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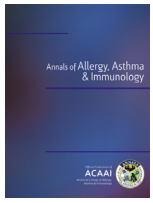

Letter

Prurigo nodularis and Hashimoto thyroiditis

Prurigo nodularis (PN) is a chronic skin condition that presents with diffuse multiple pruritic nodules. Nodules often present on the extensor surfaces of the extremities and are 0.5 to 3.0 cm in most reported cases.[1] The nodules tend to be extremely pruritic but nonpainful. The condition is a clinical diagnosis that may be supported through histologic identification. There are no confirmatory findings, but many reports include hyperkeratosis or parakeratosis with diminished nerve fiber density. Other histologic findings include acanthosis and an inflammatory perivascular infiltrate in the lower epidermis and upper dermis.[2] The precise cause is unknown but is presumed to be due to an increased number of nerves in the papillary dermis secondary to overexpression of nerve growth factor and receptor tyrosine kinase A.[3] Mast cells can be observed near these nerves and release nerve growth factor. However, these findings are not confirmed, and recent research has suggested that reduced nerve fiber density may suggest a neuropathic cause behind this condition.[4] However, recent studies have found hypoplasia of epidermal sensory nerves independent of clinical parameters. This is a new finding in PN and suggests involvement of epidermal nerves in PN pathophysiology.[5]

Although autoimmune disorders are not classically associated with PN, there is evidence that it may involve T_H1 and T_H2 cytokines. In one study, 19 of 22 patients with PN had immunostaining with anti–pSTAT-6 throughout the epidermis.[6] Anti–pSTAT-6 is a marker for the T_H2 cytokines interleukin (IL) 4, IL-5, and IL-13. In addition, 8 patients had dispersed staining with anti–pSTAT-1, a marker for the T_H1 cytokines interferon γ and IL-27. On the basis of these patterns, T_H1 and T_H2 cytokines may participate in the pathogenesis of PN.

Hashimoto thyroiditis (HT) is a disorder characterized by autoimmune dissolution of the thyroid gland. Autoantibodies against thyroid peroxidase, thyroglobulin, and thyrotropin receptors are often implicated in this condition. Autoimmune diseases, such as HT, often include elevated levels of T_H1 cytokines. In a study by Drugarin et al,[7] elevated levels of the T_H1 cytokines IL-2, tumor necrosis factor α, and interferon γ were found in patients with HT when compared with controls. The clinical presentation includes symptoms associated with hypothyroidism, such as weight gain, depression, cold intolerance, and bradycardia.

The association of HT and skin disorders is well documented. In a systemic review by Bagnasco et al,[8] nearly one-quarter of patients with chronic idiopathic urticaria presented with serologic evidence of autoimmune thyroid disease. In addition, Nuzzo et al[9] reported a higher prevalence of thyroid antibodies in their CIU cohort when compared with their controls. Furthermore, they observed HT was more prevalent in their CIU patients vs controls as well.

A 45-year-old African American woman presented with worsening pruritus and the emergence of multiple dome-shaped raised lesions. The patient described the lesions as being pruritic, darkly pigmented, and occasionally warm to touch. She experienced no residual burning or pain with the lesions. The lesions appeared to be fixed because they persisted for months. They were located primarily on her upper extremities, neck, and torso.

She could not identify any specific triggers, such as cosmetics, food, or environmental sources. Oral antihistamines and topical corticosteroids were ineffective, whereas high-dose corticosteroids provided minimal relief. She denied associated cutaneous or mucosal swelling, fever, joint pain, photophobia, nausea, abdominal pain, malaise, weight loss, anorexia, bullae, and oral lesions. Her medical history included hypothyroidism secondary to HT, childhood atopic dermatitis, nonallergic vasomotor rhinitis, and moderate persistent asthma.

Laboratory analysis results were fairly unremarkable. A complete blood cell count with differential, complete metabolic panel, complement studies, mannose-binding lectin, IgA, IgG, and IgM were all within normal limits. Immunoglobulin and mannose-binding lectin levels were measured to assess for an underlying primary immunodeficiency because of her history of recurrent sinopulmonary infections and fatigue. Her thyrotropin level was slightly elevated, and she had positive thyroid peroxidase and thyroglobulin antibody test results. The antibody test results were consistent with her history of HT. The patient's initial biopsy specimens were unremarkable, but subsequent biopsy specimens revealed thick orthohyperkeratotic lesions and irregular hyperplasia. In conjunction with her history and clinical presentation, she was diagnosed as having PN.

Because of her failure to respond to other therapies, including topical corticosteroids and antihistamines, she was prescribed thalidomide, 50 mg once daily. The dose was gradually increased to 100 mg and then 150 mg once daily. Thalidomide is an immunomodulator that inhibits the production of IL-6, IL-10, IL-12, and tumor necrosis factor α.[10] Its precise therapeutic mechanism regarding PN is unknown but is believed to alleviate pruritus through a local effect on proliferated neural tissue.[11] The patient began to experience peripheral neuropathy with higher doses of thalidomide. As a result, her therapy was gradually reduced to 50 mg once daily. Since being prescribed thalidomide, she has not taken oral corticosteroids, and her pruritus is well controlled. Duration of treatment is case dependent because of a limited number of studies. The largest retrospective study involved 42 patients with PN treated with a mean dose of thalidomide of 100 mg/d for a mean of 2 years. The mean duration of treatment before discontinuation because of neuropathy was 89 weeks (range, 1 week to 7.5 years).[12] There was moderate to marked improvement in 50% of the patients.

PN may be mistaken for urticaria and atopic conditions, particularly in black patients. Clinicians should include PN in the differential diagnosis when evaluating perceived urticaria and generalized

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pruritus, particularly when these conditions are recalcitrant to treatment with antihistamines and corticosteroids. Furthermore, PN may have an immunologic origin and could be associated with other autoimmune conditions, such as HT. After a review of the literature, this is the first published case report, to our knowledge, of PN in a patient with HT.

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