Diagnosis of a neutrophilic dermatosis, such as pyoderma gangrenosum (PG), often is challenging at onset because it can be impossible to distinguish clinically and histopathologically from an acute infection in an immunosuppressed patient, necessitating a detailed history as well as correlation pathology with microbial tissue cultures. The dermatologist’s ability to distinguish a neutrophilic dermatosis from active infection is of paramount importance as the decision to treat with surgical debridement, in addition to an antibiotic regimen, can have grave consequences in the misdiagnosed patient. We present a case of PG occurring at a chest tube site in a patient with chronic lymphocytic leukemia (CLL) and highlight the challenges and therapeutic importance of arriving at the correct diagnosis.

**PRACTICE POINTS**

- The primary value of early recognition and diagnosis of pyoderma gangrenosum (PG) lies in the physician’s ability to distinguish PG from an infectious process.
- Surgical debridement would further exacerbate PG, making proper diagnosis of a neutrophilic dermatosis of paramount importance to avoid treatments that could have grave consequences in the misdiagnosed patient.
- Cutaneous findings are seen in one-quarter of patients with chronic lymphocytic leukemia.
- Pyoderma gangrenosum is commonly associated with inflammatory bowel disease but also can be seen in many hematologic malignancies. Physicians should be aware of this association to ensure these patients are diagnosed properly.

**Diagnosis**

Diagnosis of a neutrophilic dermatosis, such as pyoderma gangrenosum (PG), often is challenging at onset because it can be impossible to distinguish clinically and histopathologically from an acute infection in an immunosuppressed patient, necessitating a detailed patient history as well as correlation pathology with microbial tissue cultures. The dermatologist’s ability to distinguish a neutrophilic dermatosis from active infection is of paramount importance as the decision to treat with surgical debridement, in addition to an antibiotic regimen, can have grave consequences in the misdiagnosed patient.

Pyoderma gangrenosum is a neutrophilic dermatosis histologically characterized by a pandermal neutrophilic infiltrate without evidence of an infectious cause or true vasculitis. It is classically associated with inflammatory bowel disease or an underlying hematologic malignancy. Pyoderma gangrenosum in the setting of chronic...
lymphocytic leukemia (CLL) is rare, with as few as 4 cases having been described in the literature and only 1 case of PG developing after a surgical procedure.¹⁻⁴ We present a case of PG occurring at a chest tube site in a patient with CLL. We highlight the challenges and therapeutic importance of arriving at the correct diagnosis.

**Case Report**

An 87-year-old man with a history of refractory CLL was admitted to the hospital with pneumonia and pleural effusion requiring chest tube placement (left). His most recent therapeutic regimen for CLL was rituximab and bendamustine, which was administered 9 days prior to admission. After removal of the chest tube, an erythematous plaque with central necrosis surrounding the chest tube site developed (Figure 1A). During this time period, the patient had documented intermittent fevers, leukopenia, and neutropenia. Serial blood cultures yielded no growth. Because the patient was on broad-spectrum antibiotic coverage, dermatology was consulted for possible angioinvasive fungal infection.

Physical examination revealed an indurated, erythematous-violaceous, targetoid, well-defined, ulcerated plaque with central necrosis on the left side of the chest. Notably, we observed an isolated bulla with an erythematous base within the right antecubital fossa at the site of intravenous placement, suggesting pathergy.

Multiple punch biopsies revealed an ulcer with an underlying dense neutrophilic infiltrate within the dermis and subcutaneous tissues (Figure 2). Grocott-Gomori methenamine-silver, periodic acid–Schiff, and acid-fast bacillus stains were all negative for organisms. Tissue cultures for bacterial, fungal, and acid-fast bacilli revealed no growth. Due to the rapidly expanding nature of the plaque and the possibility of infection despite negative microbial stains and cultures, the patient was scheduled for surgical debridement by the surgical team.

Opportunely, after thoughtful consideration of the clinical history, histopathology, and negative tissue cultures, we made a diagnosis of PG, a condition that would have been further exacerbated by debridement and unimproved with antibiotics. Based on our recommendation, the patient received immunosuppressive treatment with prednisone 60 mg/d and triamcinolone ointment 0.1%.

**FIGURE 1.** Pyoderma gangrenosum. A, An erythematous-violaceous, targetoid, well-defined, ulcerated plaque with central necrosis on the left side of the chest. Notably, we observed an isolated bulla with an erythematous base within the right antecubital fossa at the site of intravenous placement, suggesting pathergy.

**FIGURE 2.** A, Histopathology revealed an ulcerated epidermis with an underlying dense neutrophilic infiltrate (H&E, original magnification ×40). B, High-power view revealed a dense neutrophilic infiltrate within the dermis and subcutis (H&E, original magnification ×200).
He experienced immediate clinical improvement, allowing him to be discharged to the care of dermatology as an outpatient. He continued to receive a monthly rituximab infusion. We intentionally tapered the patient’s prednisone dosage slowly over 4 months and photodocumented steady improvement with eventual resolution of the PG (Figure 1B).

