

duration of 12.5 months. Seven patients have been receiving dupilumab for more than 1 year.

One patient in our cohort had concomitant plaque psoriasis, for which he was receiving ustekinumab, 45 mg every 12 weeks, in conjunction with his dupilumab. He developed clearance of his psoriasis and near clearance of his dyshidrotic eczema and developed no treatment-related adverse events. The dosing frequency was increased to weekly for 2 partial responders. Neither of them experienced clearance of their disease while receiving this more frequent dosing regimen, nor did they develop adverse events. The one patient in our cohort who stopped dupilumab was responding appropriately but decided to discontinue because she was concerned about possible long-term adverse effects.

Dupilumab was well tolerated in our cohort, with only 3 reported adverse events. One patient developed conjunctivitis that is being managed satisfactorily with artificial tears. Two patients developed dupilumab facial redness that was refractory to treatment with topical corticosteroids, topical azoles, and topical calcineurin inhibitors. All 3 patients who developed adverse events have continued with therapy.⁵

Our series suggests that dupilumab is a generally well tolerated and frequently effective treatment for dyshidrotic eczema. Limitations include its retrospective nature and risk of misclassification bias, given lack of diagnostic criteria for dyshidrosis.

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REFERENCES

1. Nanda S, Nagrani N, MacQuhae F, Nichols A. A case of complete resolution of severe plantar dyshidrotic eczema with dupilumab. *J Drugs Dermatol*. 2019;18(2):211-212.
2. Weston GK, Hooper J, Strober BE. Dupilumab in the treatment of dyshidrosis: a report of two cases. *J Drugs Dermatol*. 2018;17(3):355-356.
3. Oosterhaven JAF, Romeijn GLE, Schuttelaar MLA. Dupilumab treatment of very severe refractory atopic hand eczema. *JAMA Dermatol*. 2018;154(8):969-970.
4. Zirwas MJ. Dupilumab for hand eczema. *J Am Acad Dermatol*. 2018;79(1):167-169.
5. Waldman RA, DeWane ME, Sloan SB, King B, Grant-Kels JM. Dupilumab ocular surface disease occurs predominantly in patients receiving dupilumab for atopic dermatitis: a multi-institution retrospective chart review. *J Am Acad Dermatol*. <https://doi.org/10.1016/j.jaad.2019.07.031>. Published online July 17, 2019.

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Dupilumab treatment of nummular dermatitis: A retrospective cohort study



To the Editor: Nummular dermatitis is an idiopathic eczematous eruption characterized by pruritic, coin-shaped lesions typically involving the extremities and, less commonly, the trunk. Although topical therapy is the mainstay of management, treatment escalation may be required in severe cases. Dupilumab is a human monoclonal antibody against the interleukin 4 receptor α subunit that has shown efficacy for moderate to severe atopic dermatitis.¹ We present a retrospective cohort study of our institutional experience with dupilumab for nummular dermatitis.

After institutional review board approval, a retrospective chart review was performed of adult patients treated in the general dermatology clinic at our institution from January 1, 2017, through July 31, 2019, with the words “nummular” and “dupilumab” or “dupixent” in clinic notes. Patients receiving a diagnosis of idiopathic nummular dermatitis who had ever received dupilumab were included.

Six patients treated with dupilumab were identified (Table 1). All patients did not meet the revised Hanifin and Rajka criteria for atopic dermatitis, which were used to establish a diagnosis of atopic dermatitis in the dupilumab clinical trials.¹ None of the patients had a history of flexural dermatitis or childhood atopic dermatitis. All had failed standard therapy, as well as emollient and dry skin care.

In total, 5 of 6 patients had a durable response to dupilumab, defined as a reduction in body surface area involvement sustained throughout the follow-up period of up to 2 years (Table 1). The sole patient without durable response had initial improvement but discontinued treatment because of fluctuating response and the development of conjunctivitis attributed to dupilumab. No other adverse events were reported.

