Pyoderma gangrenosum in a patient with cutaneous T-cell lymphoma

Randy Tang, MD, Larisa Geskin, MD, and Marc E. Grossman, MD, FACP
New York, New York

Key words: cutaneous T-cell lymphoma; lower extremities; pyoderma gangrenosum.

INTRODUCTION

Pyoderma gangrenosum (PG) is an uncommon neutrophilic dermatosis characterized classically by the development of rapidly expanding painful ulcerations often on the lower extremities. Although most commonly associated with inflammatory bowel disease, acute leukemia, myelodysplastic syndrome, or monoclonal gammopathy, PG has been reported in association with systemic lupus erythematosus, autoimmune hepatitis, relapsing polychondritis, and sarcoidosis.[1]

CASE REPORT

A 59-year-old woman with tumor stage cutaneous T-cell lymphoma (CTCL) presented with fevers and leg ulcers. She was recently discharged from the hospital for aseptic thrombophlebitis of her right upper extremity treated with vancomycin and cefepime for 7 days.

The patient had CTCL diagnosed in 2000 when she presented with patches on her thighs. Peripheral flow cytometry results were normal, but she had a positive clonal T-cell receptor gene rearrangement. Her early treatments, including topical steroids, photochemotherapy, and acitretin, only briefly controlled her disease. Subsequently she received numerous systemic agents including methotrexate, bexarotene, romidepsin, denileukin diftitox, and vorinostat; 6 cycles of etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin (EPOCH) chemotherapy; total body electron beam radiation; and an autologous stem cell transplant. Her disease was finally controlled with gemcitabine infusions twice a week eventually tapered to every other week until her current admission.

Abbreviations used:

PG:	Pyoderma gangrenosum
CTCL:	Cutaneous T-cell lymphoma
IL:	Interleukin

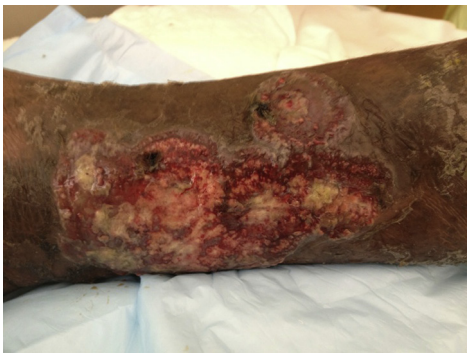

Fig 1. A 13- × 9-cm ulcer with pseudovesicular borders on patient's right medial portion of the lower leg.

On physical examination, 2 annular ulcerative plaques with pseudovesicular borders each measuring 4 × 4 cm were noted on the patient's left medial calf. Her right medial calf had a much larger severely painful rapidly enlarging ulceration with pseudovesicular borders measuring 13 × 9 cm at its widest borders (Fig 1). Both leg ulcers were not present on her previous discharge 7 days before. Two 4-mm punch biopsy sections were obtained from the right medial portion of the lower leg with half of each specimen sent for hematoxylin-eosin staining and the other half sent for tissue culture. Biopsy specimens showed a diffuse infiltrate of neutrophils in the dermis extending to the subcutis (Fig 2). Immunohistochemical stains showed no

From the Department of Dermatology and the Dermatology Consultation Service, Columbia University Medical Center.
Funding sources: None.
Conflicts of interest: None declared.
Correspondence to: Randy Tang, MD, Department of Dermatology, Columbia University Medical Center, 161 Ft. Washington Ave, 12th Floor, New York, NY 10032. E-mail: rt2486@cumc.columbia.edu.

