Among other adverse skin reactions, it causes eczematous reactions clinically typical as pompholyx[3]. To the best of our knowledge, no studies reported seborrheic dermatitis-like eczematous eruption following IVIg therapy. Here, we report a patient receiving IVIg for demyelinating polyneuropathy who developed dyshidrotic eczema and seborrheic-dermatitis like eczematous eruption 3 days following his first IVIg therapy and recurrence after the following course of IVIg therapy.

2 | CASE REPORT

A 33-year-old man admitted to outpatient clinic with a complaint of pruriginous water-filled blisters on the palms and scaly erythema on his face. He was diagnosed with demyelinating polyneuropathy a month prior and received IVIg therapy (Genivig 5% Human Immunoglobulin; Sichuan Yuanda Shuyang Pharmaceutical Co., Sichuan, China) at a dose of 0.4 g/kg/d for five consecutive days and the therapy was then suspended for 10 days. Three days after the 5-day IVIg course, pruriginous erythema and small vesicles appeared on the palms, thereafter pruriginous scaling erythema arose around his forehead, eyebrows, and ear folds. Following the 10-day treatment-free period, weekly IVIg therapy was resumed at a dose of 0.4 g/kg. After the first weekly IVIg infusion, the patient presented to the outpatient clinic with an increase in cutaneous complaints. He had no known history of any significant medical disease except for demyelinating polyneuropathy. The patient also had no history of atopy, hand eczema, seborrheic dermatitis, or superficial dermatophyte infection such as tinea pedis and drug allergies or cutaneous drug reactions. Besides IVIg, he received no new medications and he was not aware of any contact with new substances. On dermatological examination, there was pale erythema, multiple small vesicles, and squam on the bilateral palms (Figure 1), and white, moderate scaling erythema on the face, particularly the forehead, eyebrows, ear folds, and behind the ear was seen (Figure 2). Findings of a complete blood cell count and blood chemical analysis were normal. Serologic analysis for syphilis, hepatitis B and C, and human immunodeficiency virus was negative. Serologic findings for cytomegalovirus, Epstein-Barr virus, and parvovirus B19

were positive for IgG but negative for IgM. Histopathological examination of a skin punch biopsy sample from the palm showed marked spongiosis with intraepidermal vesicle formation and a dermal perivascular inflammatory infiltrate mainly composed of lymphocytes and eosinophils. A skin biopsy specimen taken from a scaling erythematous lesion on the face revealed a dermal perivascular and perifollicular inflammatory cell infiltrate composed of predominantly lymphocytes and eosinophils (Figure 3). Patch and prick tests were performed with immunoglobulin (Genivig 5%, 1/100, 1/10 in phosphate-buffered saline). All tests were negative upon immediate and delayed reading (96 hours and 1 week). Topical 0.1% mometasone furoate ointment was prescribed, and the seborrheic dermatitis-like rash regressed and vesicles on the palms resolved with desquamation. However, the lesions flared up, after the following next weekly IVIg infusion. The patient wanted to continue the IVIg therapy because of the neurologic clinical benefit. Because a recurrence of the same eruption was observed during the sequential courses of IVIg therapy, we believe these dyshidrotic eczematous and seborrheic dermatitis-like lesions were the result of the IVIg therapy.

