

Two Cancer Patients Receiving Dupilumab for Treatment of Atopic Dermatitis

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Dupilumab is the first monoclonal antibody approved for treatment of atopic dermatitis. Dupilumab targets the alpha subunit of interleukin-4 (IL-4) receptor, thereby interfering with IL-4 and IL-13 signaling (1). Long-term safety data for dupilumab is still lacking and clinical studies did not include patients with cancer. Current non-specific systemic immunosuppressive therapies for atopic dermatitis raise safety concerns when used in patients with advanced cancer. Here, we present two patients with advanced cancer receiving dupilumab with no evidence of cancer recurrence.

CASE REPORTS

Case 1. A 22-year-old woman with a history of intermittent asthma, poorly controlled atopic dermatitis since infancy, and a new diagnosis of melanoma presented with severe eczema with over 40% of body surface area involvement and eczema area and severity index (EASI) score of 62. The melanoma had a Breslow thickness of 5 mm. The patient received wide-localized excision and sentinel lymph node biopsy, which was positive.

She reported being extremely bothered by pruritus (numerical rating scale (NRS) 10/10) and inability to sleep. The symptoms were so severe that the patient had opted against adjuvant immunotherapy for her melanoma because of the risk of recrudescence of eczema. Instead, she opted for clinical and imaging surveillance.

The patient's initial regimen included wet wraps, topical mometasone 0.075% in silicone, crisaborole, and low dose mirtazapine at night. This regimen was minimally effective. After discussions with the patient, dermatologist, and oncologist, dupilumab was initiated.

After one month of treatment with dupilumab, the severity of pruritus significantly lessened (NRS 3/10),

her EASI score decreased to 1.8, and only minimal eczematous plaques were present on the lower extremities. At the most recent follow-up visit – 18 months of treatment – the patient denied any pruritus, and physical examination was only remarkable for mild lichenification of the lower extremities. **Fig. 1** shows her progressive improvement on dupilumab after 15 months of treatment. The patient is following up with oncology, and clinical exams and surveillance imaging are negative to-date.

Case 2. A 43-year-old man with a history of atopic dermatitis, human immunodeficiency virus (HIV) on antiretroviral therapy, and anal squamous cell carcinoma (SCC) presented with severe pruritus (NRS 10/10) and a diffuse, eczematous eruption on his arms and trunk. The patient was recently diagnosed with stage IIIb anal SCC and received chemotherapy and radiation. Six months after completing treatment, follow-up PET scan images were distorted due to his severe dermatitis.

Considering his HIV and recent anal SCC, a variety of topical medications including clobetasol 0.05% ointment, triamcinolone 0.1% ointment, and pimecrolimus 1% cream, were prescribed in combination with narrow-band UVB phototherapy. However, the condition did not improve, and he continued to experience frequent flares and developed secondary methicillin-resistant *Staphylococcus aureus* (MRSA) impetiginization requiring antibiotics. Given the severity of his atopic dermatitis, the impact on quality of life, and interference with cancer screening, dupilumab was initiated in coordination with his primary care provider and oncologist.

Two weeks after his first injection of dupilumab, the patient's pruritus was significantly improved (NRS 4/10), and physical examination revealed only lichenified skin and healed scars (**Fig. 2**). Additionally, biopsies of sus-

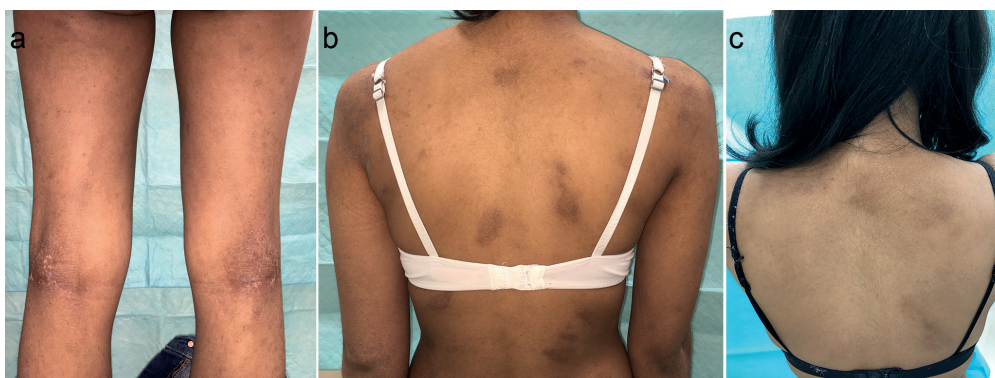


Fig. 1. Patient 1: (a) Posterior bilateral knees with mild lichenification after one month of treatment with dupilumab. (b) The back after 4 months of treatment with dupilumab showing scattered patches of postinflammatory hyperpigmentation and mild lichenification; and (c) back of patient after 15 months of treatment with dupilumab with mild postinflammatory hyperpigmentation.

