Photosensitive Atopic Dermatitis Exacerbated by UVB Exposure

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PRACTICE **POINTS**

- Photosensitive atopic dermatitis (AD) is rare but should be considered in patients with uncontrolled AD with a rash on sun-exposed skin.
- A thorough history and physical examination of these patients can provide the necessary clues for further workup.
- Phototesting should be performed to confirm the diagnosis and evaluate the degree of sensitivity to UV light and the specific wavelength eliciting the cutaneous response.
- Photoprovocation and photopatch testing also can be useful to confirm the diagnosis.

Photosensitive atopic dermatitis (AD) is a rare disease entity that many physicians are not familiar with, thus it often is misdiagnosed. It can be life altering, as patients often strictly avoid the sun and may only leave the house at night. Effective treatments are available, and therefore diagnosis is key to improve quality of life for these patients. We describe a case of photosensitive AD exacerbated by UVB exposure. The diagnosis was made with phototesting, and the patient was able to begin treatment with narrowband UVB (NB-UVB) hardening while on immunosuppression. The literature on photosensitive AD is limited, and this entity typically is not found in the main dermatology textbooks. Our case emphasizes the diagnostic problems and complexity of photosensitive AD. Histopathologic findings are nonspecific. A thorough history and physical examination can provide the necessary clues for further workup. Phototesting should be performed to confirm the diagnosis and evaluate the degree of sensitivity to UV light and the specific wavelength eliciting the cutaneous response. Photoprovocation and photopatch testing also can be useful to confirm the diagnosis.

Cutis. 2017;100:180-184.

Atopic dermatitis (AD) is the most common inflammatory skin condition, affecting approximately 15% to 20% of the global population.[1,2] Atopic dermatitis is characterized by a chronic relapsing dermatitis with pruritus, often beginning in infancy or childhood. Atopic dermatitis is caused by a defect in epidermal barrier function, which results in increased transepidermal water loss.[1] The criteria for AD include a pruritic skin condition plus 3 or more of the following: history of involvement of the skin creases, history of asthma or hay fever, history of AD in a first-degree relative (in children), 1-year history of generally dry skin, visible flexural eczema, and an age of onset of less than 2 years. Adults with AD frequently present with hand or facial dermatitis.[1]

UV light therapies including narrowband UVB (NB-UVB), UVA1, and psoralen plus UVA (PUVA) have all been used as effective treatments of AD.[3,4] UV light is beneficial for AD patients due to its immunomodulatory effects, thickening of the stratum corneum, and the reduction of *Staphylococcus aureus* in the skin.[2] Most patients with AD improve with light therapy; however, it is estimated that 1% to 3% of patients with AD will experience a paradoxical worsening of their AD after exposure to UV light.[2,5] This condition is referred to as photosensitive AD and is characterized by a photodistributed rash in patients who fulfill the criteria of AD. Photosensitive AD has a female predominance and generally affects patients with late-onset disease with development of AD after puberty.[2,5] The pathogenesis for the development of photosensitivity in patients with AD who previously tolerated exposure to sunlight is unknown.[5] We describe a case of photosensitive AD exacerbated by UVB exposure.

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The authors report no conflict of interest.

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Case Report

A 55-year-old Asian woman presented for evaluation of a rash on the head, neck, and arms. She reported that she had developed a pruritic rash with edema after sun exposure at 16 years of age. Since then, the rash has been intermittent and completely resolved at times with periods of decreased sun exposure; however, the rash recently had been persistent and worsening despite practicing strict sun protection with daily sunscreen application, protective clothing, and sun avoidance. She was not taking systemic medications or supplements at the time but was applying high-potency topical corticosteroids and calcineurin inhibitors with minimal improvement under the care of a dermatologist.

