Recalcitrant prurigo nodularis treated successfully with dupilumab

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INTRODUCTION

Prurigo nodularis (PN) is a chronic pruritic condition that reduces quality of life. PN may exist in 50% of cases as an overlap syndrome with atopic dermatitis (AD), although its etiology has not been clearly established.[1] Because of a paucity of data and randomized controlled trials, treatment of PN is challenging. Consequently, patients often endure multiple unsuccessful therapeutic trials. We report on 2 patients with PN who did not respond to a variety of treatments and subsequently achieved clearance of lesions with dupilumab.

Abbreviations used:

AD: atopic dermatitis
IL: interleukin
PN: prurigo nodularis

REPORT OF CASES

Patient 1

A 53-year-old white woman with hypercholesterolemia presented to the dermatology clinic with multiple, extremely pruritic, symmetrically distributed, excoriated, lichenified papules of the trunk and extremities (Fig 1, *A*). Punch biopsy of lichenified nodules on the legs found an acanthotic epidermis with mild spongiosis and dermis containing a scattered mononuclear infiltrate with slight fibrosis, consistent with lichen simplex chronicus. Clinically, our patient's lesions were consistent with PN. The therapeutic course over several years included high-potency topical steroids, intralesional triamcinolone, 10 mg/mL, oral antihistamines, prednisone, broad-band ultraviolet B phototherapy, etanercept, methotrexate, ustekinumab, mycophenolate mofetil, lenalidomide, and thalidomide, all of which failed to control her disease or resulted in adverse effects requiring discontinuation. Cyclosporine controlled her disease at 3 to 5 mg/kg/d, and she could not be weaned from it for more than 3 years. Dupilumab monotherapy therapy was subsequently initiated, using the dosing regimen as indicated for atopic dermatitis, 600 mg subcutaneous injection at week 0 followed by 300 mg subcutaneous injection every 2 weeks. The patient achieved decreased pruritus within the first 2 injections and sustained improvement in subsequent weeks (Fig 1, *B*). The patient had new-onset alopecia, which was not felt to be dupilumab related; however, she elected to stop dupilumab, resulting in lesion recurrence requiring resumption of cyclosporine.

Patient 2

A 40-year-old African-American female with hypothyroidism and hypercholesterolemia presented with extremely pruritic, multiple hyperpigmented, lichenified papules and nodules involving the trunk and extremities, including palms and soles. Because the clinical picture was consistent with PN, biopsy was deferred. Therapies tried over several years included antihistamines, high-potency topical steroids, intralesional triamcinolone, 10 mg/mL, doxepin, narrow-band ultraviolet B phototherapy, naltrexone, gabapentin, thalidomide, apremilast, and tofacitinib, all with inadequate results or intolerable side effects. Cyclosporine, 3 to 5 mg/kg/d, prednisone, and methotrexate, 15 to 20 mg/wk were

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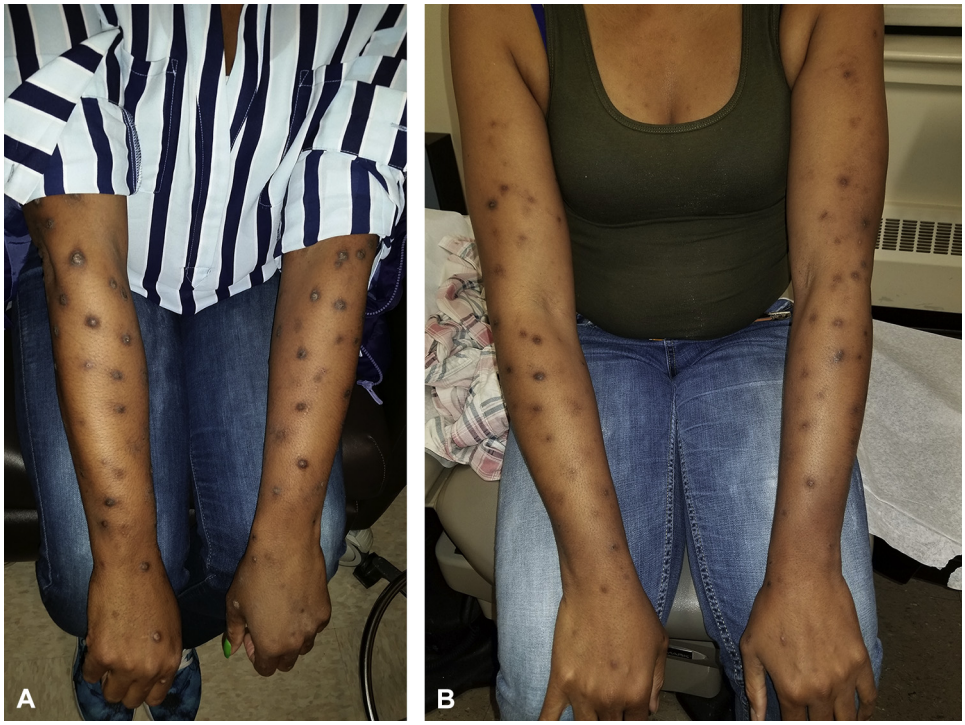

Fig 1. Clinical photo of patient 2, before dupilumab therapy (**A**) and after dupilumab therapy (**B**).

able to control the patient's disease, although attempts to wean off these agents were unsuccessful. Dupilumab therapy was subsequently initiated, 600 mg subcutaneous injection at week 0 followed by 300 mg subcutaneous injection every 2 weeks, and the patient rapidly achieved decreased pruritus and dramatic albeit not full skin clearance over the last year. She is off all other medications. No side effects from dupilumab monotherapy were noted.

DISCUSSION

Current therapies for PN aim to suppress the itch-scratch cycle and include a myriad of topical agents, such as steroids, calcineurin inhibitors, and neuromodulators like capsaicin. Topical agents are frequently unsuccessful, and systemic agents are often needed, including intralesional steroids, antipruritic agents such as oral antihistamines, neuromodulators like gabapentin and pregabalin, and phototherapy. In more severe cases, immunosuppressive agents such as thalidomide, cyclosporine, mycophenolate mofetil, azathioprine, and methotrexate have been used with varying success and come with a host of undesirable side effects.[2] Recently, substance P and various neuropeptides have been implicated in a neurogenic etiology of pruritus in PN, and have guided the use of neurokinin-1 antagonists (serlopitant and aprepitant) in these patients.[3]

Associations with atopic dermatitis and PN have long been suggested, with PN being subcategorized into early-onset atopic and late-onset nonatopic forms that both involve chronic inflammation and itch.[4] Studies find the role of T-helper type 2–associated cytokines, such as interleukin (IL)-4, 13, and 31 as hallmark regulators of itch. One study found a 50-fold upregulation of IL-31 messenger RNA in PN biopsy samples.[5] Blockade of these immunomodulatory axes have accordingly emerged as promising therapeutic approaches for chronic pruritic conditions. Nemolizumab and dupilumab, inhibitors of IL-31 and the IL-4/13 receptor, respectively, have proven to be efficacious in reducing pruritus in AD patients.[6] Indeed, 2 recent case series describe the success of dupilumab in a total of 7 PN patients.[7,8] The new wave of cytokine modulation in AD may be the key to providing dramatic relief for PN patients.

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