Persistent Peripheral Eosinophilia and Cutaneous Non-Hodgkin's Lymphoma: A Case Report and Review of the Literature

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Peripheral eosinophilia can be the presenting sign in many cutaneous diseases but is often missed as a marker of a serious undiagnosed underlying disease such as atopic dermatitis, urticaria, drug eruption, bullous pemphigoid, inflammatory bowel disease, helminthic infection, Churg-Strauss syndrome, rheumatoid arthritis, or lymphoma. We report a case of non-Hodgkin's lymphoma presenting as persistent eosinophilia with a diffuse nodular cutaneous eruption.

Case Report

A 76-year-old previously healthy man presented to our clinic with a 3-week history of a diffuse cutaneous eruption. Previous pertinent history included a 3-month history of diarrhea and peripheral eosinophilia. The patient had undergone an extensive work-up including stool cultures for ova and parasites, upper endoscopy with small-bowel biopsies, chest x-ray, barium enema, small-bowel series, sigmoidoscopy, gall bladder ultrasound, and complete blood cell count. These tests revealed peripheral eosinophilia and chronic inflammation of the small bowel on biopsy. The remaining tests were normal. The patient had been placed on a 2-month prednisone course for presumptive eosinophilic gastroenteritis with no significant improvement. A repeat complete blood cell count demonstrated persistent eosinophilia (eosinophil count of 1900/μL; normal, 0–500/μL) but a normal white blood cell count.

Physical examination demonstrated multiple large erythematous, well-marginated plaques scattered diffusely over the patient's back (Figure), upper thighs, and arms. A biopsy of one of the plaques demonstrated a superficial and deep perivascular and interstitial mononuclear cell infiltrate. The infiltrate was composed of lymphoid-appearing cells with large

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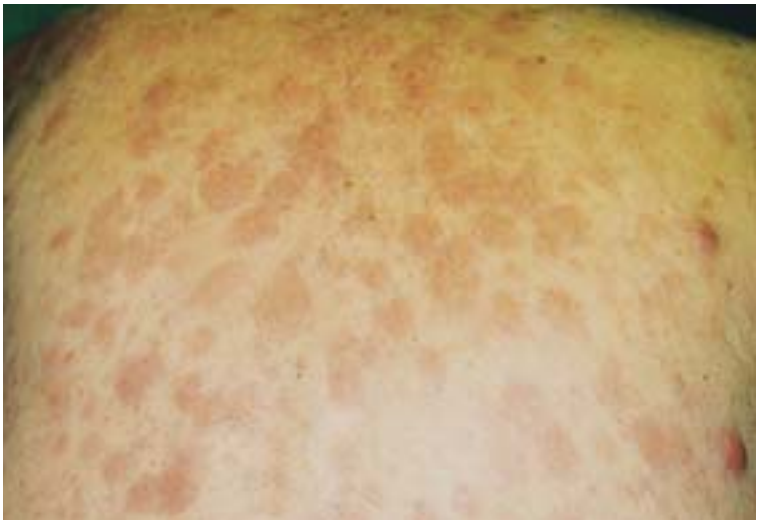

Physical examination demonstrated multiple large erythematous, well-marginated plaques scattered diffusely over the back.

Table 1.

Peripheral Eosinophilia as a Presenting Sign of Non-Hodgkin's Lymphoma

Author	Year	No. of Patients	White Blood Cell Count and Level of Eosinophilia
Goldman et al[9]	1995	1	9600/mm^3 with 10% eosinophils
Jacobs et al[10]	1982	1	Varies between 28,000–35,000/mm^3 —52% mature eosinophils —5% eosinophil band form —4% eosinophilmyelocytes
Henderson et al[11]	1969	2	Case 1: 18,300/mm^3 with 45% eosinophils Case 2: 32,500/mm^3 with 76% eosinophils
Catovsky et al[12]	1980	1	39,000–49,999/mm^3 with 20%–60% eosinophils
Watanabe et al[13]	1989	1	10,900/mm^3 with 32% eosinophils
Lorenzana et al[14]	1989	1	21,500/mm^3 with 13% eosinophils

hyperchromatic cleaved nuclei with scant cytoplasm. Mitotic figures were noted in the infiltrate. Immunoperoxidase staining revealed cells that were positive for the T-cell marker CD3 and negative for a large battery of B-cell markers including L26, CD31, CD34, neutrophil elastase, and myeloperoxidase. These markers confirmed that the infiltrate was consistent with a non-Hodgkin's lymphoma.

