To the Editor:

Neutrophilic dermatoses—a group of inflammatory cutaneous conditions—include acute febrile neutrophilic dermatosis (Sweet syndrome), pyoderma gangrenosum, and neutrophilic dermatosis of the dorsal hands. Histopathology shows a dense dermal infiltrate of mature neutrophils. In 2005, the histiocytoid subtype of Sweet syndrome was introduced with histopathologic findings of a dermal infiltrate composed of immature myeloid cells that resemble histiocytes in appearance but stain strongly with neutrophil markers on immunohistochemistry.1 We present a case of histiocytoid pyoderma gangrenosum with histopathology that showed a dense dermal histiocytoid infiltrate with strong positivity for neutrophil markers on immunohistochemistry.

An 85-year-old man was seen by dermatology in the inpatient setting for a new-onset painful abdominal wound. He had a medical history of myelodysplastic syndrome (MDS), high-grade invasive papillary urothelial carcinoma of the bladder, and a recent diagnosis of low-grade invasive ascending colon adenocarcinoma. Ten days prior he underwent a right colectomy without intraoperative complications that was followed by septic shock. Workup with urinalysis and urine culture showed minimal pyuria with *Pseudomonas aeruginosa*. Additional studies, including blood cultures, abdominal wound cultures, computed tomography of the abdomen and pelvis, renal ultrasound, and chest radiographs, were unremarkable and showed no signs of surgical site infection, intra-abdominal or pelvic abscess formation, or pulmonary embolism. Broad-spectrum antibiotics—vancomycin and piperacillin-tazobactam—were started. Persistent fever (\(T_{\max}\) of 102.3 °F [39.1 °C]) and leukocytosis (45.3 × 10^9/L [4.2–10 × 10^9/L]) despite antibiotic therapy, increasing pressor requirements, and progressive painful erythema and purulence at the abdominal surgical site led to debridement of the wound by the general surgery team on day 9 following the initial surgery due to suspected necrotizing infection. Within 24 hours, dermatology was consulted for continued rapid expansion

Histiocytoid Pyoderma Gangrenosum: A Challenging Case With Features of Sweet Syndrome

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of the wound. Physical examination of the abdomen revealed a large, well-demarcated, pink-red, indurated, ulcerated plaque with clear to purulent exudate and superficial erosions with violaceous undermined borders extending centrifugally from the abdominal surgical incision line (Figure 1A). Two punch biopsies sent for histopathologic evaluation and tissue culture showed dermal edema with a dense histiocytic infiltrate with nodular foci and admixed mature neutrophils to a lesser degree (Figure 2). Special staining was negative for bacteria, fungi, and mycobacteria. Immunohistochemistry revealed positive staining of the dermal inflammatory infiltrate with CD68, myeloperoxidase, and lysozyme, as well as negative staining with CD34 (Figure 3). These findings were suggestive of a histiocytoid neutrophilic dermatosis such as Sweet syndrome or pyoderma gangrenosum. Due to the morphology of the solitary lesion and the abrupt exacerbation shortly after surgical intervention, the patient was diagnosed with histiocytoid pyoderma gangrenosum. At the same time, the patient’s septic shock was treated with intravenous hydrocortisone (100 mg 3 times daily) for 2 days and also achieved a prompt response in the cutaneous symptoms (Figure 1B).

Sweet syndrome and pyoderma gangrenosum are considered distinct neutrophilic dermatoses that rarely coexist but share several clinical and histopathologic features, which can become a diagnostic challenge. Both conditions can manifest clinically as abrupt-onset, tender, erythematous papules; vesiculopustular lesions; or bullae with ulcerative changes. They also exhibit pathergy; are associated with underlying systemic conditions such as infections and/or malignancy; demonstrate a dense neutrophilic infiltrate in the dermis on histopathology; and respond promptly to systemic corticosteroids. Bullous Sweet syndrome, which can present as vesicles, pustules, or bullae that progress to superficial ulcers, may represent a variant of neutrophilic dermatosis characterized by features seen in both Sweet syndrome and pyoderma gangrenosum, suggesting that these 2 conditions may be on a spectrum. Clinical features such as erythema with a blue, gray, or purple hue; undermined and ragged borders; and healing of skin lesions with atrophic or cribiform scarring may favor pyoderma gangrenosum, whereas a dull red or plum color and resolution of lesions without scarring may support the diagnosis of Sweet syndrome. Although both conditions can exhibit pathergy secondary to minor skin trauma such as venipuncture and biopsies, Sweet syndrome rarely has been described to develop after surgery in a patient without a known history of the condition. In contrast, postsurgical pyoderma gangrenosum has been well described as secondary to the pathergy phenomenon.

