Dupilumab in HIV-positive patients: A case series report of 4 patients

Ameen Alawadhi, MD,[a] Damira Karibayeva, MD,[b] and Alice B. Gottlieb, MD, PhD[a]
New York, New York and Pittsfield, Massachusetts

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INTRODUCTION

Atopic dermatitis (AD) is a common inflammatory skin disorder affecting 10%-30% of children and 2%-10% of adults.[1] The hallmark features of AD are xerosis and pruritus, in which the skin appears prominently dry and is associated with a relentless desire to rub and scratch the skin, the latter being a cause of considerable impact on a patient's quality of life. AD is further characterized by its chronic course, hereditary nature, and association with other atopic disorders such as asthma and hay fever.

Treatment for AD has traditionally been largely focused on topical agents. This was partly because most of the systemic treatment options for AD had either a low efficacy or an unacceptable safety profile. Thus, the treatment of more severe or less responsive cases of AD was severely limited.

In 2017, dupilumab was approved for the treatment of AD, and the landscape of AD management drastically changed. Dupilumab is a monoclonal antibody that targets the alpha subunit of the interleukin 4 receptor (IL-4Rα), thus modulating the signaling of both IL-4 and IL-13. Its marked efficacy, paired with a limited set of side effects, allowed it to quickly become a first-line treatment option for moderate-to-severe cases of AD.

Although no formal study has been conducted to assess the exact prevalence of atopic disorders in patients with HIV/AIDS, these patients have been observed to have a higher incidence of atopic disorders. The exact mechanism for this increase is not entirely understood, but it is presumed to be in part due to the increased helper T cell type 2 (TH2) cytokine release observed in HIV/AIDS.[2]

Abbreviations used:

AD:	atopic dermatitis
BSA:	body surface area
HAART:	highly active antiretroviral therapy
IGA:	investigator global assessment
TH2:	helper T cell type 2

Given the many concerns regarding treatment with monoclonal antibodies in patients with HIV/AIDS, we examined the safety of using dupilumab as a treatment option for HIV/AIDS patients who suffered from moderate-to-severe AD. To date, there have not been any large-scale studies or case series assessing the efficacy and safety of dupilumab in HIV/AIDS patients. We present a case series of 4 patients treated with dupilumab, all of whom were diagnosed with moderate or severe AD and HIV (Table I).

CASE 1

A 51-year-old male with a medical history of asthma, hay fever, and HIV controlled with highly active antiretroviral therapy (HAART) (CD4 count, 837 cells/μL, undetectable viral load) presented with complaints of severe xerosis and pruritus for 5 years, which he attributed to being HIV-positive (Figs 1 and 2). The patient tried numerous topical therapies, without improvement. Physical examination revealed severe erythematous lichenified scaly plaques on the face, trunk, and extremities, with an

From the Icahn School of Medicine at Mount Sinai, New York,[a] and Berkshire Medical Center, Pittsfield.[b]

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Correspondence to: Ameen Alawadhi, MD, Department of Dermatology, The Icahn School of Medicine at Mount Sinai, 10 Union Square E, New York, NY 10003. E-mail: drameenalawadhi@gmail.com.

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Table I. Patient demographics and clinical characteristics

Case number	Age	Sex	Duration of follow-up (months)	VL/CD4 count before treatment	VL/CD4 count at follow-up	BSA%/IGA before treatment	BSA%/IGA at follow-up
1	51	M	6	837 cells/μL/undetectable	1001 cells/μL/undetectable	95%/4	30%/1-2
2	42	M	8	245 cells/μL/undetectable	259 cells/μL/undetectable	50%/3	5%/1
3	59	M	3	425 cells/μL/38 cp/mL	594 cells/μL/23 cp/mL	90%/4	40%/1
4	54	M	7	701 cells/μL/undetectable	606 cells/μL/undetectable	NA	NA/0

BSA, Body surface area; *IGA*, investigator global assessment; *NA*, not available.

