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ABSTRACT

Introduction
Neutrophilic eccrine hidradenitis (NEH) is a rare and benign condition, which belongs to the spectrum of neutrophilic dermatoses. In this paper, we present a case of NEH during administration of chemotherapy for the treatment of acute myeloid leukemia along with histological and clinical findings.

Case Report
This paper presents the case of a 69-year-old man with a history of ulcerative colitis, dyslipidemia, and hypertension. He was diagnosed with acute myeloid leukemia. From day 1 of admission until day 7, the patient was administered Cytarabine 200 mg/m². In addition, Idarubicin (12 mg/m²) was initiated on day 3. On day 21, a morbiliform, diffused, pruritic, infiltrated rash was observed. A fresh cutaneous biopsy revealed that these lesions were of viral origin or reaction, without signs of malignant proliferation. The Periodic Acid Schiff coloration test was negative for infection. The lesions regressed spontaneously after the introduction of Amphotericin B and Vancomycin.

Conclusion
We concluded that NEH is self-limiting and non-life threatening. However, early diagnosis of the condition is necessary to avoid unwarranted medication and surgery. NEH can be successfully managed with the use of topical or systemic corticosteroids. Analgesics may be useful in case of pain. Dose adjustment or changing the chemotherapeutic agent is recommended to avoid possible recurrence.

Keywords: Neutrophilic eccrine hidradenitis, neutrophilic dermatoses, ulcerative colitis, dyslipidemia, hypertension
TITLE: Neutrophilic eccrine hidradenitis during treatment of acute myeloid leukemia

INTRODUCTION
Neutrophilic eccrine hidradenitis (NEH) belongs to the spectrum of neutrophilic dermatoses. It was first described by Harris et al. [1] in 1982 as a non-altered neutrophilic infiltration around the eccrine sweat glands in the deep dermis with extra-cutaneous aseptic localization of neutrophils. The condition is benign and rare and is most commonly encountered in acute myeloid leukemia (AML) patients undergoing chemotherapy.

NEH has also been known to occur in association with other neoplastic and non-neoplastic diseases such as testicular carcinoma, Hodgkin’s lymphoma, non-Hodgkin lymphoma, and osteogenic sarcoma; administration of drugs such as paracetamol, non-steroidal anti-inflammatory drugs, zidovudine, and stavudine; presence of infective pathogens such as human immunodeficiency virus, Serratia spp., and Enterobacter spp.; and chronic inflammatory processes such as rheumatic diseases [2,3]. The condition has also been reported to occur in the healthy population, among both adults and children. It affects both sexes with a slight male predominance.

In this paper, we present a case of NEH developing during chemotherapy for acute myeloid leukemia along with the clinical and histological findings. The condition abated spontaneously with only symptomatic treatment.

CASE REPORT
The patient was a 69-year-old man with a history of ulcerative colitis, dyslipidemia, and hypertension. The patient had initially visited his local physician in December 2015 for asthenia since several weeks with dyspnea on exertion as well as a few episodes of fever with diarrhea. Laboratory tests revealed leukocytosis (white blood cell count, 36,400/mm³) with blast cells at 65%, platelets at 74000/mm³, and hemoglobin at 7.3 g/dl. The patient was then referred to the emergency department for continuation of his care. On admission, the patient was diagnosed with AML. From day 1 of admission to day 7, the patient was administered Cytarabine 200
mg/m², i.e., 394 mg/d. In addition, Idarubicin (12 mg/m²) was initiated on day 3. Written informed consent was obtained from the patient for inclusion of his data in the study.

A gradual improvement was noted in leukocytosis with aplasia on day 4; the WBC reduced to 2400/mm³, polymorphonuclear neutrophils (PNN) 300/mm³, hemoglobin 8.2 g/dl, and platelets 22000/mm³. Complete recovery from aplasia was recorded on day 27, with WBC count 800/mm³, PNN 1,400, hemoglobin 8.6 g/dl, and platelets 435000/mm³.

On the infectious level

A febrile episode was recorded on day 1 on initiation of Ceftriaxone, with persistence of the fever for 48 hours. The Ceftriaxone was discontinued and replaced with Piperacillin on day 3. On the same day, a lesion was noted on the upper lip and Acyclovir was introduced. On day 7, the patient developed dyspnea, without coughing or sputum production. Blood gas analysis revealed a PO₂ gas of 70 mm Hg, and radiology showed evidence of bilateral, mainly hilar, alveolo-interstitial lesions, which were suggestive of fluid overload. In addition, the absence of micronodule or ground-glass lesions indicated a fungal infection. Accordingly, Amphotericin B was initiated. The patient developed lower limb lesions that were round, well-circumscribed, and with infiltration, as well as several bilateral, oral lesions with severe mucositis. Thus, Vancomycin was introduced on day 7.