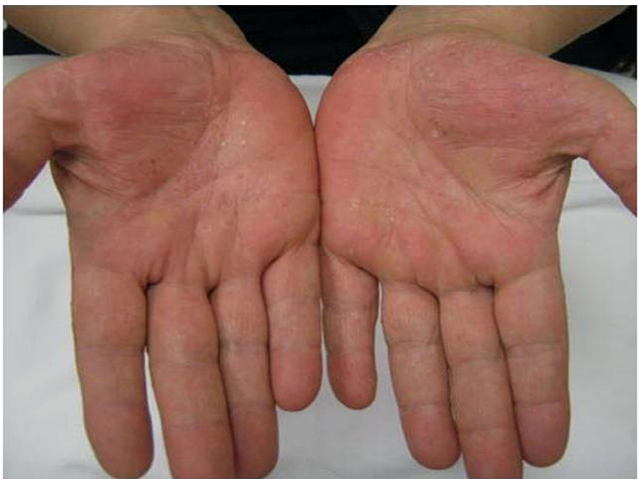

FIGURE 1 Multiple small vesicles and squam on the bilateral palms

3 | DISCUSSION

IVIg is widely used for various inflammatory and autoimmune diseases with good clinical evidence for the effectiveness and safe side-effect profile. Cutaneous adverse reactions to IVIg therapy are rare, including pruritus, eczematous reactions, urticaria, and anecdotal case reports including alopecia, erythema multiforme lichenoid dermatitis, purpuric erythema, and vasculitis.[4-7]

The vesicular eczematous eruption, characterized by pruritic, tense, vesicles localized to the palms and soles (pompholyx or dyshidrotic eczema), was recently described as an IVIg adverse effect. However, its precise etiology is unclear; it was associated with contact allergens, fungal infections, or generalized eczema.[8] When associated with IVIg, the eruption may remain localized to the palms and/or soles or may cause a widespread eczematous rash by spreading to face, trunk, or buttocks. The symptoms usually occur 2 to 5 days after the infusions and may last up to 30 days.[9] When the IVIg therapy was readministered, most of the cases developed the same skin eruption.[8,10]

Miyamoto et al described a case of diffuse eczema affecting the face, trunk, extremities, and palmoplantar region following IVIg therapy for peripheral neuropathy. The patient's skin rash regressed with systemic steroid treatment, and no IVIg therapy was readministered.[11] Vecchietti et al documented four cases of intense eczematous cutaneous eruption approximately 10 days after high-dose IVIg infusion (0.4 g/kg for five consecutive days) for polyradiculoneuritis, characterized by an eczematous rash on the palms and soles initially and then becomes generalized to the whole body. IVIg therapy was discontinued and no recurrent skin rash observed.[10]. Berk-Krauss et al