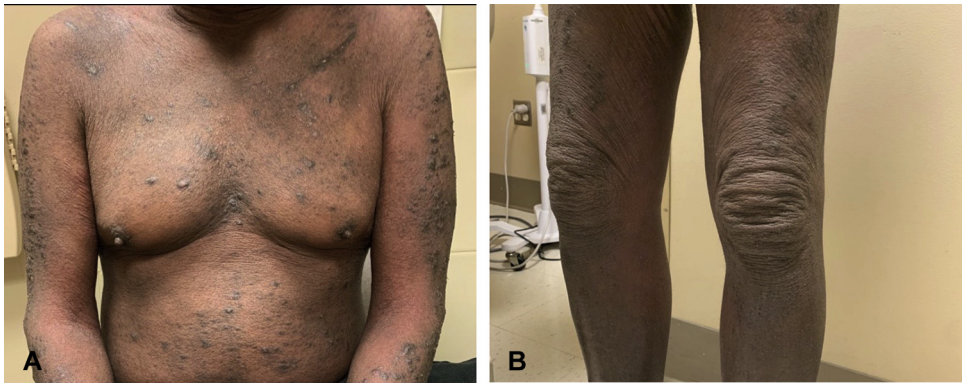

Fig 1. Erythematous lichenified scaly plaques and hyperpigmented papules with excoriations.

investigator global assessment (IGA) of 4 and body surface area (BSA) of 95%. Hyperpigmented papules with or without overlying erosions and linear excoriations were also present on most skin surfaces. The patient was diagnosed with erythrodermic AD and prurigo nodularis and started on dupilumab. After 1 month of treatment, the patient reported a significant improvement in his symptoms, and a physical examination showed an IGA of 1-2 and BSA of 30%. The patient was followed up monthly for 6 months, and laboratory tests did not show any changes in the CD4 count or viral load. The patient also reported an improvement in the asthma and hay fever symptoms since the initiation of the dupilumab injections; he is no longer using his inhaler.

CASE 2

A 42-year-old male with HIV controlled with HAART (CD4 count, 245 cells/μL, undetectable viral load) presented to our clinic complaining of a rash and severe pruritus with an intensity of 10/10 for more than a year. The IGA was 3, and BSA was 50%. A physical examination revealed excoriated erythematous plaques over the trunk, extremities, and scalp. The patient underwent a biopsy, which revealed subacute spongiotic dermatitis with multifocal parakeratosis, consistent with an eczematous process. Treatment with ultraviolet B phototherapy and topical corticosteroids was initiated, but it failed to improve his symptoms. Consequently, the ultraviolet B and topical corticosteroids were discontinued, and dupilumab treatment was initiated. On his 2-month follow-up appointment after starting dupilumab, the patient reported a significant improvement in the symptoms; a physical examination showed an IGA of 1 and BSA of 5%, with the pruritus intensity reduced to 1-2/10. The patient also reported mild dryness of 1 eye, which was relieved with lubricating eye drops. The patient was followed up every 4-8 weeks over a duration of 8 months. Laboratory tests during the treatment period revealed no significant changes in the CD4 count and viral load.

CASE 3

A 59-year-old male patient with a medical history of AD, asthma, gout, and HIV controlled with HAART (CD4 count, 425 cells/μL; viral load, 38 cp/mL), presented for a follow-up of an exacerbation of his AD (Figs 3 and 4). The patient had AD since he was a teenager, which usually manifested as localized patches that were controlled with topical corticosteroids. Clinical examination revealed widespread erythematous patches and plaques with overlying scales, lichenification, and some areas of weeping involving the face, trunk, arms, and legs. The lesions were associated with severe pruritus and a burning sensation. The BSA was 90%, and IGA was 4. Treatment with topical steroids and topical

