Dupilumab for the treatment of severe photodermatitis

Mary Patricia Smith, BS, Karen Ly, BA, Quinn Thibodeaux, MD, Kristen Beck, MD, Timothy Berger, MD, Rita Khodosh, MD, Wilson Liao, MD, and Tina Bhutani, MD
San Francisco, California

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Photodermatoses constitute a heterogenous group of cutaneous conditions caused or exacerbated by ultraviolet radiation and/or visible light. Examples include photosensitive atopic dermatitis, chronic actinic dermatitis, polymorphous light eruption, and solar urticaria. Presentations vary, and can include erythematous papules or plaques, urticaria, vesicles, and lichenification, with a sharp demarcation between sun-exposed and sun-protected areas, and are accompanied by pruritus.[1-4] Treatment of all types of photodermatoses is anchored in photoprotection, and management of refractory cases can be challenging. Here we present 4 cases of severe photodermatitis effectively treated with dupilumab, a monoclonal antibody directed against the interleukin-4 receptor α subunit.[5]

REPORT OF CASES

Four patients with treatment-resistant photodermatoses each reported an exacerbation of symptoms after exposure to sunlight. Although no biopsies or minimal erythema dose testing were performed, the patient demographics, disease history, and clinical findings in cases 1 and 2 make photosensitive atopic dermatitis the most likely diagnosis, whereas cases 3 and 4 are consistent with chronic actinic dermatitis. Treatment with topical glucocorticoids failed in all 4 cases, and none of the patients had an adequate response to systemic therapies as described in the Table I. In all 4 patients, treatment was begun with dupilumab in the standard dosing regimen (600-mg induction dose followed by 300 mg every 2 weeks). Each patient was followed up for clinical response, treated with concurrent therapy adjustments, and monitored for adverse events. No adverse events were reported.

Case 1

A 36-year-old woman had photosensitive atopic dermatitis since age 18 that did not improve on trials of cyclosporine, hydroxychloroquine, or azathioprine. On examination in July 2017, she had excoriated, erythematous papules on the posterior neck, upper back, axillae, and inner forearms and vesicular papules on the palms. Dupilumab was initiated in August 2017 with continuation of azathioprine and topical glucocorticoids. She had significant improvement after the first dose of dupilumab, reporting both reduced itch and improved rash, and consequently discontinued all other therapies. Her dermatitis remains well controlled on dupilumab monotherapy.

Case 2

A 25-year-old woman presented with a lifelong history of photosensitive atopic dermatitis refractory to a combination of cyclosporine, hydroxychloroquine, and methotrexate. Her course was complicated by hospitalization for eczema herpeticum in December 2016. On examination in April 2017, she had diffuse xerosis of the face, neck, and chest and erythematous, lichenified plaques on bilateral inner arms and legs. Dupilumab was started in May 2017 with continuation of hydroxychloroquine and methotrexate, and she showed significant improvement by week 4 of treatment. By 8 weeks, she had

From the Department of Dermatology, University of California, San Francisco.

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Correspondence to: Mary Patricia Smith, BS, Department of Dermatology, UCSF, 515 Spruce Street, San Francisco, CA, 94118. E-mail: mary.smith2@ucsf.edu.

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Table I. Patient characteristics and response to dupilumab therapy

Case	Sex/age (y)	History of photodermatitis (y)	Previous therapies	Concomitant therapies	Clinical response & changes to concomitant therapies	Adverse events
1	F/36	18	Azathioprine (PO), cyclosporine (PO), glucocorticoids (T), hydroxychloroquine (PO)	Glucocorticoids (T), azathioprine (PO)	Significant response with reduced itch and rash by week 2 of dupilumab; first discontinued topical glucocorticoids and subsequently azathioprine; since September 2017, well controlled on dupilumab monotherapy	None
2	F/25	25	Cyclosporine (PO), glucocorticoids (T), hydroxychloroquine (PO), methotrexate (PO), non-medicated emollient (T)	Hydroxychloroquine (PO), methotrexate (PO)	Significant response with reduced itch and rash by week 4 of dupilumab; discontinued topical glucocorticoids; as of February 2019, stable on weekly dupilumab plus concomitant hydroxychloroquine; no additional occurrences of eczema herpeticum	None
3	M/49	1	Cetirizine/ pseudoephedrine (PO), diphenhydramine (PO), glucocorticoids (T, PO), methotrexate (PO), titanium dioxide/ zinc oxide sunscreen (T)	Glucocorticoids (T)	Significant response with reduced itch and rash by week 8 of dupilumab; since September 2018, much improved with few pruritic spots that improve with topical glucocorticoids	None
4	M/59	3	Azathioprine (PO), cyclosporine (PO), glucocorticoids (T, PO), hydroxychloroquine (PO), mycophenolate mofetil (PO), tacrolimus (T), thalidomide (PO)	Cyclosporine (PO), thalidomide (PO)	Significant response with reduced itch and rash by week 8 of dupilumab plus concomitant thalidomide and cyclosporine; as of February 2019, stable on biweekly dupilumab while tapering cyclosporine	None