Cutaneous manifestations

On day 7, the patient developed purple indurated lesions on the skin. The lesions were present on the upper and lower limbs and the abdomen and were well-circumscribed (Figures 1 (A), (B)). The genitalia were spared. Other findings of physical examination were unremarkable. No other abnormalities were noted. Punch biopsy of the skin revealed PNN-rich inflammatory dermal lesions surrounding apocrine (sweat) glands, which were consistent with NEH (Figures. 2 (A), (B) and Figure 3). No vasculitis was observed. The epidermis was normal.
No special care was required after dermatological advice. The Periodic Acid Schiff coloration test was negative for infection. The lesions regressed spontaneously after the introduction of Amphotericin B and Vancomycin. On day 21, a morbiliform, diffuse, pruritic, infiltrated rash was observed. A fresh cutaneous biopsy revealed that these lesions were of viral origin or reaction, without signs of malignant proliferation. The standard management for spontaneous eruption is to administer dexchlorpheniramine for the pruritus.

On day 22, the catheter was changed due to local inflammation. The fever abated completely after the introduction of Amphotericin B and Vancomycin. Antibiotics could be discontinued on complete recovery of aplasia and persistence of apyrexia. No bacteriological or mycological studies were required.

**DISCUSSION**

The differentiation of NEH from other similar conditions, particularly, infections, drug eruptions, and malignancies, is important. Several theories have been proposed regarding the pathogenesis of NEH, including the direct cytotoxic effect of chemotherapy agents or abnormal activation of neutrophils [4]. However, the actual mechanism underlying the pathogenesis of NEH remains elusive. From our experience, we suggest that prolonged administration of chemotherapeutic agents at low doses causes accumulation of the drugs in the eccrine glands, which may induce local inflammatory changes and epithelial cell necrosis. The development of NEH could also be attributed to the dose of the chemotherapeutic agents or to the duration or number of cycles of exposure. Our patient was febrile during the episode of NEH and was at risk of infection. However, bacterial and fungal cultures were negative. Vancomycin and Amphotericin B were administered. However, anti-infectious medications have been implicated in the NEH.

Typically, NEH has an acute onset and disappears spontaneously 1–5 weeks after discontinuing chemotherapy. The disease most commonly presents with skin lesions frequently associated with fever. The lesions generally appear as solitary or multiple, erythematous papules or even plaques on the trunk and limbs. Periorbital and facial lesions and appearance of dark plaques, annular lesions, and sclerodermoid
changes have also been reported. However, the lesions are rarely accompanied by pain and tenderness.

The diagnosis is established by the detection of neutrophilic infiltration around eccrine glands with necrosis in biopsy samples. Some non-specific epidermal changes may also be present, such as spongiosis, isolated keratinocyte necrosis, and vacuolization of the basal layer.

Our experience in this case confirms that NEH is self-limiting and non-life-threatening. However, early diagnosis of the condition is necessary to avoid unwarranted medication and surgery [5]. It is necessary to differentiate this condition from other neutrophilic dermatoses with similar clinical or histological signs, including sweet syndrome, pyoderma gangrenosum, and erythema elevatum diutinum. NEH is successfully managed with topical or systemic corticosteroids for symptom relief. Analgesics may be useful in case of pain. Dose adjustment or changing the chemotherapeutic agent is recommended to avoid possible recurrence.

CONCLUSION
Based on our findings, we concluded that NEH can be successfully managed with the use of topical or systemic corticosteroids. To avoid possible recurrence, it is recommended to adjust the dose or change the chemotherapeutic agent.

CONFLICT OF INTEREST
The authors declare that there does not exist any financial interest or conflict of interest.

AUTHOR’S CONTRIBUTIONS
Wajd Ahmed Althakfi
Group 1 - Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2 - Drafting the article, Critical revision of the article
Group 3 - Final approval of the version to be published
REFERENCES


FIGURE LEGENDS

Figure 1: Dermatological lesions: well-circumscribed, indurated lesions on (A) –the upper limbs; (B) –the lower limbs.

Figure 2: (A) – Histopathological images are obtained by using Hematoxylin and eosin stain and observing it at low magnification power of 5X: Neutrophilic infiltration is observed around eccrine glands; (B) – Histopathological images are obtained by using Hematoxylin and eosin stain and observing it at medium magnification power of 10X: Neutrophilic infiltration is observed around eccrine glands.

Figure 3: High magnification power of 40x and Hematoxylin and eosin stain are used. Neutrophils surrounding and infiltrating the sweat gland epithelium with gland atrophy are observed.

FIGURES

Figure 1: Dermatological lesions: well-circumscribed, indurated lesions on (A) –the upper limbs; (B) –the lower limbs.
Figure 2: (A) – Histopathological images are obtained by using Hematoxylin and eosin stain and observing it at low magnification power of 5X: Neutrophilic infiltration is observed around eccrine glands; (B) – Histopathological images are obtained by using Hematoxylin and eosin stain and observing it at medium magnification power of 10X: Neutrophilic infiltration is observed around eccrine glands.

Figure 3: High magnification power of 40x and Hematoxylin and eosin stain are used. Neutrophils surrounding and infiltrating the sweat gland epithelium with gland atrophy are observed.