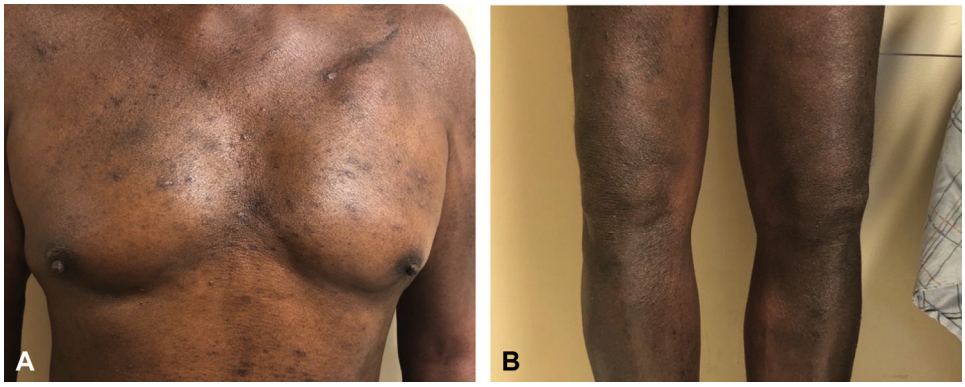

Fig 2. After 1 month of treatment with dupilumab.

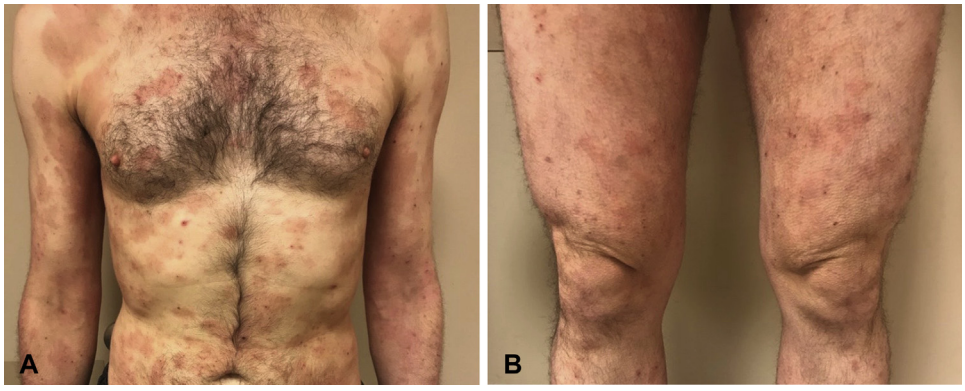

Fig 3. Excoriated erythematous plaques over the trunk and extremities.

calcineurin inhibitors had failed. A decision to start treatment with dupilumab was made. During his follow-up visit 1 month later, the patient reported a significant improvement in his symptoms. Physical examination showed hyperpigmented patches and plaques with mild scaling on the same areas that were associated with mild pruritus, with a BSA of 40% and IGA of 1. The patient had monthly follow-up appointments for 3 months, without significant changes in laboratory tests (CD4 count, 594 cells/μL; viral load, 23 cp/mL).

CASE 4

A 54-year-old male with a medical history of hepatitis B virus and HIV controlled with HAART (CD4 count, 701 cells/μL; undetectable viral load) presented with an intertriginous rash in the axillary and groin area, with a severe pruritus intensity of 7.5/10, which was initially thought to be a fungal infection. He underwent treatment with topical and oral antifungals but without improvement. A physical examination showed bilateral velvety hyperpigmented plaques of the axilla, inner thighs, groin, and posterolateral neck. A biopsy revealed subacute spongiotic dermatitis, consistent with an eczematous reaction pattern. Another biopsy showed secondary changes that were associated with lichen simplex chronicus. The patient was diagnosed with flexural eczema and lichen simplex chronicus. Treatment with several classes of topical corticosteroids, oral corticosteroids, topical crisaborole, and topical tacrolimus had failed to improve his condition. The patient was subsequently started on dupilumab. After 3 months of treatment, the patient reported a significant improvement in his symptoms, and a physical examination showed an IGA of 0. The patient was followed up for 7 months, without significant changes in the CD4 count or viral load.