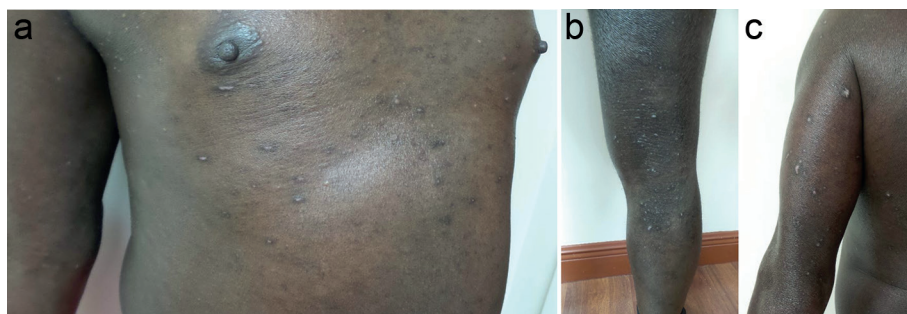


Fig. 2. Patient 2: (a) chest, (b) leg, and (c) back two weeks after receiving his first injection of dupilumab showing scattered lichenified papules and nodules.

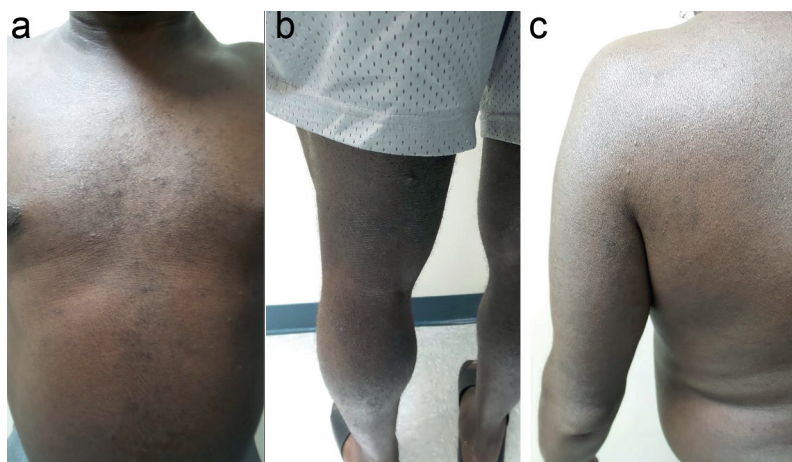


Fig. 3. Patient 2: (a) chest, (b) leg, and (c) back after 9 months of treatment with dupilumab with total clearance of previous lesions.

picious axillary and inguinal nodes were negative for malignancy, CT imaging was stable, and remission was documented. Nine months later, the patient continued to report improvement on dupilumab (**Fig. 3**), having only one localized flare with MRSA infection that responded to antibiotics.

DISCUSSION

Hesitation often arises among prescribers giving immunomodulatory therapies to patients with cancer because of the risk of propagating their condition. Previous immunosuppressant treatments for atopic dermatitis, such as azathioprine and cyclosporine, have posed safety concerns for cancer patients (2–4). Dupilumab, as a targeted treatment, may be more suitable for these cases. A recent systematic review of preclinical and clinical trials showed that there is no risk of malignancy when specifically targeting the IL-13 and IL-4 pathway (5). Herein we present cases that suggest that dupilumab may safely control atopic dermatitis in patients with advanced cancer. Of note, it is always important to evaluate each patient individually and to climb the full therapeutic ladder before dupilumab is indicated in

such patients. Larger studies with long-term follow-up are warranted.

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REFERENCES

1. Gooderham MJ, Hong HC, Eshtiaghi P, Papp KA. Dupilumab: A review of its use in the treatment of atopic dermatitis. *J Am Acad Dermatol* 2018; 78: S28–36.
2. Cho HG, Kuo KY, Xiao K, Batra P, Li S, Tang JY, et al. Azathioprine and risk of multiple keratinocyte cancers. *J Am Acad Dermatol* 2018; 78: 27–28.e1.
3. Sinha A, Velangi S, Natarajan S. Non-hodgkin's lymphoma following treatment of atopic eczema with cyclosporin A. *Acta Derm Venereol* 2004; 84: 327–328.
4. Paul CF, Ho VC, McGeown C, Christophers E, Schmidtman B, Guillaume JC, et al. Risk of malignancies in psoriasis patients treated with cyclosporine: A 5 y cohort study. *J Invest Dermatol* 2003; 120: 211–216.
5. Braddock M, Hanania NA, Sharafkhaneh A, Colice G, Carlsson M. Potential risks related to modulating interleukin-13 and interleukin-4 signalling: a systematic review. *Drug Saf* 2018; 41: 489–509.