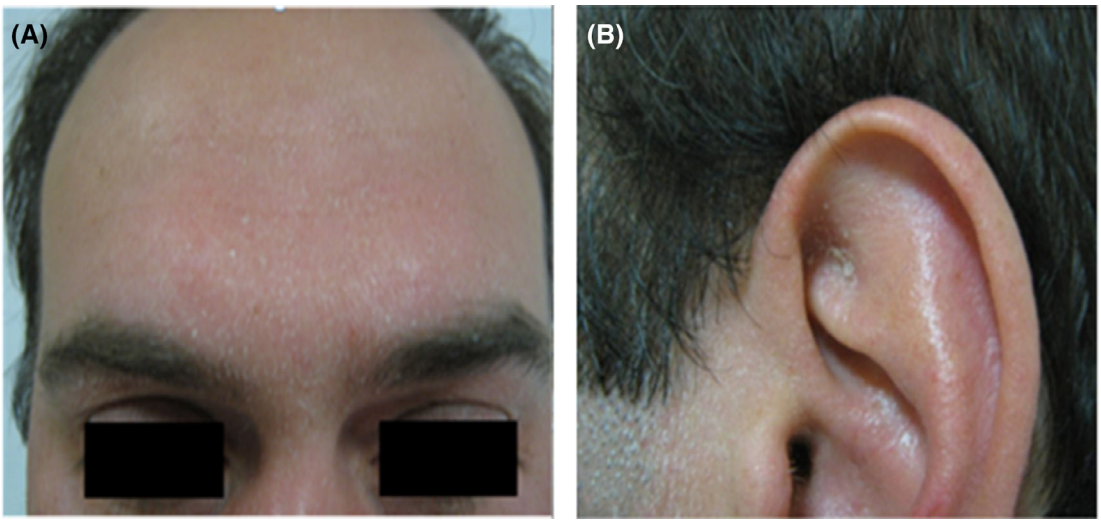

FIGURE 2 A, B, Scaling erythema on the forehead, eyebrows, and ear folds

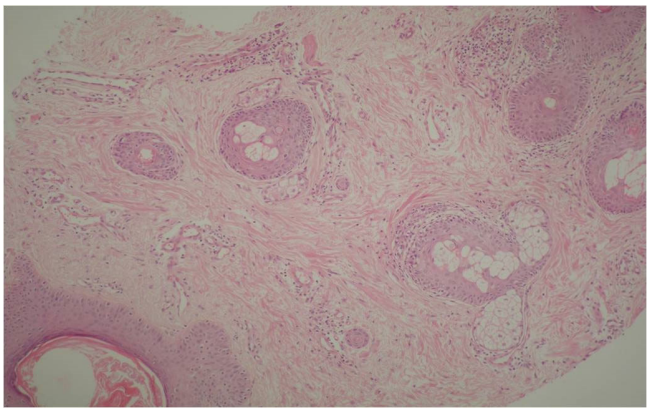

FIGURE 3 Dermal perivascular and perifollicular inflammatory cell infiltrate composed of predominantly lymphocytes and eosinophils (hematoxylin and eosin, original magnification: ×10)

described two cases with dermatomyositis who developed an eczematous generalized skin rash that emerged after receiving IVIg. One patient reported the same cutaneous eruption 2 days after receiving the second IVIg course and no further cutaneous reactions after her third and fourth IVIg therapies. Other case reported a mild dyshidrotic eczema on palms after subsequent IVIG doses.[12]

In our patient, dyshidrotic eczema on the palms began 3 days after the cessation of the first 5-day IVIg therapy. There was no vesicular eczematous eruption in other parts of the body, such as face or trunk. But, the patient developed flaky grayish-white scales on the skin near the eyelashes, forehead, sides of the nose, ear folds, and behind the ears, following the dyshidrotic eczema as differed from the reports in the literature. The cutaneous complaints increased after the first weekly IVIg infusion, following the 10-day treatment-free period. The seborrheic dermatitis-like rash and vesicles on palms regressed with the topical corticosteroid ointment. However, the symptoms recurred after the following weekly IVIg infusion, which was a conspicuous point of the strong temporal association with relapse when IVIg was readministered. In the follow-up, mild eczematous attacks such as dyshidrosis and seborrheic dermatitis that started within 2 to 3 days following IVIg infusion were observed but controlled easily with topical steroids.

IVIg is a purified polyvalent antibody product, produced from a large donor pool of human plasma. Due to different purification methods used among manufacturers, traces of other immunologically active molecules such as soluble major histocompatibility complex molecules and soluble CD4 and CD8 were observed besides IgG. The diversity in the preparation may influence the side effects and safety of the IVIg preparations.[4,9] The pathogenesis of adverse cutaneous reactions to IVIg remains unclear, although higher doses and faster flow rates, which result in high-dose administration of drugs within a short time, have been suggested. Rhee et al suggested that pompholyx may be due to a delayed-type hypersensitivity in response to an unidentified substance within IVIg. The high perspiration rate of affected areas of the skin may enable accumulation of these potential allergens.[13] On the contrary, it has been suggested that IVIg may act like a B-cell superantigen, followed by selective activation of certain B cells.[14]

Recently, the spectrum of possible side effects of IVIg has been enlarged by the report of eczematous reactions of unknown pathophysiologic mechanisms. Here, we intended to contribute the literature by reporting this case. Although the adverse reactions seen in our patient is not life-threatening, it is important to recognize the nature of these reactions as the side effects of IVIg. Further study is warranted to clarify the mechanisms of these two dermatologic manifestations.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this report are available from the corresponding author upon reasonable request.

