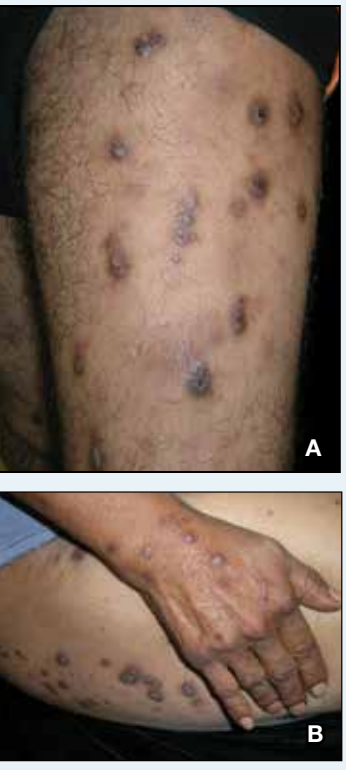
DX ACROSS THE SKIN COLOR SPECTRUM

Break the Itch-Scratch Cycle to Treat Prurigo Nodularis

Waleed Adawi, MD[a]; Richard P. Usatine, MD[b]; Candrice R. Heath, MD[c]

Simultaneously published in *Cutis* and *Federal Practitioner.* doi:10.12788/fp.0548



A A 45-year-old Hispanic man with prurigo nodularis presented with hyperpigmented lesions on the leg due to frequent scratching.

B A 60-year-old Black woman with prurigo nodularis presented with hyperpigmented lesions on the hand, arm, and thigh due to frequent scratching.

Photographs courtesy of Richard P. Usatine, MD.

Prurigo nodularis (PN) is a chronic inflammatory skin condition characterized by firm hyperkeratotic nodules that develops when patients persistently scratch or rub intensely itchy areas of the skin. This potent itch-scratch cycle can be traced back to a dysfunctional interplay between cutaneous nerve fibers and the local immune environment.[1-3] Pruritis lasting at least 6 weeks is a hallmark symptom of PN and can be accompanied by pain and/or a burning sensation.[4] The lesions are symmetrically distributed in areas that are easy to scratch (eg, arms, legs, trunk), typically sparing the face, palms, and soles; however, facial lesions have been reported in pediatric patients with PN, who also are more likely to have back, hand, and foot involvement.[5,6]

PN can greatly affect patients' quality of life, leading to increased rates of depression and anxiety.[7-9] Patients with severe symptoms also report increased sleep disturbance, distraction from work, self-consciousness leading to social isolation, and missed days of work/school.[9] In one study, patients with PN reported missing at least 1 day of work, school, training, or learning; giving up a leisure activity or sport; or refusing an invitation to dinner or a party in the past 3 months due to the disease.[10]

Epidemiology

PN has a prevalence of 72 per 100,000 individuals in the United States, most commonly affecting adults aged 51 to 65 years and disproportionately affecting African American and female patients.[11-13] Most patients with PN experience a 2-year delay in diagnosis after initial onset of symptoms.[10] Adults with PN have an increased likelihood of having other dermatologic conditions, including atopic dermatitis (AD) and psoriasis.[11] Nearly two-thirds of pediatric patients with PN present with AD, and those with AD showed more resistance to first-line treatment options.[5]

Key Clinical Features

Compared to White patients, who typically present with lesions that appear erythematous or pink, patients with darker skin tones may present with hyperpigmented nodules that are larger and darker.[12] The pruritic nodules often show signs of scratching or picking (eg, excoriations, lichenification, and angulated erosions).[4]

Worth Noting

Diagnosis of PN is made clinically, but skin biopsy may be helpful to rule out alternative diseases. Histologically, the hairy palm sign may be present in addition to other histologic features commonly associated with excessive scratching or rubbing of the skin.

Patients with PN have a high risk for HIV, which is not surprising considering HIV is a known systemic cause of generalized chronic pruritus. Other associations include type 2 diabetes mellitus and thyroid, kidney, and liver disease.[11,13] Workup for patients with PN should include a complete blood count with differential; liver and renal function testing; and testing for C-reactive protein, thyroid-stimulating hormone, and lactate dehydrogenase.[4,14] Hemoglobin A_{1c} and HIV testing as well as a hepatitis panel should be considered when appropriate. Because generalized pruritus may be a sign of malignancy, chest radiography and lymph node and abdominal ultrasonography should be performed in patients who have experienced itch for less than 1 year along with B symptoms (fever, night sweats, ≥ 10% weight loss over 6 months, fatigue).[14] Frequent scratching can disrupt the skin barrier, contributing to the increased risk for skin infections.[13] All patients with a suspected PN diagnosis also

should undergo screening for depression and anxiety, as patients with PN are at an increased risk for these conditions.[4]

Treatment of PN starts with breaking the itch-scratch cycle by addressing the underlying cause of the pruritus. Therapies are focused on addressing the immunologic and neural components of the disease. Topical treatments include moderate to strong corticosteroids, calcineurin inhibitors (tacrolimus or pimecrolimus), capsaicin, and antipruritic emollients. Systemic agents include phototherapy (narrow-band UVB or excimer laser), gabapentin, pregabalin, paroxetine, and amitriptyline to address the neural component of itch. Methotrexate or cyclosporine can be used to address the immunologic component of PN and diminish the itch. That said, methotrexate and cyclosporine often are inadequate to control pruritus.[10] Of note, sedating antihistamines are not effective in treating itch in PN but can be used as an adjuvant therapy for sleep disturbances in these patients.[15]

The only drugs currently approved by the US Food and Drug Administration to treat PN are the biologics dupilumab (targeting the IL-4 receptor) approved in 2022 and nemolizumab (targeting the IL-31 receptor) approved in 2024.[16-18] The evidence that these injectable biologics work is heartening in a condition that has historically been very challenging to treat.[16,18] It should be noted that the high cost of these 2 medications can restrict access to care for patients who are uninsured or underinsured.