PO, Oral; *T*, topical.

near-complete resolution of both itch and rash. As she experienced flares in sun-exposed areas before each dupilumab injection, she was transitioned to weekly dosing in July 2017. As of December 2018, she has discontinued methotrexate, and her condition is stable on dupilumab and hydroxychloroquine. Furthermore, the patient has experienced no recurrences of eczema herpeticum.

Case 3

A 49-year-old man with a several years' history of mild eczematous and nummular dermatitis presented with worsening erythematous and edematous plaques on the sun-exposed areas of the face, eyelids, ears, and neck. This evolution of symptoms toward severe photosensitivity was most consistent with chronic actinic dermatitis. In August 2017, the

patient's symptoms worsened, and although he experienced some relief with a prednisone taper, his rash returned soon after. Methotrexate was initiated, along with a prednisone bridge, but both had to be discontinued almost immediately because of a positive QuantiFERON-TB Gold test. Treatment with dupilumab was initiated in October 2017, resulting in significant improvement with reduced itch and rash within 8 weeks.

Case 4

A 59-year-old man presented in February of 2016 with an intensely pruritic, worsening rash on his bilateral hands, forearms, face, and neck. In September 2016, his examination found erythematous, scaly, and excoriated papules and plaques on the forehead, face, neck, arms, and legs as well as lichenified nodules on the dorsal hands and forearms. His examination and symptoms were most consistent with chronic actinic dermatitis. His symptoms did not improve with attempts to limit sun exposure, the use of fragrance-free products, or treatment with topical glucocorticoids and hydroxychloroquine. Treatment with azathioprine and, subsequently, mycophenolate mofetil were attempted, but quickly discontinued due to significant leukopenia. He had some improvement with a combination of prednisone, cyclosporine, thalidomide, and topical tacrolimus, but lack of disease control prompted the initiation of dupilumab in August 2018. Two months after the addition of dupilumab, his itch and rash improved significantly, allowing for the taper of cyclosporine, which is still in progress.

DISCUSSION

Management of photodermatoses has traditionally involved strict photoprotection coupled with topical and oral glucocorticoids, cyclosporine, azathioprine, mycophenolate mofetil, or methotrexate.[1,4] Because long-term use of these medications carries significant risks, identification of safe and effective alternatives is necessary.

The four cases presented here demonstrate successful treatment of severe photodermatitis with dupilumab. The first 2 cases highlight improvement in patients with photosensitive atopic dermatitis, whereas the final 2 cases highlight improvement in patients with chronic actinic dermatitis. Although some of our patients required continuation of other therapies, their rapid clinical improvement shortly after the addition of dupilumab suggests that this agent was primarily responsible for disease control. Given that photodermatoses are a heterogenous group of diseases, it would be difficult to postulate the exact mechanism by which dupilumab improved these patients' conditions. However, their robust and durable responses suggest that this drug targets key inflammatory pathways that are common to atopic dermatitis and chronic actinic dermatitis, such as the T-helper type 2 cells that produce interleukin-4 and interleukin-13.

Our goal in presenting these cases is to provide clinicians with another potential treatment option for photodermatoses, such as photosensitive atopic dermatitis and chronic actinic dermatitis, that are frequently refractory to traditional therapies. We recognize that this case series is limited by a small sample size, diagnoses based on history and clinical findings rather than histology or minimal erythema dose testing, and a short follow-up period. Larger longer-term studies are needed to further explore the effectiveness of dupilumab as a treatment for this these and other photodermatoses.

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