The patient received a lumbar puncture and bone marrow biopsy for staging purposes. The bone marrow biopsy showed evidence of a T-cell lymphoma, but the lumbar puncture results were within normal limits. The patient was diagnosed with stage IV non-Hodgkin's lymphoma according to the Ann Arbor staging classification (diffuse involvement of 1 or more extra lymphatic organs). He received several courses of cyclophosphamide, doxorubicin, vincristine, and prednisone. There was rapid decline in his clinical status, leading to peripheral and cranial nerve palsy. Four months after diagnosis, the patient expired from respiratory arrest at an outlying hospital.

Comment

The non-Hodgkin's lymphomas are a group of malignancies of the lymphoid system that represent 4% of all cancer deaths in the United States.[1] The incidence of these lymphomas has been increasing for the last 2 decades. Approximately 75% of lymphomas of the skin are of B cell origin, with the remaining comprising Sézary syndrome, mycosis fungoides, and adult T-cell leukemia and lymphoma.[2]

The cutaneous presentation of non-Hodgkin's lymphoma may be subdivided into 2 major groups: mycosis fungoides representing the largest percentage of patients and primary and secondary cutaneous lymphomas as the significantly smaller group. These lymphomas have been difficult to classify because of the multiple clinical conditions and terms used to describe cutaneous lymphoid infiltrates that simulate lymphoma in the skin.[3-6]

Our patient had a persistent peripheral eosinophilia for 8 months, during which his lymphoma remained undiagnosed until his cutaneous eruption became apparent. This case is noteworthy for its unusual presentation of persistent peripheral eosinophilia and generalized cutaneous eruption that resulted in the diagnosis of systemic non-Hodgkin's lymphoma. To our knowledge, only 2 authors have reported cases of peripheral eosinophilia and cutaneous disease in the presentation of non-Hodgkin's lymphoma. Finan and Winkelmann[7] described a single case of lymphocytic lymphoma with necrotizing granulomas resembling Churg-Strauss syndrome. Pestell[8] reported a second similar case.

Peripheral eosinophilia is a known sign of underlying non-Hodgkin's lymphoma but has only been noted as a presenting sign of this disease in isolated cases (Table 1).[9-14] Henderson and Mejia[11] reported 2 cases that showed an elevated white blood cell count with eosinophilia in the 45% to 76% range. No mention of cutaneous disease was made in these cases. The most common presentation of non-Hodgkin's lymphoma is persistent painless superficial adenopathy (67%).[2] Extra nodal disease is seen in only 30% to 40% of patients at presentation.[1] Several authors have noted that non-Hodgkin's lymphoma

Table 2.

Characteristics of Skin Disease in Non-Hodgkin's Lymphoma With Skin as the Presenting Sign

Author	Year	No. of Patients	Type of Skin Lesion
Burke et al[16]	1981	37	3 multiple 12 single 22 disseminated
Kawasaki et al[18]	1994	7	Solitary nodules, multiple lesions
Wolk[19]	1977	16	9 with single nodule or tumor 3 with localized multiple nodules 4 with widespread nodules and plaques
Illie[20]	1986	2	Both single tumors in skin and subcutaneous tissue
Kahn et al[21]	1974	1	Widespread plaques
Rijlaarsdam[17]	1990	35	35 red to violaceous nodules —10 solitary lesions —23 skin lesions circumscribed area —2 multiple lesions
Riyat[22]	1995	38	6 with skin infiltration at subcutis

that appears to be limited to the skin at the time of presentation may actually have generalized disease.[15-17]

Several studies examined the spectrum of cutaneous findings in non-Hodgkin's lymphoma without eosinophilia. Saxe et al[15] examined 36 patients with cutaneous involvement at the time of diagnosis of lymphoma. Fourteen of these 36 (39%) had disease confined to the skin at the time of presentation. Burke et al[16] reported a series of 50 cases of non-Hodgkin's lymphoma in which the initial diagnosis of lymphoma was established by skin biopsy. Burke and colleagues reported 22 of 37 (59%) patients who presented with disseminated cutaneous disease. Rijlaarsdam[17] examined 35 patients with skin involvement of non-Hodgkin's lymphoma but only 2 (6%) with widespread cutaneous disease (Table 2). Riyat[22] found 35 patients with cutaneous infiltration of non-Hodgkin's lymphoma but none with widespread disease.

Our case is particularly illustrative of the fact that the findings of persistent eosinophilia may warrant a high index of suspicion for non-Hodgkin's lymphoma when no infectious cause is found. A cutaneous eruption along with persistent peripheral eosinophilia demand a thorough history, physical examination, and timely skin biopsy to determine etiology. In such cases, non-Hodgkin's lymphoma should be considered highly on the differential diagnosis to ensure early and appropriate treatment.

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