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A case of filgrastim-induced neutrophilic dermatosis of the dorsal hands in a patient with Felty syndrome

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Abstract

Neutrophilic dermatosis of the dorsal hands (NDDH) is a variant of Sweet syndrome that presents with erythematous bullae, papules/plaques, or pustules on the dorsal hands. It is most commonly associated with hematologic and solid organ malignancies, though cases of NDDH associated with inflammatory bowel disease, rheumatologic disorders, and medication exposure have also been described in the literature. Felty syndrome is a rare complication of long-standing rheumatoid arthritis characterized by neuropathy, splenomegaly, and neutropenia. Granulocyte colony stimulating factors (e.g., filgrastim) can be utilized to rescue the neutropenia observed in Felty syndrome, but this treatment may subsequently cause Sweet syndrome. Herein, we present a 64-year-old man with Felty syndrome and a complex medical history who presented with sudden onset, painful blisters located on the dorsal and palmar aspects of his bilateral hands. Given the patient's past medical history, a broad differential diagnosis, including disseminated fungal and viral infection was initially considered. A punch biopsy of the skin lesion disclosed neutrophilic dermatosis, which together with laboratory data satisfied the von den Driesch criteria for Sweet syndrome. As the lesions were localized exclusively on the patient's hands, the qualification of NDDH was also endorsed.

Keywords: Felty syndrome, rheumatoid arthritis, Sweet syndrome

Introduction

Neutrophilic dermatosis of the dorsal hands (NDDH) is a subtype of Sweet syndrome that manifests as indurated, painful, erythematous papules/plaques admixed with possible ulcers and pustules localizing to the dorsal hands. This entity was first described by Strutton et al. in 1995 [1]. The nomenclature *neutrophilic dermatosis of the dorsal hands* would later be coined by Galaria et al. in 2000 [2]. Histology of NDDH reveals a dense neutrophilic infiltrate with possible papillary dermal edema. Neutrophilic dermatosis of the dorsal hands has been most commonly reported in the setting of hematologic and solid organ malignancies; it also may be associated with inflammatory bowel disease, rheumatologic disorders, and medication exposure [3].

Felty syndrome (FS) is a rare complication of long-standing rheumatoid arthritis that presents with cutaneous ulcerations, mononeuropathy multiplex, and splenomegaly in addition to symmetric, bilateral joint pain. Patients with FS often tend to develop profound neutropenia, which may be treated with granulocyte colony stimulating factors (GCSF), such as filgrastim [4]. Herein, we present a patient with FS who developed NDDH after initiating filgrastim treatment.

Case Synopsis

A 64-year-old man presented to the emergency department for sudden onset, painful blisters located on the dorsal and palmar aspects of his bilateral hands. He also endorsed low grade fevers and chills but denied headache, dyspnea, cough, abdominal pain, dysuria, hematuria, and myalgia. Past medical history was significant for chronic

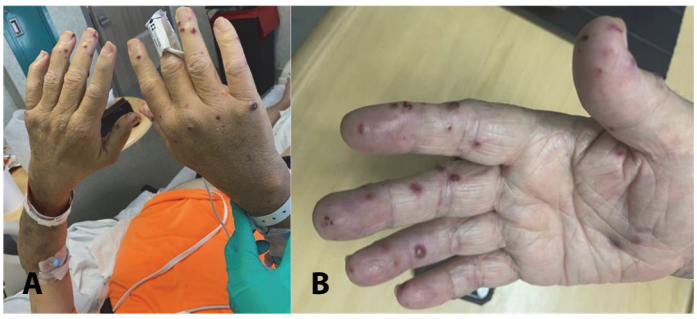

Figure 1. *Distant **A)** and closer **B)** view of the rash on the patient's hand reveals violaceous papules, nodules, and vesicles admixed with occasional pustules.*

kidney disease, heart failure with reduced ejection fraction, non-alcoholic fatty liver disease, pulmonary mucormycosis, and rheumatoid arthritis complicated by FS. He denied illicit drug use, recent travel, and sexual activity over the past two years. Six days prior to presentation, the patient had received his first dose of filgrastim.

Physical examination revealed violaceous papules, nodules, and hemorrhagic vesicles admixed with occasional pustules on the dorsal and palmar aspects of the patient's hands (**Figure 1**). The lesions were painful but non-pruritic. No lesions were noted over the arms, trunk, back, or head and neck, but a solitary vesicle was observed over the superior gluteal cleft. Neither lymphadenopathy nor hepatosplenomegaly were appreciated. Complete blood count disclosed a leukocyte count of 8100/mm^3 (90% neutrophils); erythrocyte sedimentation rate (ESR) was found to be 55mm/hr.

Initially, a broad differential diagnosis was proposed. Erythema elevatum diutinum was considered given the lesion morphology and the underlying rheumatoid arthritis. Disseminated herpes simplex virus (HSV) and varicella zoster virus (VZV) as well disseminated fungal infections (e.g., cryptococcosis, histoplasmosis) were principally considered as infectious etiologies.

A punch biopsy of a lesion on the patient's right fourth finger revealed a dense neutrophilic infiltrate occupying the entire thickness of the dermis, extending into the subcutaneous fat (**Figure 2**). Multiple stains for infectious agents, including acid fast bacilli, bacteria, and fungal elements failed to reveal any organisms; HSV and VZV immunohistochemical stains were also negative. Blood cultures and orthopoxvirus polymerase chain reaction also later returned negative. A simple search for common malignancies in the patient's demographic was negative. Altogether, considering the biopsy results, clinical findings (sudden onset painful skin lesions and low-grade fevers), and laboratory data (erythrocyte sedimentation rate >20mm/hr, leukocyte count >8,000/mm^3, with 90% neutrophils), a diagnosis of Sweet syndrome was made per the von den Driesch criteria [5]. Also, given that the lesions were limited to the patient's hands, a further qualification of NDDH was made.