ORCID

Zennure Takci https://orcid.org/0000-0001-7257-5792
Atiye Akbayrak https://orcid.org/0000-0003-2999-2691
Ayse Serap Karadag https://orcid.org/0000-0003-4333-8274

REFERENCES

1. Kazatchkine MD, Kaveri SV. Immunomodulation of autoimmune and inflammatory diseases with intravenous immunoglobulin. *N Engl J Med*. 2001;345:747-755.
2. Orbach H, Katz U, Sherer Y, Shoenfeld Y. Intravenous immunoglobulin: adverse effects and safe administration. *Clin Rev Allergy Immunol*. 2005;29(3):173-184.
3. Gerstenblith MR, Antony AK, Junkins-Hopkins JM, Abuav R. Pompholyx and eczematous reactions associated with intravenous immunoglobulin therapy. *J Am Acad Dermatol*. 2012;66(2):312-316.
4. Cohen Aubart F, Barete S, Amoura Z, Francès C, Lyon-Caen O, Lebrun-Vignes B. Intravenous immunoglobulins-induced eczematous eruption: a long-term follow-up study. *Eur J Intern Med*. 2009;20(1):70-73.
5. Howse M, Bindoff L, Carmichael A. Facial vasculitic rash associated with intravenous immunoglobulin. *BMJ*. 1998;317:1291.
6. Leclech C, Maillard H, Penisson-Besnier I, Laine-Cessac P, Verret JL. Unusual skin reaction after intravenous infusion of polyvalent immunoglobulins: 3 case reports. *Presse Med*. 1999;28:531.
7. Yockey SM, Ahmed I. Intravenous immunoglobulin-induced lichenoid dermatitis: a unique adverse reaction. *Mayo Clin Proc*. 1997;72:1151-1152.
8. Uyttendaele H, Obadiah J, Grossman M. Dyshidrotic-like spongiotic dermatitis after intravenous immunoglobulin therapy. *J Drugs Dermatol*. 2003;2(3):337-341.
9. Dalakas MC. The use of intravenous immunoglobulin in the treatment of autoimmune neuromuscular diseases: evidence-based indications and safety profile. *Pharmacol Ther*. 2004;102(3):177-193.
10. Vecchietti G, Kerl K, Prins C, Kaya G, Saurat JH, French LE. Severe eczematous skin reaction after high-dose intravenous immunoglobulin infusion: report of 4 cases and review of the literature. *Arch Dermatol*. 2006;42(2):213-217.
11. Miyamoto J, Böckle BC, Zillikens D, Schmidt E, Schmuth M. Eczematous reaction to intravenous immunoglobulin: an alternative cause of eczema. *JAMA Dermatol*. 2014;150(10):1120-1122.
12. Berk-Krauss J, Lee K, Lo Sicco KI, Liebman TN. Eczematous reaction to IVIG for the treatment of dermatomyositis. *Int J Womens Dermatol*. 2018;4(3):170-173.

13. Rhee DY, Park GH, Chang SE, et al. Pompholyx after intravenous immunoglobulin therapy for treatment of Guillain-Barré syndrome. *J Eur Acad Dermatol Venereol*. 2009;23(5):602-604.
14. Leucht S, Uttenreuther-Fischer MM, Gaedicke G, Fischer P. The B cell superantigen-like interaction of intravenous immunoglobin (IVIG) with Fab fragments of V (H) 3–23 and 3–30/3–30.5 germline gene origin cloned from a patient with Kawasaki disease is enhanced after IVIG therapy. *Clin Immunol*. 2001;99:18-29.

How to cite this article: Takci Z, Guler Simsek G, Uzuner H, Akbayrak A, Yıldız Seckin H, Karadag AS. Dyshidrotic eczema and seborrheic dermatitis-like eczematous eruption following intravenous immunoglobulin therapy. *Dermatologic Therapy*. 2020;e14147. https://doi.org/10.1111/dth.14147