Paraneoplastic eczematous eruption associated with Hodgkin's lymphoma

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ABSTRACT

Hodgkin's disease (HD) is a common malignant lymphoma that classically presents with painless lymphadenopathy, weight loss, nocturnal sweats, fever, and generalized pruritus. Unlike other lymphoproliferative disorders, cutaneous involvement is uncommon with HD. Diffuse hyperpigmentation, prurigo nodularis, acquired ichthyosis, erythema nodosum, mycosis fungoides, herpes zoster, and vasculitis have all been described as nonspecific or paraneoplastic manifestations of HD. A small set of cases of adult new-onset recalcitrant eczema has recently been described as a nonspecific cutaneous manifestation of HD. In agreement with these reports, we present a case of a 28-year-old woman who initially presented with persistent lymphadenopathy and a pruritic eczematous dermatitis that preceded the diagnosis of HD.

KEYWORDS Eczema; Hodgkin's lymphoma; paraneoplastic; pruritic rash

Hodgkin's disease (HD) is a lymphoid malignancy defined by the presence of CD15+/CD30+ Reed-Sternberg cells. Characteristically, it affects adults in their 20s, lacks lineage-specific markers, and spreads locally. It classically presents with painless lymphadenopathy, unintentional weight loss, nocturnal diaphoresis, fever, and generalized pruritus. There is often a delay between symptom onset and diagnosis.^{1,2} Persistent painless lymphadenopathy most often presents in the neck, supraclavicular fossa, or mediastinum.³ Pruritus affects approximately 30% of patients with HD and generally begins on the lower legs before becoming more generalized.^{2,4} Unlike other lymphoproliferative disorders, cutaneous involvement with HD is uncommon.^{5,6}

CASE DESCRIPTION

A 28-year-old white woman presented with an 8-month history of right axillary and supraclavicular lymphadenopathy and a severely pruritic expanding skin eruption. Fine-needle aspiration of a right supraclavicular lymph node had previously demonstrated acute inflammatory cells admixed with atypical CD68+ cells, suggesting a histiocytic origin. Pan-cytokeratin and p63 were negative. An inflammatory process was initially favored, for which the patient was prescribed antibiotics.

Computed tomography scans of the neck, chest, and pelvis were unremarkable. In the ensuing months, the patient developed a worsening diffusely pruritic rash and right axillary mass and presented to dermatology. She denied any B symptoms. Hydroxyzine, petroleum jelly, and topical triamcinolone 0.1% cream failed to alleviate her pruritus and rash.

She had massive, nontender, firm lymph nodes of the right side of the neck, supraclavicular area, and axilla and multiple nummular eczematous plaques over the upper and lower extremities, abdomen, and right periorbital skin (*Figure 1*). Two 4-mm punch biopsies from the left arm and left calf demonstrated regular acanthosis with spongiosis, moderate exocytosis, and a superficial perivascular lymphocytic infiltrate consistent with chronic eczema or contact dermatitis. The white blood cell count was $8.5 \times 10^9/L$, with 81.8% granulocytes, 14.5% lymphocytes, hemoglobin of 12.2 g/dL, and hematocrit of 37.3%. Biopsy of a right supraclavicular lymph node showed classical CD15+/CD30+ Hodgkin's lymphoma (nodular sclerosis type). Positron emission tomography demonstrated hypermetabolic bilateral cervical, right supraclavicular, right retropectoral, extensive mediastinal, bilateral hilar, and bilateral axillary lymphadenopathy with no disease below the diaphragm. Bone marrow biopsy was negative. The patient was treated with two cycles of

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Figure 1. A 28-year-old woman with nummular eczematous plaques distributed bilaterally over the upper and lower extremities, abdomen, and right periorbital skin.

Adriamycin, bleomycin, vinblastine, and dacarbazine chemotherapy; her eczema and pruritus resolved after the second cycle, suggesting a paraneoplastic phenomenon. After resolution of her eczema, the patient was lost to follow-up.

DISCUSSION

Skin lesions associated with HD occur in 17% to 53% of patients.⁷⁻⁹ Specific dermal involvement secondary to direct extension via retrograde lymphatic spread from cancerous lymph nodes is rare and is associated with advanced (stage IV) nodal or visceral disease.¹⁰ Nonspecific skin lesions associated with HD often represent a paraneoplastic syndrome and account for the majority of reported cases, occurring in 10% to 50% of patients with HD.^{5,8-11} Diffuse hyperpigmentation, prurigo nodularis, acquired ichthyosis, erythema nodosum, mycosis fungoides, herpes zoster, and acquired perforating collagenosis have all been described as nonspecific manifestations of HD.^{10,12-15} Although eczematous dermatitis and chronic idiopathic erythroderma are known to precede the diagnosis of cutaneous T-cell lymphoma, it is not commonly associated with the diagnosis of noncutaneous lymphoma such as classical HD. Two published cases describe adult-onset recalcitrant eczema that preceded HD diagnosis and one case of eczema exacerbation that preceded non-Hodgkin's lymphoma.^{16,17} In a recent retrospective study of a large group of patients with HD, pruritus and eczema were the most common dermatological findings. The authors suggest that patients with eczema, mycosis fungoides, and HD have a similar propensity to T-cell dysregulation and increased Th2 cytokine profiles conducive to atopy, which accounts for the similar cutaneous presentations among the three diseases.¹⁰ Treatment of HD led to the resolution of the eczematous eruptions in both our patient and the patients described in the literature.

