lymphoproliferative disorder patients without a lysine methyltransferase two-dimensional mutation showed milder symptoms with a more favourable prognosis. Genetic variation, immune deficiency and Epstein–Barr virus infection play important roles in the development of the disease, which explains why this patient's clinical course was characterised by rapid progress and repeated recurrence.

In conclusion, severe atypical symptoms may occur in patients with hydroa vacciniforme-like lymphoproliferative disorder. The presence of genetic defects and/or immunodeficiency may be considered in this setting.

Authors Contributions

Donghua Liu proposed the conception of the work and designed the study. Li Chang and Chaoyin Zhang contributed equally to the collection of data and the writing of the manuscript. Xue Yang provided patient care. Raqib Khan performed data analysis and revised the article. Donghua Liu supervised the manuscript. All authors critically assessed the manuscript for intellectual content.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflict of interest

The authors declare no competing financial interests. The table cited in this article has been obtained with appropriate permission.

Chaoyin Zhang, Li Chang, Xue Yang, Raqib Khan, Donghua Liu

Department of Dermatology and Venereology, First Affiliated Hospital of Guangxi Medical University, Nanning, China

Corresponding author:
Dr. Donghua Liu,
Department of Dermatology and Venereology, First Affiliated Hospital of Guangxi Medical University, No. 6, Shuang Yong Road, Nanning, Guangxi, China,
ldhgxmu@163.com

References

1. Biggs CM, Keles S, Chatila TA. DOCK8 deficiency: Insights into pathophysiology, clinical features and management. Clin Immunol 2017;181:75–82.
2. Quintanilla-Martinez L, Ridaura C, Nagl F, Saez-de-Ocariz M, Duran-McKinster C, Ruiz-Maldonado R, *et al*. Hydroa vacciniforme-like lymphoma: A chronic EBV+ lymphoproliferative disorder with risk to develop a systemic lymphoma. Blood 2013;122:3101–10.
3. Chang CH, Hsu YH. Hyper-IgE syndrome with Epstein-Barr virus associated extranodal NK/T cell lymphoma of skin. Kaohsiung J Med Sci 2010;26:206–10.
4. Chen CC, Chang KC, Medeiros LJ, Lee JY. Hydroa vacciniforme and hydroa vacciniforme-like lymphoproliferative disorder: A spectrum of disease phenotypes associated with ultraviolet irradiation and chronic Epstein-Barr virus Infection. Int J Mol Sci 2020;21:9314.
5. Cohen JI, Iwatsuki K, Ko YH, Kimura H, Manoli I, Ohshima K, *et al*. Epstein-Barr virus NK and T cell lymphoproliferative disease: Report of a 2018 international meeting. Leuk Lymphoma 2020;61:808–19.
6. Margolskee E, Jobanputra V, Jain P, Chen J, Ganapathi K, Nahum O, *et al*. Genetic landscape of T- and NK-cell post-transplant lymphoproliferative disorders. Oncotarget 2016;7:37636–48.

Dupilumab use in non-atopic chronic hand eczema: Two cases and a review of the literature

Sir,

Chronic hand eczema (CHE) is a common inflammatory disease that seriously affects people's quality of life. Chronic eczema is generally resistant to topical treatment, dupilumab has been found to be effective in few cases of hand eczema with associated atopic dermatitis. We report two cases of non-atopic CHE who are successfully treated with dupilumab.

Case 1: A 57-year-old man presented to the dermatology clinic with a 1-year history of dry, fissured, scaling eruptions on the fingertips and palms, accompanied by minor itching. He had received multiple treatments including potent topical corticosteroids and tacrolimus but with little improvement. On physical examination, his fingertips and palms exhibited dry, fissured and scaly plaques without any vesicles [Figure 1a].

How to cite this article: Li T, Li H, Zhang J. Dupilumab use in non-atopic chronic hand eczema: Two cases and a review of the literature. Indian J Dermatol Venereol Leprol 2023;89:877-9.

