

## Neutrophilic Eccrine Hidradenitis in a Primary CNS Lymphoma Patient Receiving High-Dose Chemotherapy

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### Abstract

Neutrophilic Eccrine Hidradenitis (NEH) is a rare inflammatory neutrophilic dermatosis that primarily affects eccrine sweat glands. Although it has been described in various malignancies and with therapeutic agents, it is most frequently associated with cytarabine-based induction chemotherapy for acute myelogenous leukemia. We report a rare case of NEH in a 63-year-old male with a medical history significant for primary CNS lymphoma. The patient was treated with high-dose thiotepa, busulfan, and cyclophosphamide (BuCy) followed by autologous stem cell transplantation, which was complicated by bacteremia and septic shock. Approximately three weeks after chemotherapy, he developed localized bright red, desquamating plaques on his bilateral outer hips, posterior upper thighs, and buttocks. Histological findings revealed neutrophils infiltrating and surrounding the eccrine glands accompanied by squamous syringometaplasia, apoptotic keratinocytes, and basovacuolar changes. This case serves to highlight that NEH should be considered in the differential diagnosis of erosive, erythematous plaques, especially in patients with lymphoproliferative tumors receiving high-dose chemotherapy, in order to provide appropriate clinical management.

**Keywords:** Neutrophilic eccrine hidradenitis; Primary CNS lymphoma; Chemotherapy; Eccrine glands; Neutrophils

### Introduction

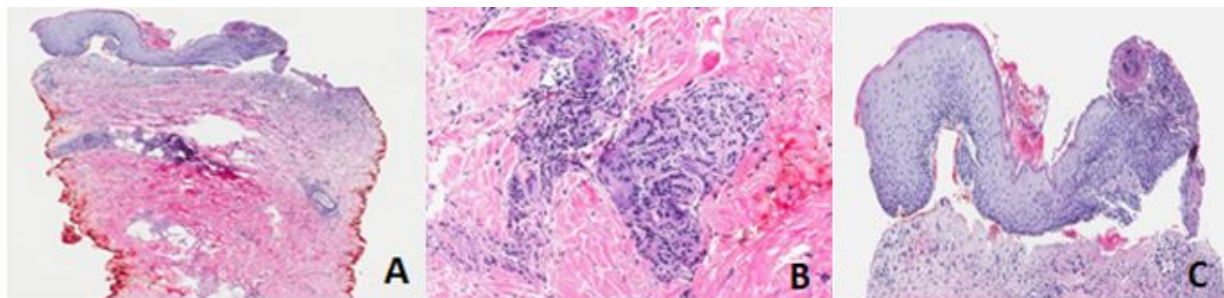
Chemotherapy with thiotepa, busulfan, and cyclophosphamide (BuCy) followed by autologous stem cell transplantation has been adopted as the treatment of the primary Central Nervous System (CNS) lymphoma [1]. High-dose chemotherapy has been associated with Neutrophilic Eccrine Hidradenitis (NEH) in patients with acute myelogenous leukemia [2]. NEH is described as a neutrophilic dermatosis characterized by neutrophilic infiltrates predominantly in the dermis without any identifiable source of infection [3]. To our knowledge, we present the first case of Neutrophilic Eccrine Hidradenitis (NEH) in an adult patient receiving high-dose chemotherapy for primary CNS lymphoma.

### Case Report

A 63-year-old male with a history of primary CNS lymphoma presented with fever and erythematous plaques on the buttocks and lower extremities. Three weeks prior to presentation, the patient was treated with high-dose chemotherapy (thiotepa and BuCy) followed by autologous stem cell transplantation, which was complicated by *Klebsiella* and *Pseudomonas* bacteremia and septic shock. On physical examination, a few well-circumscribed erythematous erosions with overlying white crust were noted on the outer thighs (Figure 1). On the buttocks and upper posterior thighs were bright red, eroded plaques with overlying fine white desquamation. A punch biopsy was performed on his right anterior thigh out of concern for acute graft versus host reaction versus a drug reaction.



**Figure 1:** Clinical appearance of desquamating plaques on the hip.



**Figure 2:** Neutrophilic eccrine hidradenitis. Histological examination demonstrates interface dermatitis with underlying superficial and deeply mixed inflammatory infiltrates with predominantly neutrophils (A). Prominent peri-eccrine inflammation with neutrophils accompanied by squamous syringometaplasia in the superficial and mid dermis (B) and apoptotic keratinocytes with basovacuolar changes (C) are shown.

Histological examination revealed prominent peri-eccrine inflammation with neutrophils and squamous syringometaplasia in the superficial and mid-dermis (Figure 2). Interface dermatitis with apoptotic keratinocytes and bilateral basovacuolar change with an underlying superficial and deep mixed inflammatory infiltrate of predominantly neutrophils were also observed. There was no evidence of vasculitis or hemorrhage. The fungal and bacterial cultures were negative. These findings were most consistent with NEH secondary to high-dose thiotepa and BuCy. While the patient's history of recent autologous stem cell transplantation was concerning for acute graft versus host reaction, the changes in eccrine glands seen in NEH are not observed in this diagnosis. The patient was treated with triamcinolone 0.1% ointment and silver sulfadiazine cream twice daily.