Table I. Clinical characteristics and treatment course of 6 patients with nummular dermatitis treated with dupilumab

Case no./sex/ race/age at dupilumab initiation, years	Areas of involvement of nummular dermatitis at dupilumab initiation (BSA, %)	Duration of nummular dermatitis at dupilumab initiation, years	Personal history of atopy (AD, allergic rhinitis, asthma)	Family history of atopy	Patch testing results	Concomitant dermatologic diagnoses	Results (pathology, cultures)	Previous failed therapies (duration if known)	Response to dupilumab (BSA at most recent visit, %)
Responders									
1/M/ white/ 77	Upper extremities (elbows, hands), chest, back, abdomen, lower extremities (BSA not recorded)	10	No	No	N/A	Grover disease; no history of venous stasis, did not meet revised Hanifin and Rajka criteria for AD	Biopsy (OSH): spongiotic dermatitis with eosinophils, lichenified KOH (OSH): tinea, hyphal and yeast elements; treated	Topical steroids (10 y), prednisone (intermittent × 7 y), topical tacrolimus (2 y), mycophenolic acid (3 mo), intramuscular triamcinolone (1 dose)	100% clearance noted at 31 wk at first follow-up; response maintained through 428 d at writing
2/M/ other/ 85	Lower extremities, buttocks, palms, soles (7%–8%)	7	No	None documented	N/A	None; no history of venous stasis, did not meet revised Hanifin and Rajka criteria for AD	Biopsy (right dorsal foot): chronic spongiotic dermatitis with eosinophils KOH: hyphae; treated	Topical steroids (≥1.5 y), urea (≥1.5 y), NB-UVB (<1 mo, had to stop because of logistic issues)	90% improvement with BSA <1% noted at 5 wk; response maintained through 757 d at article writing
3/M/ Asian/ 45	Lower extremities (feet, ankles, lower legs) (15%)	5	No	None documented	N/A	Seborrheic dermatitis of scalp/ears/neck; no history of venous stasis, did not meet revised Hanifin and Rajka criteria for AD	Biopsy (OSH): consistent with nummular dermatitis per patient; results not documented	Topical steroids (2.5 y), topical tacrolimus	90%–95% improvement with BSA <1% at 76 d; response maintained through 120 d at article writing
4/M/ white/ 90	Back, hands, lower extremities (8%–10%)	3	Allergic rhinitis only, no history of flexural rash, childhood AD, or asthma	None documented	Budesonide 0.01% (2+); dexamethasone-21 phosphate 1% (2+); hydrocortisone-17- butyrate 1% (2+); amcinonide 0.1% (1+); triamcinolone acetonide 0.1% (1+); desoximetasone 1% (2+); betamethasone- 17-valerate 0.12% (1+);	Allergic contact dermatitis (only partial improvement with years of allergen avoidance); no history of venous stasis, did not meet revised Hanifin and Rajka criteria for AD	Biopsy (L, lower back): spongiotic dermatitis with eosinophils Culture (lower back): normal skin flora HSV/VZV PCR (lower back): not detected	Topical steroids (2.5 y), topical tacrolimus (≥4 y), NB-UVB (7 mo)	90% improvement with BSA <1% noted at 13 wk at first follow-up; response maintained through 221 d at article writing

Continued

Table I. Cont'd

Case no./sex/ race/age at dupilumab initiation, years	Areas of involvement of nummular dermatitis at dupilumab initiation (BSA, %)	Duration of nummular dermatitis at dupilumab initiation, years	Personal history of atopy (AD, allergic rhinitis, asthma)	Family history of atopy	Patch testing results	Concomitant dermatologic diagnoses	Results (pathology, cultures)	Previous failed therapies (duration if known)	Response to dupilumab (BSA at most recent visit, %)
5/M/ white/ 70	Upper extremities, back, abdomen (12%), lower extremities	4	Allergic rhinitis, asthma, no history of flexural rash or childhood AD	None documented	dexamethasone 0.5% (1+); prednisone 1% (1+); tixocortol-21- pivalate 0.1% (1+); triamcinolone acetone 0.1%; neomycin (1+); carba mix (1+); nickel (1+)	None; no history of venous stasis, did not meet revised Hanifin and Rajka criteria for AD	None	Topical steroids (4 y), calcipotriene (3 y), urea	90%–95% improvement with BSA <1% noted at 20 wk at first follow-up; response maintained through 202 d at article writing
Nonresponder 6/F/white/ 70	Face, neck, upper extremities (arms, hands), lower extremities (soles spared), torso	4	No	None documented	Clobetasol 1.0% (1+); budesonide 0.01% (1+); tixocortol- 21-pivalate 0.1% (questionable result); hydrocortisone- 17-butyrate 1.0% (questionable result)	Hand dermatitis; allergic contact dermatitis (only partial improvement with allergen avoidance); no history of venous stasis, did not meet revised Hanifin and Rajka criteria for AD	Biopsy (OSH): spongiotic dermatitis with eosinophils and superficial perivascular dermatitis Repeated biopsy (L hip, L knee): spongiotic dermatitis with eosinophils	Topical steroids, topical tacrolimus, crisaborole (≥2 y, ongoing), NB-UVB (6 mo, stopped because of burn), prednisone (≥2 y), methotrexate (6 mo), mycophenolic acid (1.5 y, stopped because of intolerance), cyclosporine (2 y; restarted with dupilumab for ≥1.5 y, ongoing)	Improvement with BSA <1% and reduced pruritus noted at 1 wk at first follow-up; response maintained until development of repeated flares starting from 2 mo follow-up; dupilumab discontinued at 1 y secondary to conjunctivitis