On physical examination the patient had thin, well-demarcated, erythematous papules and plaques with scaling, primarily on sun-exposed skin on the forehead (Figure 1A), cheeks (Figure 1B), eyelids, upper lip, neck (Figures 1B and 1C), upper chest (Figure 1C), and dorsal aspect of the hands, with excoriated pink papules on the forearms, shoulders, and back. A punch biopsy of the right neck showed spongiotic dermatitis with a perivascular lymphohistiocytic infiltrate (Figure 2). Further workup was pursued including complete blood cell count, comprehensive metabolic profile, liver function panel, Sjögren syndrome antigen A/Sjögren syndrome antigen B test, antinuclear antibody test, human immunodeficiency virus 1/2 antigen/antibody test, hepatitis panel, and mycobacterium tuberculosis test, which were all within reference range. Photodermatosis was suspected and she underwent phototesting including UVA, NB-UVB, and visible light. Phototesting confirmed she had a UVB photosensitivity with a markedly decreased minimal erythema dose (MED) to NB-UVB. The MED to NB-UVB was positive at 24 hours to all tested sites, the lowest of which was 0.135 J/cm^2. Eczematous changes began to develop at day 6 at doses of 0.945 and 1.080 J/cm^2. The patient also underwent visible light testing, which was negative. The patient was patch tested for multiple standardized agents as well as personal products, all of which were negative. Subsequent photopatch testing revealed a slightly positive reaction to benzophenone 4, a common ingredient in sunscreens.

The patient was then started on mycophenolate mofetil and prednisone. Repeat MED testing to NB-UVB was performed. Her repeat MED to NB-UVB was determined to be 0.405 J/cm^2, and hardening commenced at 3 times per week at 70% of the MED (0.2835 J/cm^2). She began to flare and develop an eczematous reaction, thus the dose was decreased to 50% of the MED (0.2025 J/cm^2), which she tolerated.

