“Look Beyond the Skin”: A case report about chronic pruritus

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Abstract
A healthy 23-year-old female developed generalized pruritus over a year that began on her feet and gradually progressed to involve more than 50% of her entire body surface area. Punch skin biopsies were inconclusive, whereas a two-view chest x-ray was suspicious for lymphadenopathy. A chest computed tomography scan with contrast identified an anterior mediastinal mass which was biopsied and diagnosed as a nodular sclerosis type of Hodgkin’s lymphoma. Subsequently, appropriate therapy was initiated resulting in complete resolution of the patient’s chronic itch. This case underscores the clinical significance of a comprehensive systemic evaluation in chronic pruritus of unclear etiology.

Keywords
Pruritus, systemic diseases, malignancy, quality of life

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Introduction
Chronic pruritus is a frequent cause of office visits among the adult population.1,2 It is defined as an itch that lasts longer than 6 weeks and can be associated with various underlying systemic processes.3–5 A comprehensive diagnostic assessment is recommended for chronic pruritus of unclear etiology.6 However, a widespread application of this clinical approach is lacking, which can lead to suboptimal therapeutic outcomes and poor quality of life.2,7 We describe a case of chronic, intractable itching in a young adult as a manifestation of underlying Hodgkin’s lymphoma to highlight the need for a timely and relevant diagnostic evaluation in chronic pruritus of undetermined origin.

Case report
A 23-year-old female was seen in the outpatient dermatology clinic for one-and-a-half years of generalized pruritus. The pruritus began on her feet, gradually progressing to involve both upper and lower extremities, buttocks, trunk, as well as the palms and soles over subsequent months. The itching was moderate to severe (VAS: 7-8), persisted throughout the day and night, was exacerbated by heat and alcohol intake, and relieved slightly with ice packs. Skin papules appeared after 3–4 months. Review of systems was positive for mild, intermittent shortness of breath, fatigue, poor appetite, and rare night sweats. No personal history of allergic rhinitis, asthma, autoimmune diseases, substance abuse, or recent psychological stressors. Diagnostic tests performed at an outside healthcare facility showed normal serum IgE and tryptase. A punch skin biopsy from the left forearm showed findings consistent with lichen simplex chronicus, and direct immunofluorescence was negative. She was empirically treated for scabies, tinea pedis, staphylococcal folliculitis, allergic contact dermatitis, and prurigo nodularis without any considerable improvement. Several antihistamines, along with topical and systemic steroids, were trialed without benefit.

A complete skin examination revealed several erythematous, excoriated papules in various stages of healing, diffusely spread on bilateral feet, legs, buttocks, arms, chest, and back. Post-inflammatory hyperpigmentation was prominent on bilateral legs and feet, with some scarring present (Figure 1). Subsequently, a comprehensive diagnostic workup for chronic pruritus revealed low hemoglobin (11.4 g/dL), thrombocytosis (498 × 10⁹/L), lymphopenia (0.61 × 10⁹/L), elevated ESR (42 mm/h) and LDH (305 U/L). Liver enzymes, creatinine, thyroid function tests,
serum protein electrophoresis, antinuclear antibody level, and tryptase were normal. Screening for Hepatitis B and C, HIV, and syphilis was negative. Indirect immunofluorescence, bullous pemphigoid 180/230 IgG Ab, and desmoglein 1/3 IgG Ab were negative/normal. Punch biopsies obtained from the right dorsal forearm and right buttock showed erosion, prurigo nodule-like changes, and healing skin response (Figure 2). Direct immunofluorescence showed granular deposition with IgA in a few superficial dermal vessels, but there was no evidence for vasculitis on H&E sections. A 2-view chest x-ray (Figure 3(a) and (b)) was concerning for lymphadenopathy or neoplasm due to presence of right para-mediastinal and hilar opacities. A chest computed tomography (CT) scan revealed a large right anterior mediastinal mass (7.8 cm × 1.5 cm × 12.7 cm) with intrathoracic lymph node involvement (Figure 4(a) and (b)). Subsequently, a right anterior mediastinoscopy (Chamberlain procedure) was performed, with biopsy specimens showing the classic nodular sclerosis type of Hodgkin’s lymphoma with positive B-cell lymphoma-6 (BCL-6) and multiple myeloma oncogene-1 (MUM-1) biomarkers. Patient had a stage IIB (2B) disease as identified on a positron emission tomography-CT (PET-CT) scan and appropriate treatment was initiated. In accordance with the National Comprehensive Cancer Network (NCCN) guidelines, she completed 4 cycles of ABVD (Adriamycin, Bleomycin, Vinblastine, Dacarbazine) chemotherapy, along with consolidative radiation therapy (Dose: 30.6 Gy in 17 fractions), over a period of 6 to 8 months. Her pruritus improved significantly following the first cycle of chemotherapy and resolved completely without recurrence upon completion of scheduled chemotherapy and radiation therapy. The patient has been in remission for over 2 years and undergoes annual oncology follow-up with appropriate laboratory work (CBC, CMP, ESR, and LDH) and imaging (chest, abdomen, and pelvis CT scan with contrast).