AD, Atopic dermatitis; BSA, body surface area; F, woman; M, man; N/A, not applicable; NB-UVB, narrowband ultraviolet B light; OSH, outside hospital.

The pathogenesis of nummular dermatitis is unclear. It has been described in association with xerosis, venous stasis, and infection.²⁻⁴ Nummular dermatitis must be distinguished from atopic dermatitis with nummular morphology, which is particularly observed in childhood.⁵ Nummular lesions have also been associated with contact sensitization, which may represent primary allergic contact dermatitis or secondary development of allergic contact dermatitis to medicaments for nummular dermatitis lesions.² This latter scenario was favored for patients 4 and 6, who had clinically relevant positive patch test results to corticosteroids, neomycin, or both, but only partially improved with allergen avoidance. Some have advocated that nummular dermatitis be viewed as a morphology rather than a unique disease state; regardless of viewpoint, any underlying causes should be addressed whenever possible before nummular lesions are deemed idiopathic.

Our findings suggest that nummular dermatitis may involve hyperactivation of the Th2 axis that is sensitive to dupilumab inhibition. Circulating Th2 lymphocyte burden was previously correlated with disease activity in a case of chronic nummular dermatitis secondary to odontogenic infection in a nonatopic male patient.⁵ Further investigation into the pathogenesis of nummular dermatitis is necessary.

In conclusion, we report the successful use of dupilumab at standard dosing in the treatment of 5 of 6 patients with nummular dermatitis and no history of stasis dermatitis or atopic dermatitis, in accordance with the revised Hanifin and Rajka criteria. We are not aware of similar reports. Our findings suggest that dupilumab may be an effective off-label treatment for nummular dermatitis that has failed conventional therapy. Further study is required to corroborate these findings.

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REFERENCES

1. Beck LA, Thaci D, Hamilton JD, et al. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med*. 2014;371(2):130-139.
2. Bonamonte D, Foti C, Vestita M, Ranieri LD, Angelini G. Nummular eczema and contact allergy: a retrospective study. *Dermatitis*. 2012;23(4):153-157.
3. Julian-Gonzalez RE, Orozco-Covarrubias L, Duran-McKinster C, Palacios-Lopez C, Ruiz-Maldonado R, Saez-de-Ocariz M. Less common clinical manifestations of atopic dermatitis: prevalence by age. *Pediatr Dermatol*. 2012; 29(5):580-583.
4. Bendl BJ. Nummular eczema of stasis origin. The backbone of a morphologic pattern of diverse etiology. *Int J Dermatol*. 1979;18(2):129-135.
5. Satoh T, Takayama K, Sawada Y, Yokozeki H, Nishioka K. Chronic nodular prurigo associated with nummular eczema: possible involvement of odontogenic infection. *Acta Derm Venereol*. 2003;83(5):376-377.

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Missed drug-induced bullous pemphigoid leads to longer immunosuppression than recognized cases: A 9-year retrospective review



To the Editor: Drug-induced bullous pemphigoid (BP), a BP variant associated with more than 50 medications and often indistinguishable from classic BP,¹⁻³ is difficult to recognize without a thorough medication history, particularly in patients with polypharmacy. This multicenter retrospective study reports rates of potential missed drug-induced BP and compares its presentation and management to recognized cases.

Biopsy- and immunofluorescence-proven BP cases from January 2010 through January 2019 were identified using International Classification of Diseases, ninth revision (694.5) and 10th revision (L12.0) codes; GEM and RLY reviewed medication histories. Gestational, mucous membrane, and immune checkpoint inhibitor-induced pemphigoid and cases without medical records for 6 months preceding BP onset were excluded. Cases identified by treating dermatologists as drug induced (based on timing, drug class, and response to drug withdrawal) were classified as such. Cases for which any new medication was added within 6 months preceding BP onset and treating dermatologists neither