Received: August, 2022 **Accepted:** October, 2022 **EPub Ahead of Print:** March, 2023 **Published:** October, 2023

DOI: 10.25259/IJDVL_721_2022 **PMID:** 37067123

Figure 1a: Case 1 at baseline

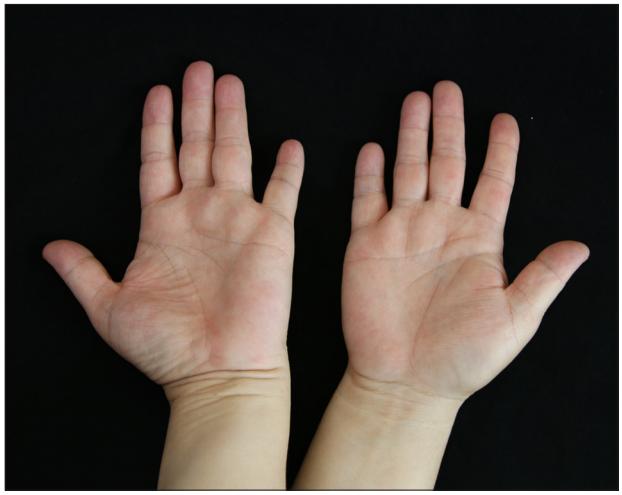

Figure 1b: Case 1 after 12 weeks of treatment

Laboratory studies and the patch test showed no positive results. Due to the absence of a history of allergic disorders, non-atopic hyperkeratotic CHE was diagnosed but the underlying aetiology remained unknown. Traditionally, oral retinoids or immunosuppressive agents are administered when the topical therapy is inadequate. However, given the safety profile, the patient preferred a biological agent so he received a 600 mg injection of dupilumab as a loading dose and 300 mg injection every 2 weeks thereafter. Surprisingly, his persistent lesions improved completely after 3 months [Figure 1b]. The dermatology life quality index score decreased from 11.9 points at baseline to 3.6 points 3 months later. The treatment was well tolerated and no side effect was observed.

Case 2: A 58-year-old woman presented with a 20-year history of progressive desquamative and fissured eruption on her fingertips [Figure 2a], accompanied by minor pain. There were no vesicles and no rashes on any other part of the body. She had received potent corticosteroids and tacrolimus under occlusion but the effect was poor. No allergen was detected through the patch test. Similar to case 1, she had no history of atopy and non-atopic hyperkeratotic CHE was diagnosed. After consulting with the patient, she chose a biological agent over a conventional topical treatment. The treatment of dupilumab was initiated with 600 mg subcutaneously on day 1 followed by 300 mg subcutaneously every 14 days. Her response was so impressive that a 90% improvement was observed in just 2 weeks, and she completely recovered in 6 weeks [Figure 2b]. Six weeks later, the dermatology life