Discussion

Chronic itch is a common and distressing symptom that lasts for more than 6 weeks.1,6 The International Forum for the Study of Itch classifies chronic pruritus into (Group I), comprising of itching secondary to dermatologic disorders, (Group II), which describes itching seen with systemic diseases, while (Group III), includes pruritus resulting from frequent scratching as seen with neurologic disorders. Mixed pruritus with more than one causative factor and pruritus of undetermined origin are other known categories.6,8 Pruritus in malignancy is either a result of local tumor reaction or treatment, or is a paraneoplastic sign that can often precede the clinical diagnosis of malignancy.4 It is often identified in a variety of hematological, with around 30% of Hodgkin’s lymphoma patients presenting with chronic pruritus as a primary symptom. Paraneoplastic itching has unique features as it usually occurs around the beginning of illness, often exacerbates at night and vanishes completely following remission of the neoplasm.8,9 In our patient, chronic pruritus was the presenting complaint for an underlying lymphoproliferative disorder.

Recent literature suggests that initial work up for generalized chronic pruritus with unclear etiology should include complete blood count, hepatic, renal and thyroid function tests, and imaging, such as chest x-ray and/or chest CT scan.
Additional tests are based on the patient’s unique clinical presentation. However, there is a considerable paucity of prospective epidemiological studies to guide this practice, and healthcare providers are frequently challenged with accurate assessment of chronic pruritus. Chronic pruritus can affect all aspects of a patient’s well-being and greatly reduces quality of life. It is imperative to consider paraneoplastic pruritus in patients with long standing itch, as a delayed diagnosis of malignancy poses a risk for suboptimal therapeutic outcomes. For our patient, a chest x-ray showed right paramediastinal and hilar opacities, which ultimately led to her diagnosis of Hodgkin’s lymphoma. Consequently, her pruritus resolved completely without recurrence within a few months of targeted chemo- and radiotherapy.

**Conclusion**

This case highlights the clinical significance of a comprehensive workup including relevant imaging studies, such as a chest x-ray in patients with chronic pruritis of unidentified
etiology to reduce potential diagnostic delay, suboptimal therapeutic outcome, and a poor quality of life

Author contribution
All persons who meet authorship criteria are listed as authors, and all authors certify of sufficient participation in the concept, design, analysis, writing, and revision of the manuscript.

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Informed consent
Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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References
1. Shive M, Linos E, Berger T, et al. Itch as a patient-reported symptom in ambulatory care visits in the United States. J Am Acad Dermatol 2013; 69(4): 550–556.
2. Sedlack S, Yosipovitch G, Kerby MB, et al. High unmet need in severe chronic pruritus in the United States: results from a survey of practicing community dermatologists. Itch 2018; 3: e18.
3. Lipman ZM, Ingrasci G and Yosipovitch G. Approach to the patient with chronic pruritus. Med Clin North Am 2021; 105(4): 699–721.
4. Larson VA, Tang O, Ständer S, et al. Association between itch and cancer in 16,925 patients with pruritus: experience at a tertiary care center. J Am Acad Dermatol 2019; 80(4): 931–937.
5. Fett N, Haynes K, Propert KJ, et al. Predictors of malignancy development in patients with chronic pruritus. J Dermatol Sci 2016; 82(2): 123–128.
6. Yosipovitch G and Bernhard JD. Clinical practice. Chronic pruritus. N Engl J Med 2013; 368: 1625–1634.
7. Lipman ZM, Yap QV, Rosen J, et al. The association of chronic pruritus with patients' quality of life: a cross-sectional study. J Am Acad Dermatol 2022; 86(2): 448–450.
8. Ständer S, Weisshaar E, Mettang T, et al. Clinical classification of itch: a position paper of the international forum for the study of itch. Acta Derm Venereol 2007; 87(4): 291–294.
9. Yosipovitch G. Chronic pruritus: a paraneoplastic sign. Dermatol Ther 2010; 23(6): 590–596.
10. Crombie JL and LaCasce AS. Current considerations in AYA Hodgkin lymphoma. Br J Haematol 2019; 184(1): 72–81.