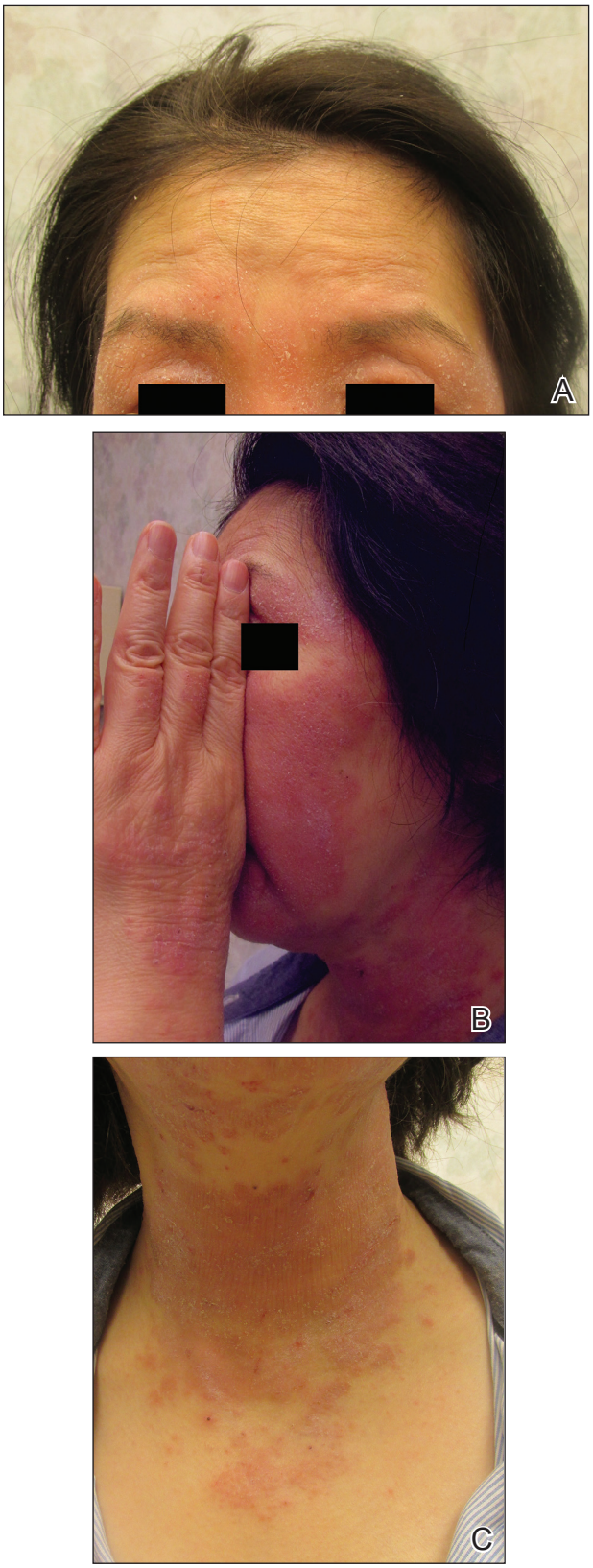

FIGURE 1. Photosensitive atopic dermatitis on the face (A and B), neck (B and C), and upper chest (C) showing thin erythematous papules and plaques with scaling.

Comment

Classification and Clinical Presentation—The literature on photosensitive AD is scant, and this disease entity is rare. Alternative names include photoaggravated AD, photosensitive eczema, and light-exacerbated eczema.[5]

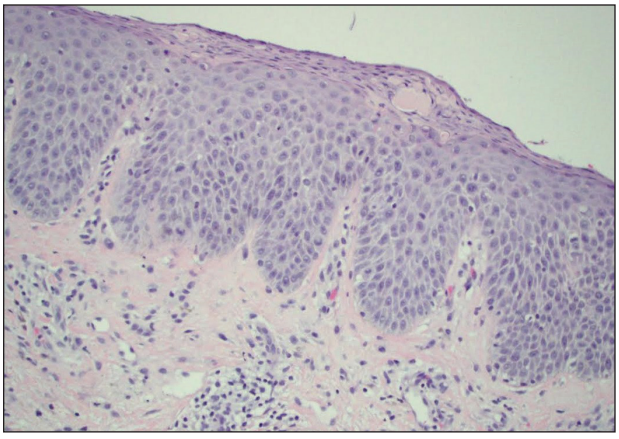

FIGURE 2. Biopsy of the right neck showed spongiosis, mild uneven psoriasiform hyperplasia, and a superficial perivascular infiltrate of lymphocytes with eosinophils (H&E, original magnification ×40).

Two main studies have been conducted in recent years that were intended to characterize photosensitive AD. ten Berge et al[5] conducted a retrospective study of 145 patients with AD that were phototested in 2009. They found that 3% of their total AD patient population had photosensitive AD.[5] In 2016, Ellenbogen et al[2] performed a similar single-center retrospective analysis of 17 patients with long-standing AD who suddenly developed photosensitivity.

Patients with photosensitive AD typically present with lesions on sun-exposed skin with coexisting eczematous lesions in sites with a predilection for AD.[2] In the study conducted by ten Berge et al,[5] 2 main reaction patterns were observed: erythematous papules with pruritus and an eczematous reaction. The authors suggested one subset of patients demonstrated polymorphous light eruption (PMLE), a common photoinduced eruption thought to represent a delayed-type hypersensitivity, coexisting with AD while the other subset had true photosensitive AD.[5,6] Ellenbogen et al[2] also found 2 reaction patterns, which they labeled papular (PMLE type) and eczematous (photosensitive AD type). The authors contested the theory of coexisting PMLE in AD because PMLE gets better in the summer with UV radiation hardening.[2] On the contrary, photosensitive AD worsens with uncontrolled exposure to sunlight. Only with controlled exposure to small doses of UV radiation at a time does this condition improve. Ellenbogen et al[2] believe both reaction patterns are consistent with photosensitive AD and the PMLE type should be termed *papular photosensitive AD type.*

Histopathology—The histopathologic findings of photosensitive AD are nonspecific but are characterized by spongiotic dermatitis with a perivascular lymphohistiocytic infiltrate.[2]