## Discussion

NEH is a rare neutrophilic dermatosis primarily affecting the eccrine glands [2]. Although most cases are reported in association with cytarabine-based induction chemotherapy for acute myelogenous leukemia [2], NEH is rarely observed in lymphoproliferative disorders [2]. It has been previously reported in one case of Hodgkin's lymphoma

and one pediatric case of a non-Hodgkin's lymphoma [4,5]. Demographics and clinical characteristics of these cases are summarized in Table 1 [4-15]. NEH has also been described in adult patients with other malignancies and solid tumors, including chronic lymphocytic leukemia, osteogenic sarcoma, testicular carcinoma, metastatic breast cancer, Bechet disease, HIV and Wilms tumor [2,4,5]. Granulocyte colony-stimulating factor, acetaminophen, anti-retroviral agents, and other chemotherapeutic agents (i.e. anthracyclines, mitoxantrone, cyclophosphamide, bleomycin, imatibib, methotrexate, and topotecan) have been reported to induce NEH as well [2,4,5]. Belot et al. reported one case without an associated disease or therapeutic agent [16].

NEH clinically manifests 2 days to 3 weeks following the induction of chemotherapy [2]. As demonstrated in Table 1, it presents as erythematous plaques typically located on the face, trunk, palms, or extremities, with or without associated fever or neutropenia [2,5,6]. Differential diagnosis may include erythema multiforme, leukemia cutis, drug hypersensitivity, vasculitis, bullous pyoderma, Sweet's syndrome and pyoderma gangrenosum [17].

Case	Gender	Age	Underlying leukemia/lymphoproliferative disorder	Clinical presentation	References
Bailey et al	M	11	Non-Hodgkin's lymphoma	Widespread erythematous papulopustules	4
Beutner et al	M	44	Hodgkin's lymphoma	Erythematous macules and plaques with associated fever	5
Srivastava et al	F	73	Acute myelogenous leukemia	Erythematous plaques mimicking facial cellulitis	6
Katsanis et al	F	11	Acute myelogenous leukemia	Erythematous eruption	7
Salik et al	F	4	Acute myelogenous leukemia	Tender erythematous and painful papules involving the trunk, extremities and face	8
Taghy et al	M	47	Acute myelogenous leukemia	Itchy, erythematous-papular palmer lesion with fever	9
Grahovac et al	F	51	Acute myelogenous leukemia	Periorbital cellulitis-like lesions and blanching urticarial papules and plaques on the trunk	10

Copaescu et al	M	58	Acute myelogenous leukemia	Dark erythematous, violaceous and edematous plaques on the right and left periorbital areas, on the nose root, and on the neck	11
Sanober et al	M	62	Acute myelogenous leukemia	Bilateral periocular erythematous and edematous maculopapular lesions	12
Ng et al	F	30	Acute myelogenous leukemia	Fever, chills, and painful cutaneous eruption over the right shin and left elbow	13
Bardenstein et al	M	30	Acute myelogenous leukemia	Periobital swelling, fever, and neutropenia.	14
Brehler et al	F	43	Acute myelogenous leukemia	Tender nodules in bilateral axillae	15

**Table 1:** Demographic and clinical characteristics of cases with associated leukemia and lymphoproliferative diseases.

The diagnosis of NEH is based on histological findings [18]. It is characterized by dense neutrophilic infiltrating and surrounding the eccrine glands, which may be accompanied by dermal edema and/or hemorrhage, squamous syringometaplasia, and necrosis of the eccrine coils and glands [2]. Epidermal spongiosis, basal vacuolization, and focal necrotic keratinocytes may also be present [9]. These findings in our case confirmed the diagnosis. Histopathological differential diagnosis includes, but is not limited to, acute urticaria, graft versus host disease, erythema nodosum, erythema multiforme, cellulitis, sweet syndrome, and erysipelas [3].

The pathogenesis of NEH has not been well-characterized. Harris et al., postulated that NEH may arise secondary to a direct cytotoxic effect of a therapeutic agent secreted in the sweat on the eccrine glands [19]. The damage of the glands may stimulate an inflammatory response and neutrophilic chemotaxis, which would lead to cellular damage and necrosis of the epithelial cells [2]. This may account for a majority of NEH cases, including our case, in patients receiving high-dose chemotherapy. In contrast, other investigators proposed that NEH is part of the spectrum of neutrophilic dermatoses [18].

NEH is generally a benign, self-limiting condition [6]. Current treatment includes non-steroidal anti-inflammatory drugs and topical corticosteroids, which should be used with caution in patients with neutropenia [2]. Shear et al., demonstrated that administration of dapsone 48 hours prior to chemotherapy prevented recurrent NEH in a patient [20]. It is also important to exclude infection as well as another differential diagnosis by fungal and bacteria cultures to avoid unnecessary use of antibiotic or changes in chemotherapy regimens [11,17].

## Conclusion

NEH is a neutrophilic dermatosis characterized by neutrophilic infiltrates within and around eccrine glands. It should be considered in the differential diagnosis of eroded, erythematous plaques, especially in patients receiving high-dose chemotherapy for primary CNS lymphoma. A diagnosis of NEH should be based on histological findings to avoid unnecessary use of antibiotics and changes in chemotherapy regimens.

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