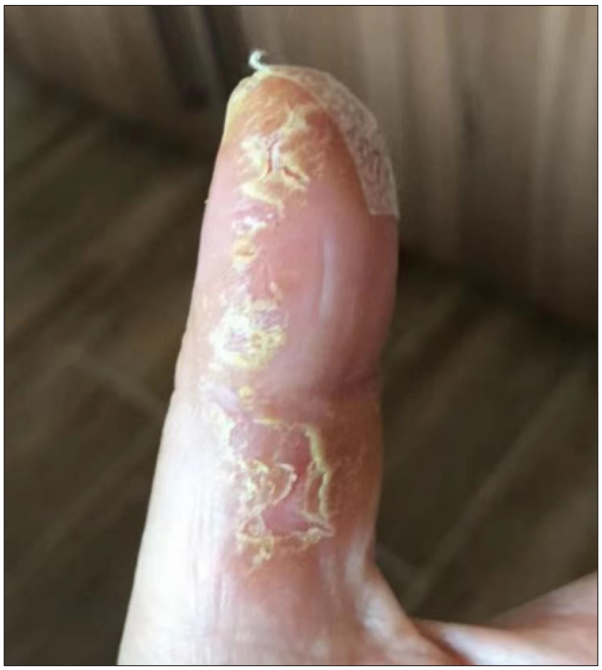

Figure 2a: Case 2 at baseline

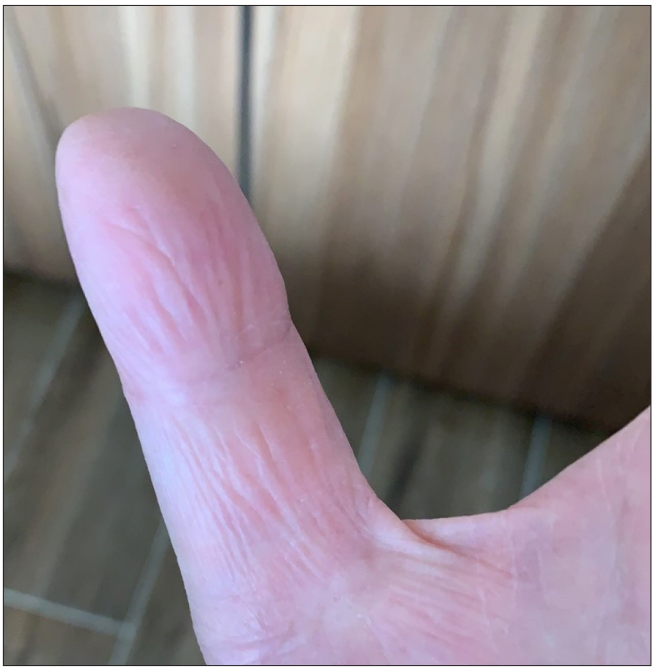

Figure 2b: Case 2 after 6 weeks of treatment

Table 1: Published and our cases of non-atopic CHE treated with dupilumab

Case	Sex, age	Clinical pattern and severity	History of atopy	Patch test	Disease duration	Previous therapy	Response to dupilumab	Adverse events
Halling *et al.*, 2020	M, 67	Vesicular CHE, severe	No	−	3 years	tCS, Pho, Mtx, Azt, CsA	Almost clear in 4 weeks	N/S
Zhu *et al.*, 2020	M, 43	Hyperkeratotic CHE, severe	No	−	5 years	tCS, Pho, alitretinoin, Mtx, CS	Almost clear in 4 weeks	N/S
Loman *et al.*, 2021	M, 65	Hyperkeratotic CHE, moderate	No	−	4 years	tCS, Mtx, alitretinoin	Only improvement of itch in 16 weeks	N/S
	M, 47	Hyperkeratotic CHE, severe	No	−	9 years	tCS, Mtx, alitretinoin, CsA	Almost clear in 16 weeks	N/S
	F, 65	Hyperkeratotic CHE, severe	No	−	4 years	tCS, Azt, alitretinoin	Almost clear in 16 weeks	N/S
Our cases	M, 57	Hyperkeratotic CHE, severe	No	−	1 year	tCS, topical tacrolimus	Almost clear in 12 weeks	None
	F, 58	Hyperkeratotic CHE, severe	No	−	20 years	tCS, topical tacrolimus	Almost clear in 6 weeks	None

tCS, topical corticosteroids; Pho, phototherapy; Mtx, methotrexate; Azt, azathioprine; CsA, cyclosporine; N/S, not significant

quality index score decreased from 10.7 points at baseline to 4.8 points. No adverse events were reported and the response was maintained until the time of writing.

Dupilumab, a fully human monoclonal antibody that blocks IL-4 and IL-13, is proven for the treatment of atopic dermatitis. CHE is a potential new indication for dupilumab since numerous studies have shown remarkable effects in CHE patients with atopy.[1]

We found only five previous reports of non-atopic patients with persistent CHE treated with dupilumab [Table 1].[2–4] All of the seven cases including ours were treated with dupilumab at standard FDA-approved dosing, and the lesions of six cases were almost cleared in 4–16 weeks. Only one case had little improvement, which may be caused by continuous occupational exposure to irritants and friction. Crepy *et al.*[5] reported a similar case in which an atopic CHE with documented occupational exposure had a poor response to dupilumab.

In conclusion, we have described two cases that strengthen the evidence that dupilumab's efficacy in non-atopic CHE is equally promising. In addition, based on the scientific evidence, those with continuous occupational exposure may have a limited response to dupilumab whether they were of atopic or not.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest.

Tingting Li, Houmin Li, Jianzhong Zhang

Department of Dermatology, Peking University People's Hospital, Beijing, China.

Corresponding author:
Dr. Jianzhong Zhang,
Department of Dermatology,
Peking University People's Hospital,
Beijing, China.
rmzjz@126.com

References

1. Voorberg AN, Romeijn GLE, de Bruin-Weller MS, Schuttelaar MLA. The long-term effect of dupilumab on chronic hand eczema in patients with moderate to severe atopic dermatitis—52 week results from the Dutch BioDay Registry. Contact Dermatitis 2022;87:185–91.
2. Halling AS, Zachariae C, Thyssen JP. Severe treatment-resistant acute and recurrent vesicular chronic hand eczema successfully treated with dupilumab. Contact Dermatitis 2020;83:37–8.
3. Zhu GA, Honari G, Ko JM, Chiou AS, Chen JK. Dupilumab for occupational irritant hand dermatitis in a nonatopic individual: A case report. JAAD Case Rep 2020;6:296–8.
4. Loman L, Diercks GFH, Schuttelaar MLA. Three cases of non-atopic hyperkeratotic hand eczema treated with dupilumab. Contact Dermatitis 2021;84:124–7.
5. Crepy MN, Nosbaum A, Bensefa-Colas L. Blocking type 2 inflammation by dupilumab does not control classic (type 1-driven) allergic contact dermatitis in chronic hand eczema. Contact Dermatitis 2019;81:145–7.