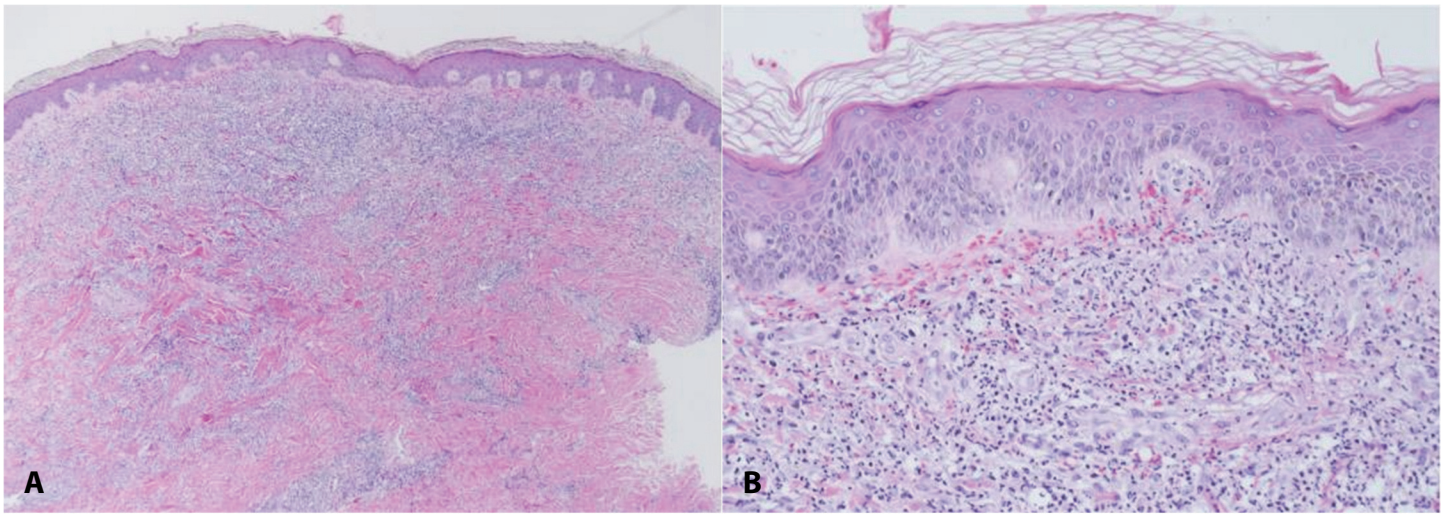

Figure 2. *H&E histopathology of 3cm punch biopsy of a lesion on the patient's right fourth finger **A)** reveals a dense neutrophilic infiltrate within the dermis extending into the subcutaneous fat, 40×. **B)** Higher magnification view illustrating neutrophilic infiltration into upper dermis, 200×.*

Case Discussion

Sweet syndrome, or acute febrile neutrophilic dermatosis, is a condition that presents with a constellation of cutaneous (abrupt onset painful nodules/plaques) and inflammatory findings (e.g., pyrexia, elevated ESR). Sweet syndrome can occur due to a variety of etiologies, including autoimmune processes (e.g., inflammatory bowel disease), infectious triggers, iatrogenic agents, and malignancy. Sweet syndrome also commonly occurs in the setting of GCSF treatment. Although the pathogenesis of Sweet syndrome in the setting of GCSF treatment is not completely understood, it is suggested that GCSF results in an overexuberant neutrophilic response with subsequent neutrophil localization to the dermis [3]. In our patient, the temporal association between initiation of filgrastim and Sweet syndrome manifestation strongly suggests filgrastim administration to be the most likely etiology of the SS.

Neutrophilic dermatosis of the dorsal hands is a variant of Sweet syndrome. Histologically, NDDH is identical to Sweet syndrome, but differs in its localization. In a 2019 systematic review of 123 patients with NDDH, Micallef et al. observed 78% of NDDH cases to involve both hands; 30.9% of cases reported involvement of other sites, though only 4.1% of cases described palmar involvement. The investigators also noted hematologic and solid organ malignancies to be the most common co-morbidities, seen in 14.3% and 15.5% of patients, respectively [6]. A recent single center study of 27 patients with NDDH further emphasizes the link between NDDH and malignancy, with 44% of patients having a hematologic dyscrasia and 19% having a solid organ cancer [7]. Our report, which describes NDDH involving both the dorsal and palmar aspects of the hands and occurring in association with FS, represents an uncommon presentation of NDDH.

Sweet syndrome is usually exquisitely responsive to corticosteroids [3], yet given the patient's significant comorbidities (including pulmonary mucormycosis and congestive heart failure), corticosteroid treatment was not pursued. Additionally, during his hospital course, the patient decided to pursue hospice care (the patient was terminally ill due to pulmonary mucormycosis); thus, he refused any further treatment.

Conclusion

Altogether, our patient presentation is unique for a number of reasons. First, it conceptualizes an interesting illness script: a patient with rheumatoid arthritis, whose clinical course is complicated by FS, then subsequently complicated by neutropenia, requiring GCSF treatment, which ultimately triggers Sweet syndrome. Second, the anatomic localization of lesions in our patient (involving both the palmar and dorsal aspects of the hand) is uncommon, as NDDH usually only involves the dorsal hands. Finally, the occurrence of NDDH in the setting of filgrastim administration in a patient with FS is also noteworthy, as NDDH is most commonly observed in the setting of malignancy.

Potential conflicts of interest

The authors declare no conflicts of interest.

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