In conclusion, our case emphasizes the importance of maintaining a high index of suspicion for HD in any adult patient presenting with a new-onset eczematous dermatitis. Although pruritus is the most common presenting cutaneous manifestation of HD, the differential diagnosis of new-onset

adult eczema should include HD along with cutaneous T-cell lymphoma such as mycosis fungoides. Early detection is crucial in the prognosis of a paraneoplastic process. A thorough workup including lymph node examination with biopsy of any enlarging nodes, skin biopsies, chest x-ray, complete blood count with a peripheral smear, basic blood chemistries, and close follow-up for any adult presenting with new onset pruritus or eczema is highly recommended.

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1. Lehmann LE, Anupindi S, Harris NL. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 18-2003. A 15-year-old girl with pain in the left leg and back, pruritus, and thoracic lymphadenopathy. *N Engl J Med.* 2003;348:2443-2451. doi:10.1056/NEJMcpc030007.
2. Cavalli F. Rare syndromes in Hodgkin's disease. *Ann Oncol.* 1998;9(Suppl 5):S109-S113. doi:10.1093/annonc/9.suppl_5.s109.
3. Connors JM. Clinical manifestations and natural history of Hodgkin's lymphoma. *Cancer J.* 2009;15:124-128. doi:10.1097/PPO.0b013e3181a282d8.
4. Gobbi PG, Attardo-Parrinello G, Lattanzio G, Rizzo SC, Ascari E. Severe pruritus should be a B-symptom in Hodgkin's disease. *Cancer.* 1983;51:1934-1936. doi:10.1002/1097-0142(19830515)51:10<1934::aid-cnrcr2820511030>3.0.co;2-r.
5. Stadie V, Marsch WC. Itching attacks with generalized hyperhidrosis as initial symptoms of Hodgkin's disease. *J Eur Acad Dermatol Venereol.* 2003;17:559-561. doi:10.1046/j.1468-3083.2003.00737.x.
6. Hayes TG, Rabin VR, Rosen T, Zubler MA. Hodgkin's disease presenting in the skin: case report and review of the literature. *J Am Acad Dermatol.* 1990;22(Pt 2):944-947. doi:10.1016/0190-9622(90)70131-z.
7. Arroyo A, Sánchez J, Vélez-García E. Cutaneous manifestations of Hodgkin's disease. *Cutis.* 1983;32:79-82.
8. Smith JL, Butler JJ. Skin involvement in Hodgkin's disease. *Cancer.* 1980;45:354-361. doi:10.1002/1097-0142(19800115)45:2<354::aid-cnrcr2820450227>3.0.co;2-#.
9. White RM, Patterson JW. Cutaneous involvement in Hodgkin's disease. *Cancer.* 1985;55:1136-1145. doi:10.1002/1097-0142(19850301)55:5<1136::aid-cnrcr2820550532>3.0.co;2-t.
10. Rubenstein M, Duvic M. Cutaneous manifestations of Hodgkin's disease. *Int J Dermatol.* 2006;45:251-256. doi:10.1111/j.1365-4632.2006.02675.x.
11. Introcaso CE, Kantor J, Porter DL, Junkins-Hopkins JM. Cutaneous Hodgkin's disease. *J Am Acad Dermatol.* 2008;58:295-298. doi:10.1016/j.jaad.2005.11.1055.
12. Tilakaratne W, Dissanayake M. Paraneoplastic pemphigus: a case report and review of literature. *Oral Dis.* 2005;11:326-329. doi:10.1111/j.1601-0825.2005.01116.x.
13. Shelnitz LS, Paller AS. Hodgkin's disease manifesting as prurigo nodularis. *Pediatr Dermatol.* 1990;7:136-139. doi:10.1111/j.1525-1470.1990.tb00670.x.
14. Eigentler TK, Metzler G, Brossart P, Fierlbeck G. Acquired perforating collagenosis in Hodgkin's disease. *J Am Acad Dermatol.* 2005;52:922. doi:10.1016/j.jaad.2004.12.053.
15. Rizos E, Milonis HJ, Pavlidis N, Elisaf MS. Acquired ichthyosis: a paraneoplastic skin manifestation of Hodgkin's disease. *Lancet Oncol.* 2002;3:727.
16. Callen JP, Bernardi DM, Clark RA, Weber DA. Adult-onset recalcitrant eczema: a marker of noncutaneous lymphoma or leukemia. *J Am Acad Dermatol.* 2000;43(Pt 1):207-210. doi:10.1067/mjd.2000.105502.
17. Winkelmann RK, Rajka G. Atopic dermatitis and Hodgkin's disease. *Acta Derm Venereol.* 1983;63:176-177.