

Neutrophilic Dermatositis of the Dorsal Hands in a Patient Treated With Chemotherapy for Acute Myelogenous Leukemia

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The proper nomenclature and classification of the group of diseases known as neutrophilic dermatoses is a topic of ongoing interest and study. Specifically, the possible relationship between neutrophilic dermatosis of the dorsal hands (NDDH) and Sweet disease (SD), or their existence as separate and discrete entities, has been explored in the literature. We present the case of a 63-year-old woman with acute myelogenous leukemia (AML) who developed NDDH 4 weeks after undergoing chemotherapy. Results from a punch biopsy revealed leukocytoclasia and endothelial swelling around the dermal vessels, with no evidence of fibrinoid necrosis of the vessel walls. This case may lend support to the concept that NDDH is a variant of SD rather than a distinct clinical entity.

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Case Report

The dermatology service was consulted to evaluate a 63-year-old woman admitted for a labial abscess who presented with a 2-week history of painful lesions on the back of both hands and intermittent fevers. Her medical

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history included polycythemia rubra vera that evolved to myelodysplastic syndrome (refractory anemia with excess blasts type 2 [RAEB-2]) and then progressed to acute myelogenous leukemia (AML). Four weeks prior to the development of cutaneous symptoms, the patient completed a 2-week course of cytarabine liposome and idarubicin hydrochloride and results of a bone marrow biopsy confirmed complete remission of her AML.

Physical examination revealed multiple tender erythematous nodules and large coalescing pustules on the dorsal and lateral aspects of both hands (Figure). The nodules and pustules appeared to be in various stages of development and resolution; some had eroded and were covered with hemorrhagic crust. Her white blood cell count was $9.1 \times 10^9/L$ (reference range, $4.5\text{--}11.0 \times 10^9/L$) with 79% polymorphonuclear cells, hemoglobin level was 10.9 g/dL (reference range, 14.0–17.5 g/dL), platelet count was $10 \times 10^9/L$ (reference range, $150\text{--}350 \times 10^9/L$), erythrocyte sedimentation rate was 117 mm/h (reference range, 0–20 mm/h), and C-reactive protein was 8.4 mg/L (reference range, 0.08–3.1 mg/L). Results of a punch biopsy from the right dorsal hand demonstrated a dense dermal neutrophilic infiltrate and papillary dermal edema. Dermal vessels were dilated and there was extravasation of red blood cells. A neutrophilic infiltrate with leukocytoclasia and endothelial swelling also was seen around the dermal vessels, but there was no fibrinoid necrosis of the vessel walls.

A diagnosis of neutrophilic dermatosis of the dorsal hands (NDDH) was made and the patient was treated with topical fluocinonide per her request for conservative therapy. She showed minimal improvement over 2 weeks and was subsequently treated with prednisone 1 mg/kg daily tapered over 3 weeks with rapid improvement and resolution of her symptoms. Three months after the onset



Neutrophilic dermatosis on the dorsal (A) and lateral (B) aspects of both hands upon initial presentation to the dermatology service.

of cutaneous symptoms, the patient remained free of cutaneous symptoms, but her circulating blasts rose from 4% to 78%, signifying relapse of AML.

Comment

In 1964, Sweet¹ reported on an original case series of 8 patients with fever; neutrophilic leukocytosis; painful plaques on the face, neck, and limbs; and a dense dermal neutrophilic infiltrate, which formed the foundation for a group of diseases that would become known as neutrophilic dermatoses.

The term *neutrophilic dermatosis* now encompasses a variety of diseases with similar clinical and histopathologic findings, most notably acute febrile neutrophilic dermatosis (classic Sweet disease [SD]), pyoderma gangrenosum, and NDDH. The optimal classification of these conditions is still a matter of debate and the presence or absence of vasculitis, although not included in Sweet's¹ original criteria, has been a focus of the discussion.

The first neutrophilic dermatosis in an acral distribution, termed *pustular vasculitis of the hands*,

was reported in 6 patients with lesions resembling classic SD but localized to the dorsal and lateral aspects of the hands. The patients also exhibited the classic signs of fever, neutrophilic leukocytosis, and a prompt response to oral corticosteroids, but the presence of leukocytoclastic vasculitis led the authors to view the condition as separate and distinct from SD.² More recently, NDDH was suggested as a more accurate description of this condition.³ Three patients were noted to have clinicopathologic findings similar to the patients reported by Strutton et al,² without evidence of vasculitis. The authors proposed that NDDH be considered a subset of SD.³

Subsequent researchers also have questioned the importance of vasculitis in diagnosing neutrophilic dermatoses and support the view of NDDH as a variant of SD. Malone and colleagues⁴ reported a significant correlation with vasculitis and lesions of longer duration (17.5 vs 6 days) in patients with SD ($P=.02$). In addition, they noted the absence of vascular immunoglobulin and complement in patients with vasculitis, suggesting that the associated vasculitis in older lesions

may be an epiphenomenon, or secondary vasculitis, rather than a primary process.⁴ This report supports the view of NDDH as a variant of SD.

Our case supports the idea that NDDH is a variant of SD, as our patient's condition occurred in the setting of AML, a disease that is well-known for its association with classic SD.⁵ Additionally, clinical findings were consistent with prior reports and the biopsy specimen, demonstrating leukocytoclasia and endothelial swelling around the dermal vessels, was obtained approximately 2 weeks after the onset of lesions. The absence of fibrinoid necrosis of the vessel walls in the specimen suggests that either the biopsy was obtained too early in the course of the process for the development of fibrinoid necrosis or the vessel inflammation was secondary to the dermal neutrophilic infiltrate rather than primary vasculitis.

Interestingly, our patient was in remission of AML 4 weeks following chemotherapy with cytarabine liposome and idarubicin hydrochloride. Three months after the onset of cutaneous symptoms, she developed increasing numbers of circulating blasts, signifying hematologic relapse. A review of the reported cases of SD in 1988 described that approximately 20% (79 cases) of patients with SD have an associated malignancy, and cutaneous findings precede the diagnosis in two-thirds of cases. In many cases, SD heralds relapse of the underlying malignancy.⁶ Our case reiterates the variability in timing between symptom onset and diagnosis of malignancy and supports an association between NDDH and impending hematologic relapse.

Medication-induced SD is well-documented and most common with drugs that enhance neutrophil production, such as granulocyte-macrophage colony-stimulating factor.⁷ There also are reports of SD occurring during or within 1 week after chemotherapy with cytarabine liposome for AML.⁸⁻¹¹ Our patient was treated with cytarabine liposome and the development of cutaneous symptoms was delayed for several weeks. There is a clear relationship between cytarabine liposome and neutrophilic eccrine hidradenitis, another neutrophilic dermatosis, and some researchers suggest the drug may have a pathophysiologic role in SD via an effect on neutrophil function.¹¹⁻¹⁵ In cases of simultaneous treatment with granulocyte-macrophage colony-stimulating factor and cytarabine liposome, it is unclear what role, if any, the chemotherapy plays in the pathogenesis of SD.¹⁶

Conclusion

This case further supports the concept that NDDH is a variant of SD and the presence of vasculitis does not

signify a distinct clinical entity but rather a correlation with lesion duration. The preexisting diagnosis of AML in our patient underscores the association of NDDH with malignancy and demonstrates variability in timing between symptom onset and diagnosis of malignancy.

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