Comment
Pathogenesis of PG—Pyoderma gangrenosum lies in the spectrum of neutrophilic dermatoses, which are characterized histologically by a pandermal neutrophilic infiltrate without evidence of an infectious cause or true vasculitis. Clinically, PG typically presents as a steadily expanding ulceration with an undermined or slightly raised border, and often is associated with the pathergy phenomenon. Historically, PG is classically linked to inflammatory bowel disease; however, association with underlying malignancy, including acute myelogenous leukemia, chronic myelogenous leukemia, myeloma, and myeloid metaplasia, also has been described.\(^5\)

Pathogenesis of CLL—Chronic lymphocytic leukemia represents the most prevalent form of leukemia in US adults, with the second highest annual incidence.\(^6\) Cutaneous findings are seen in 25% of patients with CLL, varying from leukemia cutis to secondary findings such as vasculitis, purpura, generalized pruritus, exfoliative erythroderma, paraneoplastic pemphigus, infections, and rarely neutrophilic dermatoses.\(^7\) According to a PubMed search of articles indexed for MEDLINE using the term *pyoderma gangrenosum in CLL*, only 4 cases of PG occurring in the setting of CLL exist in the literature, with 1 case demonstrating development after a surgical procedure, making ours the second such case (Table).\(^1-4\)

Diagnosis—Making the diagnosis of a neutrophilic dermatosis such as PG or Sweet syndrome (SS) in the hospital setting is not only difficult but also imperative, considering that the counterdiagnosis more often

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>Patient Age, y/Sex</th>
<th>Malignancy History</th>
<th>Clinical History</th>
<th>Pathology</th>
<th>Response to Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swale et al(^3) (2005)</td>
<td>63/M</td>
<td>CLL</td>
<td>Ulcerated lesion developed on the left calf after minor trauma to the leg</td>
<td>Extensive full-thickness necrosis with predominantly neutrophilic infiltrate in the dermis and subcutis</td>
<td>Lesions were refractory to multiple treatments including high-dose steroids, cyclosporine, methotrexate, and IVIg; eventually resolved after infliximab</td>
</tr>
<tr>
<td>Solovan et al(^1) (2013)</td>
<td>62/M</td>
<td>CLL and renal cell carcinoma</td>
<td>Ulcerated lesions developed after nephrectomy at surgery site</td>
<td>Phlegmonous and granulomatous nonspecific inflammation in the deep dermis and subcutis</td>
<td>Lesions resolved after high-dose oral steroids</td>
</tr>
<tr>
<td>Sławinska et al(^2) (2016)</td>
<td>64/M</td>
<td>CLL</td>
<td>Ulcerated lesions developed after initiation of ibrutinib therapy for CLL</td>
<td>Ulcer with lymphocytic and neutrophilic inflammatory infiltrate</td>
<td>Lesions resolved after discontinuation of ibrutinib and initiation of cyclosporine and oral steroids</td>
</tr>
<tr>
<td>Wong et al(^4) (2016)</td>
<td>69/M</td>
<td>CLL</td>
<td>Recurrent ulcerated lesions on the legs</td>
<td>Neutrophilic infiltrate in the dermis and subcutis</td>
<td>Lesions were refractory to oral steroids, cyclosporine, mycophenolate mofetil, hyperbaric O(_2), and IVIg; lesions eventually resolved after remission from CLL was achieved</td>
</tr>
<tr>
<td>Current report</td>
<td>87/M</td>
<td>CLL</td>
<td>Ulcerated plaque at the site of chest tube placement</td>
<td>Ulcer with dense neutrophilic infiltrate in the dermis and subcutis</td>
<td>Lesion resolved after slow, high-dose steroid taper</td>
</tr>
</tbody>
</table>

Abbreviations: PG, pyoderma gangrenosum; CLL, chronic lymphocytic leukemia; M, male; IVIg, intravenous immunoglobulin.
is an infectious process. The distinction between individual neutrophilic dermatoses is less crucial at the onset because the initial treatment is the same.

Sweet syndrome is classically the most challenging entity within the spectrum to differentiate from PG. However, our case outlines several key distinguishing features:

- The lesion in classic PG is a rapidly expanding ulceration with undermined borders, whereas SS is less commonly associated with ulceration and instead classically presents with multiple edematous papules that progress to juicy plaques.8
- The pathergy phenomenon has been reported in SS, though it is more commonly associated with PG.9
- In reported cases of SS that were related to cutaneous trauma, lesions developed outside the area of trauma and there was documented leukocytosis and neutrophilia.10-14
- Although leukocytosis is part of the minor diagnostic criteria for SS, it is not required for the diagnosis of PG. Considering that our patient had ulcerated lesions, lesions only at the site of trauma, and leukopenia with intermittent neutropenia, the diagnosis was consistent with PG.

The primary value of early recognition and diagnosis of PG lies in the physician’s ability to distinguish PG from an infectious process, which can be challenging in an immunosuppressed patient with an underlying hematologic malignancy.

Conclusion
This case report represents our experience in arriving at the correct diagnosis of PG in a febrile neutrophilic patient with CLL. In the case of PG in a complicated patient, it is critical to initiate appropriate treatment and avoid inappropriate therapies. Aggressive surgical debridement could have resulted in a fatal outcome for our patient, highlighting the need for dermatologists to raise physician awareness of this challenging disease.

Acknowledgments—The authors acknowledge the contributions of Sarah Shalin, MD, PhD; Nikhil Meena, MD; and Aditya Chada, MD (all from Little Rock, Arkansas), for excellent patient care.

REFERENCES