Diagnosis With Phototesting—Phototesting of patients with AD should be considered if there is a suspicion for photosensitivity based on persistent disease despite use of photoprotection and local treatment.[5-7] Patients may not notice a correlation of skin exacerbations with UV exposure, especially if they are only sensitive to UVA, as it is still present on cloudy days and can penetrate glass windows.[8] Phototesting evaluates the degree of sensitivity to UV light and the specific wavelength eliciting the cutaneous response. Phototesting consists of determining the MED to UVA and UVB, the minimal phototoxic dose for PUVA, and visible light exposure. Further evaluation may include photoprovocation testing or photopatch testing, as these patients can have coexisting photocontact allergies.

The MED is defined as the minimal dose of UV light needed to induce perceptible erythema in exposed skin.[5] It is dependent on the light source and patient's skin type, and individual units may vary. To determine the MED to UVA or UVB, 2×2-cm skin fields are irradiated with increasing cumulative UVA/UVB. The dose varies by skin type and it is then read at 24 hours. The majority of patients with photosensitive AD are reported to have a normal MED; however, some studies have reported the MED to be decreased.[5,7-9] ten Berge et al[5] found 7% of their study participants exhibited a lower MED, as seen in our patient.

The minimal phototoxic dose for PUVA is defined as the least exposure dose of UVA 1 hour after ingestion of 0.4 mg/kg of methoxsalen that produces pink erythema with 4 distinct borders at 48, 72, or 96 hours after ingestion.[10] Visible light exposure is tested using a slide projector as the light source to an approximately 10×5-cm area of skin for 45 minutes. Any immediate or delayed reaction is abnormal and considered positive.[10]

Photoprovocation testing has been performed in several studies.[2,5] It consists of exposing an 8-cm area of skin to 80 J/cm^2 UVA and 10 mJ/cm^2 UVB, which is read at 24, 48, or 72 hours. A papular or eczematous reaction is considered positive.[2,11]

The results of phototesting have varied between studies. ten Berge et al[5] phototested 107 patients with AD and photosensitivity and 17% were found to be solely sensitive to UVA whereas 67% were found to be sensitive to UVA and UVB. In contrast, Ellenbogen et al[2] only tested 17 patients with AD and photosensitivity and they found that 56% (9/16) were sensitive to UVA alone while only 44% (7/16) were sensitive to UVA and UVB.

Photopatch testing can help to rule out photosensitivity due to a substance in the presence of UV light. In studies of patients with photosensitive AD (N=125), photocontact reactions occurred in 23% and were predominantly associated with sunscreens, skin care products, and fragrances.[5,12] Photopatch testing is done by placing duplicate sets of patches on nonlesional skin using the Finn Chamber technique. A published list of allergens, which were agreed upon by the European Society of Contact Dermatitis and the European Society for Photodermatology in 2000 are seen in Table 1.[13] The list contains mainly UV filters and drugs. The patients'

TABLE 1. European Photopatch Test Baseline Series Agents

Type of Agent	Name of Agent[a]
"Older" organic UV absorbers[b]	4-methylbenzylidene camphor, benzophenone-3, benzophenone-4, butyl methoxydibenzoylmethane, ethylhexyl methoxycinnamate, isoamyl *p*-methoxycinnamate, octocrylene, PABA
"Newer" organic UV absorbers[c]	*Bis*-ethylhexyloxyphenol methoxyphenyl triazine, diethylhexyl butamido triazone, diethylamino hydroxybenzoyl hexyl benzoate, drometrizole trisiloxane, ethylhexyl triazone, methylene *bis*-benzotriazolyl tetramethylbutylphenol, terephthalylidene dicamphor sulfonic acid
Topical NSAIDs	Benzydamine, etofenamate, ketoprofen, piroxicam
Topical antihistamine	Promethazine

Abbreviations: PABA, *p*-aminobenzoic acid; NSAID, nonsteroidal anti-inflammatory drug.
[a]International Nomenclature of Cosmetic Ingredients name for UV absorbers.
[b]Older products include those that are rarely used or have been removed from the market in the United States but may be available in other countries.
[c]Newer products include those that are still commonly used.

