Subcutaneous Sweet syndrome in the setting of myeloid disorders: A case series and review of the literature

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Background: The association of neutrophilic dermatoses with myeloid disorders is well known, but neutrophilic panniculitis in the same setting has only been reported infrequently.

Objective: We aimed to better characterize these lesions clinically and histologically, and to provide a comprehensive differential diagnosis and appropriate diagnostic approach.

Methods: The pathology archives were searched for cases of neutrophilic panniculitis in patients with myeloid disorders. Clinical history and histologic features were studied. Similar cases in the English-language literature were reviewed.

Results: Five biopsy specimens from 4 patients and 11 previous case reports were identified. All patients presented with erythematous tender nodules typically involving the extremities. Most were accompanied by fevers, and resolved either spontaneously or with steroids. Histologically, the subcutaneous neutrophilic infiltrates demonstrated lobular or, less frequently, septal patterns with minimal dermal involvement. Leukocytoclasis, fat necrosis, reactive stromal fibroblasts, and mild reticular dermal edema were each seen in at least 3 of our 5 biopsy specimens. No myeloid blasts, vascular changes, or non-Miescher granulomas were observed. No micro-organisms were identified in the skin nodules.

Limitations: This study is limited by the small number of cases.

Conclusions: Based on the fairly consistent clinical and histologic findings, neutrophilic panniculitis occurring in the setting of myeloid disorders is best classified as subcutaneous Sweet syndrome after exclusion of infectious panniculitis, id reaction, and leukemia cutis. These lesions may be associated with myeloid disorders, or induced by chemotherapy or other medications. (J Am Acad Dermatol 2013;68:1006-15.)

Key words: myelodysplastic syndrome; myeloid leukemia; neutrophilic dermatosis; neutrophilic panniculitis; subcutaneous; Sweet syndrome.

Neutrophilic dermatosis is known to associate with myeloid disorders including acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS).[1-9] The 2 prototypes are Sweet syndrome and pyoderma gangrenosum. Sweet syndrome is characterized clinically by acute fever and skin eruption, and histologically by dermal

Abbreviations used:

AFB: acid-fast bacillus
AML: acute myeloid leukemia
MDS: myelodysplastic syndrome

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Funding sources: None.
Conflicts of interest: None declared.
Reprints not available from the authors.
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Published online February 11, 2013.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2012.12.954

neutrophilic infiltrate, leukocytoclasis, and papillary dermal edema in the absence of vasculitis.[10] Pyoderma gangrenosum associated with myeloid disorders is typically of the bullous variant, and shows histologic overlap with Sweet syndrome.[6-9] Unlike neutrophilic dermatosis, neutrophilic panniculitis has only been reported infrequently in the setting of myeloid disorders.[11-21] These cases are particularly rare when consideration is only given to neutrophilic infiltrates confined to the subcutis (primary neutrophilic panniculitis), as opposed to extension of a heavy dermal infiltrate into the subcutis (secondary neutrophilic panniculitis).

"Neutrophilic panniculitis" is not a diagnosis per se but a histologic pattern that may be seen in a variety of disorders such as erythema induratum,[22] early erythema nodosum,[23] infectious panniculitis,[24] alpha1-antitrypsin deficiency panniculitis,[25,26] pancreatic panniculitis,[27] Behçet syndrome,[28] pustular panniculitis of rheumatoid arthritis,[29] Crohn's-associated neutrophilic panniculitis,[30] panniculitic id reaction,[31] factitial panniculitis,[32] and subcutaneous Sweet syndrome.[33] Distinction often requires careful clinicopathologic correlation. As treatment regimens differ considerably, correct diagnosis is crucial especially in immunocompromised patients.

Herein, we describe 4 cases of primary neutrophilic panniculitis occurring in the setting of AML and MDS, and review all similar reports in the English-language literature. By studying the clinical and histopathologic features, we aimed to better classify these lesions and to propose an appropriate diagnostic approach to these cases.

CAPSULE SUMMARY

- Neutrophilic dermatosis is frequently associated with myeloid disorders, whereas neutrophilic panniculitis in the same clinical setting has only been described in isolated case reports.
- The clinical presentation of neutrophilic panniculitis occurring in patients with myeloid disorders closely resembles that of classic Sweet syndrome.
- We propose the diagnosis of subcutaneous Sweet syndrome in these cases after exclusion of infection, id reaction, and leukemia cutis.

METHODS

After approval from the institutional review boards, the surgical pathology databases at the Massachusetts General Hospital and the University of Michigan Medical Center were searched for "neutrophilic panniculitis" in January 2010 through January 2012. Cases were filtered by clinical history of AML, MDS, or myeloproliferative disorder. Histologic slides were reviewed to select cases with subcutaneous neutrophilic infiltrate without significant dermal involvement. Pertinent clinical data were obtained from electronic medical records. To identify similar cases in the literature, PubMed was searched for "neutrophilic panniculitis" and "leukemia," "myelodysplastic," or "myeloproliferative."

RESULTS

Five skin biopsy specimens obtained from 3 patients with AML and 1 patient with MDS were identified in our databases. The clinical and histologic findings are described as follows and summarized in Tables I and II. Eleven reports of neutrophilic panniculitis in patients with AML or MDS were found in the English-language literature, and are summarized in Table III.[11-21]

Case 1

A 53-year-old man developed therapy-related AML 2 years after chemoradiation for osteosarcoma. He entered clinical remission after allogeneic stem-cell transplantation. On day 133 he experienced a relapse and was treated with mitoxantrone, etoposide, cytarabine, lenalidomide, and donor leukocyte infusion. While on maintenance lenalidomide and sorafenib, he developed fever to 102°F, fatigue, dyspnea, and painful subcutaneous nodules. Chest computed tomographic scan and cultures from bronchioalveolar lavage confirmed *Pneumocystis jiroveci* pneumonia. Blood cultures produced negative results.

Skin examination revealed erythematous nodules on buttock and thigh without fluctuance or warmth. Punch biopsy specimen submitted for flow cytometry showed no blasts. Histology revealed predominantly lobular neutrophilic panniculitis without dermal infiltrate, papillary dermal edema, or vasculitis (Fig 1). No myeloid blasts were identified on hematoxylin-eosin stain, or on CD117 or CD34 immunostains. Brown-Hopps, periodic acid—Schiff, Grocott methenamine—silver, acid-fast bacillus (AFB), and Fite stains were negative for microorganisms.

The patient improved clinically at 1-week follow-up, and his skin lesions resolved spontaneously at 2 weeks' follow-up. Five months later the patient developed a similar nodule on the abdomen, of which he declined a biopsy. The patient died in palliative care 1 month later.