Resolution of a prurigo nodule may result in a hyperpigmented macule taking months to years to fade.

Health Disparity Highlight

Patients with PN have a considerable comorbidity burden, negative impact on quality of life, and increased health care utilization rates.[12] PN is 3.4 times more common in Black patients than White patients.[13] Black patients with PN have increased mortality, higher health care utilization rates, and increased systemic inflammation compared to White patients.[12,19,20]

References

1. Cevikbas F, Wang X, Akiyama T, et al. A sensory neuron–expressed IL-31 receptor mediates T helper cell–dependent itch: involvement of TRPV1 and TRPA1. *J Allergy Clin Immunol.* 2014;133:448-460.
2. Lou H, Lu J, Choi EB, et al. Expression of IL-22 in the skin causes Th2-biased immunity, epidermal barrier dysfunction, and pruritus via stimulating epithelial Th2 cytokines and the GRP pathway. *J Immunol.* 2017;198:2543-2555.
3. Sutaria N, Adawi W, Goldberg R, et al. Itch: pathogenesis and treatment. *J Am Acad Dermatol.* 2022;86:17-34.
4. Elmariah S, Kim B, Berger T, et al. Practical approaches for diagnosis and management of prurigo nodularis: United States expert panel consensus. *J Am Acad Dermatol.* 2021;84:747-760.
5. Kyvayko R, Fachler-Sharp T, Greenberger S, et al. Characterization of paediatric prurigo nodularis: a multicentre retrospective, observational study. *Acta Derm Venereol.* 2024;104:adv15771.
6. Aggarwal P, Choi J, Sutaria N, et al. Clinical characteristics and disease burden in prurigo nodularis. *Clin Exp Dermatol.* 2021;46:1277-1284.
7. Whang KA, Le TK, Khanna R, et al. Health-related quality of life and economic burden of prurigo nodularis. *J Am Acad Dermatol.* 2022;86:573-580.
8. Jørgensen KM, Egeberg A, Gislason GH, et al. Anxiety, depression and suicide in patients with prurigo nodularis. *J Eur Acad Dermatol Venereol.* 2017;31:E106-E107.
9. Rodriguez D, Kwatra SG, Dias-Barbosa C, et al. Patient perspectives on living with severe prurigo nodularis. *JAMA Dermatol.* 2023;159:1205-1212.
10. Misery L, Patras de Campaigno C, Taieb C, et al. Impact of chronic prurigo nodularis on daily life and stigmatization. *J Eur Acad Dermatol Venereol.* 2023;37:E908-E909.
11. Huang AH, Canner JK, Khanna R, et al. Real-world prevalence of prurigo nodularis and burden of associated diseases. *J Invest Dermatol.* 2020;140:480-483.e4.
12. Sutaria N, Adawi W, Brown I, et al. Racial disparities in mortality among patients with prurigo nodularis: a multicenter cohort study. *J Am Acad Dermatol.* 2022;82:487-490.
13. Boozalis E, Tang O, Patel S, et al. Ethnic differences and comorbidities of 909 prurigo nodularis patients. *J Am Acad Dermatol.* 2018;79:714-719.e3.
14. Müller S, Zeidler C, Ständer S. Chronic prurigo including prurigo nodularis: new insights and treatments. *Am J Clin Dermatol.* 2024;25:15-33.
15. Williams KA, Roh YS, Brown I, et al. Pathophysiology, diagnosis, and pharmacological treatment of prurigo nodularis. *Expert Rev Clin Pharmacol.* 2021;14:67-77.
16. Kwatra SG, Yosipovitch G, Legat FJ, et al. Phase 3 trial of nemolizumab in patients with prurigo nodularis. *N Engl J Med.* 2023;389:1579-1589.
17. Beck KM, Yang EJ, Sekhon S, et al. Dupilumab treatment for generalized prurigo nodularis. *JAMA Dermatol.* 2019;155:118-120.
18. Yosipovitch G, Mollanazar N, Ständer S, et al. Dupilumab in patients with prurigo nodularis: two randomized, double-blind, placebo- controlled phase 3 trials. *Nat Med.* 2023;29:1180-1190.
19. Wongvibulsin S, Sutaria N, Williams KA, et al. A nationwide study of prurigo nodularis: disease burden and healthcare utilization in the United States. *J Invest Dermatol.* 2021;141:2530-2533.e1.
20. Sutaria N, Alphonse MP, Marani M, et al. Cluster analysis of circulating plasma biomarkers in prurigo nodularis reveals a distinct systemic inflammatory signature in African Americans. *J Invest Dermatol.* 2022;142:1300-1308.e3.