DISCUSSION

AD is a common skin condition that is more prevalent in the HIV/AIDS population.[2] Due to the immune deficient state in HIV/AIDS, once topical treatments and phototherapy fail, systemic treatment options for HIV/AIDS patients with AD are severely lacking. However, with the introduction of dupilumab as a treatment option for AD, there have been a few case reports describing the efficacy and safety of this drug when used to treat moderate/severe AD in well-controlled HIV/AIDS patients. There have not

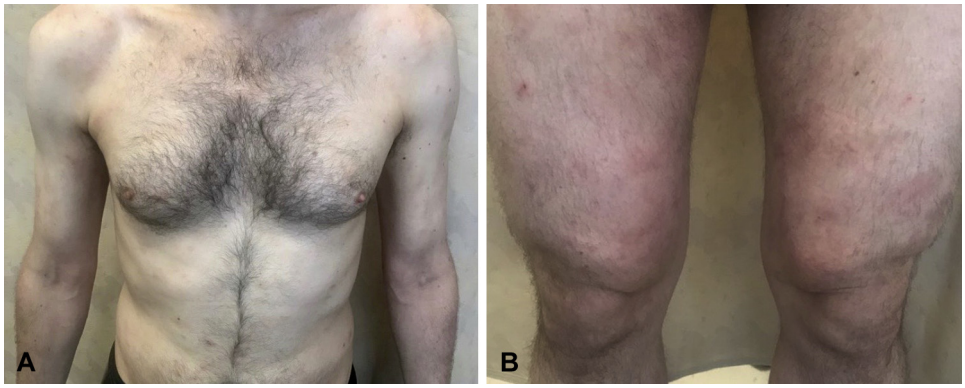

Fig 4. After 2 months of treatment with dupilumab.

been any large trials or case series published to assess its efficacy and safety.[3]

The mechanism of action of dupilumab is particularly interesting in this context. It has been observed that in HIV/AIDS, one of the main aberrations in immunity is a shift from helper T cell type 1 toTH2 immune responses.[4] This shift increases not only the patients' susceptibility to infection but also the risk of developing allergic TH2-mediated disorders. In fact, several studies have shown an increased prevalence of both AD and asthma in HIV/AIDS patients.[5] Thus, given the fact that the mechanism of action of dupilumab involves suppressing TH2 responses by inhibiting IL-4 and IL-13, dupilumab may potentially treat AD and also prevent and treat other allergic disorders, which has been observed in a case report of dupilumab showing both improvement in AD and asthma in a patient in whom the asthma had failed to improve with other treatments.[6]

Although dupilumab is generally considered to be both safe and nonimmunosuppressive, given its immunomodulatory nature, there will always be concerns when it is used for patients who are either immunosuppressed or have an increased risk of a current or future malignancy. A notable example is the recent case review describing the progression to Sézary syndrome in patients with mycosis fungoides who were given dupilumab.[7]

To our knowledge, our study is the first case series conducted to assess the efficacy and safety of dupilumab in the treatment of AD in patients with well-controlled HIV/AIDS. As described in the individual case summaries, all 4 patients had significant improvement in their disease scores, and none of these patients experienced any additional adverse events, new infections, or any changes in their viral load or CD4 counts throughout the study period.

Our study shows that dupilumab may represent a safe and effective option for treating AD in patients with well-controlled HIV/AIDS, but there is a need for larger studies to reliably confirm these results.

REFERENCES

1. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-351.
2. Garg T, Sanke S. Inflammatory dermatoses in human immunodeficiency virus. *Indian J Sex Transm Dis AIDS*. 2017;38(2):113-120.
3. Mollanazar N, Qiu C, Aldrich J, et al. Use of dupilumab in patients who are HIV-positive: report of four cases. *Br J Dermatol*. 2019;181(6):1311-1312.
4. Yechiel B. The changes in the T helper 1 (Th1) and T helper 2 (Th2) cytokine balance during HIV-1 infection are indicative of an allergic response to viral proteins that may be reversed by Th2 cytokine inhibitors and immune response modifiers - A review and hypothesis. *Virus Genes*. 2004;28(1):5-18.
5. Rudikoff D. The relationship between HIV infection and atopic dermatitis. *Curr Allergy Asthma Rep*. 2002;2(4):275-281.
6. Brodska P, Panzner P, Sedlacek D, Terl M, Cetkovska P. Use of dupilumab in a patient with atopic dermatitis, severe asthma, and HIV infection. *Dermatol Ther*. 2020:e14159. https://doi.org/10.1111/dth.14159.
7. Espinosa M, Nguyen M, Aguirre A, et al. Progression of cutaneous T-cell lymphoma after dupilumab: Case review of 7 patients. *J Am Acad Dermatol*. 2020;83:197-199.