Adapted with permission from Goncalo et al.[13]

TABLE 2. Differential Diagnoses for Photosensitive AD

Factor	Photosensitive AD	Chronic AD	Photoallergic Contact Dermatitis
History	History of AD or fulfills the criteria of AD	History of ambient sun exposure; often presents in men aged >70 y	History of known reaction to a contact allergen
Distribution	Photodistributed lesions with involvement of non–sun-exposed skin and typical AD lesions	Photodistributed lesions; non–sun-exposed skin spared	Photodistributed lesions; non–sun-exposed skin spared
Photoprovocation testing	Positive	Positive	Negative
MED on phototesting	Normal	Decreased	Normal

Abbreviations: AD, atopic dermatitis; MED, minimal erythema dose.

Adapted with permission from Ellenbogen et al.[2]

own products also should be tested in addition to the published list of allergens, but a maximum of 30 patches should be placed at one time. The patches are removed at either 24 or 48 hours; some researchers have found greater sensitivity with the 48-hour time period, while others have not found a significant difference.[10] One set of skin fields then is covered with an impermeable occlusive dressing as a control while the other is irradiated with 5 J/cm^2 of a broad-spectrum UVA light source. UVA fluorescent lamps are the light source of choice because of their widespread availability, reproducible broad spectrum, and beam uniformity.[10] In the study conducted by ten Berge et al,[5] photopatch testing was performed on 125 patients, and 29 patients were found to be positive to one or more substances. Ellenbogen et al[2] photopatch tested 5 patients with photosensitive AD and a clinical suspicion of photoallergy; however, all 5 were negative. Our patient underwent traditional patch testing due to clinical suspicion of a coexisting contact allergy, which was negative.

Differential Diagnosis—The differential diagnosis for photosensitive AD includes PMLE with coexisting AD, chronic AD, and photoallergic contact dermatitis. Photosensitive AD worsens with increasing exposure to uncontrolled sunlight, in contrast to patients with PMLE who experience UV radiation (UVR) hardening with increasing UV exposure during the summer months,

resulting in improvement of skin lesions. Patients with chronic AD generally report a history of chronic ambient sun exposure and exhibit well-demarcated eczematous lesions in a photodistributed pattern with sparing of sun-protected skin.[2] In contrast, photosensitive AD involves both sun-exposed and covered areas of the body. Chronic AD will have a positive photoprovocation test with a decreased MED (Table 2). Photoallergic contact dermatitis also will have photodistributed eczematous lesions with relative sparing of non–sun-exposed skin; however, these patients generally have negative photoprovocation testing with a normal MED.[2] These patients may or may not have a history of reaction to a known allergen, but they likely will have a positive photopatch test.

Treatment—The treatment of photosensitive AD is based on the severity of the photosensitivity. Treatment for mild disease is limited to sun protection in addition to topical corticosteroids or topical calcineurin inhibitors. For moderate disease and unsatisfactory relief with proper sun protection, UVR hardening is recommended. If severe disease is present, immunosuppression with medications such as corticosteroids, cyclosporine, and mycophenolate mofetil is suggested to prevent flaring of disease during UVR hardening.[2,5,8,14]

Conclusion

Photosensitive AD is a rare entity characterized by a photodistributed rash and involvement of non–sun-exposed skin. Patients will either have a history of AD or fulfill the criteria of AD. They have positive photoprovocation testing and generally have a normal MED. They may have positive photopatch testing with coexisting photoallergies. Histopathology is nonspecific but shows spongiotic dermatitis with perivascular lymphohistiocytic infiltrate. Diagnosis is essential, as this disease can be life altering and affect quality of life. Effective treatment options are available, and the therapeutic ladder is based on severity of disease.[2,5]

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