Our patient was favored to have pyoderma gangrenosum given the solitary lesion, its abrupt development after surgery, and the morphology of the lesion that exhibited a large violaceous to red ulcerative and exudative plaque with undermined borders with atrophic scarring. In patients with skin disease that cannot be distinguished with certainty as either Sweet syndrome or pyoderma gangrenosum, it is essential to recognize that, as neutrophilic dermatoses, both conditions can be managed with either the first-line treatment option of high-dose systemic steroids or one of the shared alternative first-line or second-line steroid-sparing treatments, such as dapsone and cyclosporine.

Although the exact pathogenesis of pyoderma gangrenosum remains to be fully understood, paraneoplastic pyoderma gangrenosum is a frequently described phenomenon. Our patient’s history of multiple malignancies, both solid and hematologic, supports the likelihood of malignancy-induced pyoderma gangrenosum; however, given his history of MDS, several other conditions were ruled out prior to making the diagnosis of pyoderma gangrenosum. Classically, neutrophilic dermatoses such as pyoderma gangrenosum have a dense dermal neutrophilic infiltrate. Concurrent myeloproliferative disorders can alter the maturation of leukocytes, subsequently leading to an atypical appearance of the inflammatory cells on histopathology. Further, in the setting of myeloproliferative disorders, conditions such as leukemia cutis, in which there can be a cutaneous infiltrate of immature or mature myeloid or lymphocytic cells, must be considered. To ensure our patient’s abdominal skin changes were not...
a cutaneous manifestation of hematologic malignancy, immunohistochemical staining with CD20 and CD3 was performed and showed only the rare presence of B and T lymphocytes, respectively. Staining with CD34 for lymphocytic and myeloid progenitor cells was negative in the dermal infiltrate and further reduced the likelihood of leukemia cutis. Alternatively, patients can have aleukemic cutaneous myeloid sarcoma or leukemia cutis without an underlying hematologic condition or with latent peripheral blood or bone marrow myeloproliferative disorder, but our patient’s history of MDS eliminated this possibility. After exclusion of cutaneous infiltration by malignant leukocytes, our patient was diagnosed with histiocytoid neutrophilic dermatosis.

Multiple reports have described histiocytoid Sweet syndrome, in which there is a dense dermal histiocytoid infiltrate on histopathology that demonstrates myeloid lineage with immunologic staining. The typical pattern of histiocytoid Sweet syndrome includes a predominantly unaffected epidermis with papillary dermal edema, an absence of vasculitis, and a dense dermal infiltrate primarily composed of immature histiocytelike mononuclear cells with a basophilic elongated, twisted, or kidney-shaped nucleus and pale eosinophilic cytoplasm. In an analogous manner, Morin et al described a patient with congenital hypogammaglobulinemia who presented with lesions that clinically resembled pyoderma gangrenosum but revealed a dense dermal infiltrate mostly made of large immature histiocytoid mononuclear cells on histopathology, consistent with the histopathologic features observed in histiocytoid Sweet syndrome. The patient ultimately was diagnosed with histiocytoid pyoderma gangrenosum. Similarly, we believe that our patient also developed histiocytoid pyoderma gangrenosum. As with histiocytoid Sweet syndrome, this diagnosis is based on histopathologic and immunohistochemical findings of a dense dermal infiltrate composed of histiocyte-resembling immature neutrophils.

Typically, pyoderma gangrenosum responds promptly to treatment with systemic corticosteroids. Steroid-sparing agents such as cyclosporine, azathioprine, dapsone, and tumor necrosis factor α inhibitors also may be used. In the setting of MDS, clearance of pyoderma gangrenosum has been reported upon treatment of the underlying malignancy, high-dose systemic corticosteroids, cyclosporine with systemic steroids, thalidomide, combination therapy with thalidomide and interferon alfa-2a, and ustekinumab with vacuum-assisted closure therapy. Our patient’s histiocytoid pyoderma gangrenosum in the setting of solid and hematologic malignancy cleared rapidly with high-dose systemic hydrocortisone.
In the setting of malignancy, as in our patient, neutrophilic dermatoses may develop from an aberrant immune system or tumor-induced cytokine dysregulation that leads to increased neutrophil production or dysfunction. Although our patient’s MDS may have contributed to the atypical appearance of the dermal inflammatory infiltrate, it is unclear whether the hematologic disorder increased his risk for the histiocytoid variant of neutrophilic dermatoses. Alegria-Landa et al reported that histiocytoid Sweet syndrome is associated with hematologic malignancy at a similar frequency as classic Sweet syndrome. It is unknown if histiocytoid pyoderma gangrenosum would have a strong association with hematologic malignancy. Future reports may elucidate a better understanding of the histiocytoid subtype of pyoderma gangrenosum and its clinical implications.

REFERENCES