JAAD Case Reports 2015;1:93-5.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2015.01.010

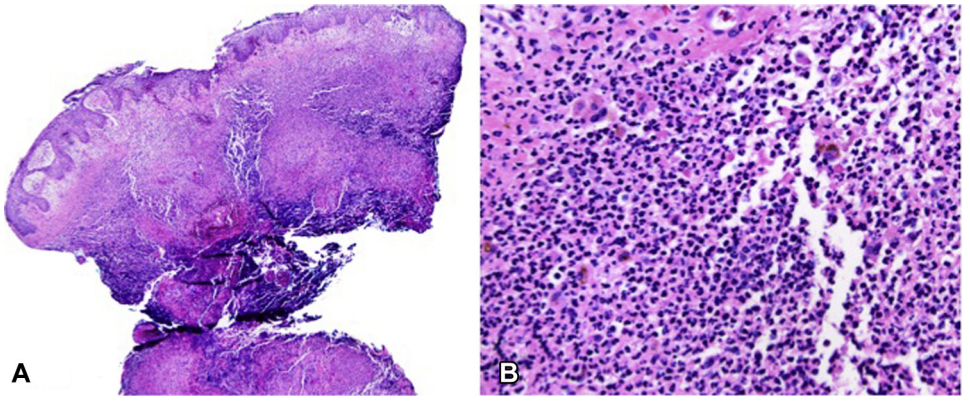

Fig 2. Right medial portion of the lower leg punch biopsy. **A**, Dense dermal infiltrate of neutrophils extending into the subcutis. **B**, High-power demonstrates diffuse infiltrate of neutrophils. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×10; **B**, ×40.)

evidence of lymphoma. Results of stains and tissue cultures for fungi, bacteria, and mycobacteria were normal. Laboratory workup found a C-reactive protein level of 322 mg/L (reference range, <2.90 mg/L) and an erythrocyte sedimentation rate of 75 mm/h (reference range, 0−20 mm/h) as the only laboratory abnormalities. The clinical and pathologic findings were consistent with the diagnosis of pyoderma gangrenosum.

DISCUSSION

There are no reports to date of PG occurring concurrently in association with CTCL or CTCL complicated by PG. Hussain et al[2] reported an 83-year-old man who had an ulcerative plaque with undermined edges on the right upper thigh with a skin biopsy consistent with pyoderma gangrenosum. He was treated successfully with minocycline and oral prednisone. Two months after cessation of therapy, the patient had a widespread eruption confirmed by skin biopsy as CTCL.[2] Additionally, there have been rare reports of CTCL presenting as PG-like lesions.[3-5]

Our patient with PG in the course of her CTCL was treated initially with prednisone at 1 mg/kg. When no response was noted after 2 days, minocycline, 100 mg twice a day, was added. Her lesions stopped progressing, and she reported significant reduction in pain after 4 days of treatment. She was discharged on hospital day 15 and continued taking minocycline twice daily for 2 months. Prednisone was tapered over a course of 5 months. At 6 months, her lesions were all healed with postinflammatory hyperpigmentation or minimal indurated dyschromia (Fig 3). Unfortunately, the patient had disease progression with rapid increase in number of tumors all over her body with several becoming ulcerated, painful, and superinfected.

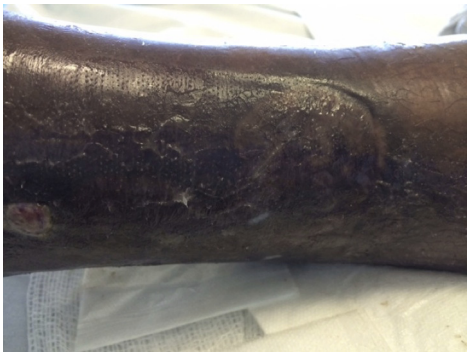

Fig 3. Patient at 6-month follow-up. Minimal indurated plaque after treatment with prednisone and minocycline.

She declined further treatment and ultimately opted for hospice care.

Association of PG with inflammatory disorders is well established, suggesting that dysregulation of the immune system plays a role in the disease pathogenesis.[6] Increased production of proinflammatory cytokines such as interleukin (IL)-8, a very potent neutrophil chemotactic factor, has been seen in PG[7] and linked to ulcer formation. IL-8 is rarely found in CTCL biopsies, but when it is elevated in the epidermis of CTCL patients, it is always associated with accumulation of neutrophils.[8]

CTCL is also considered a disease of immune dysregulation with chronic antigenic stimulation possibly playing a role in its pathogenesis. In particular, CTCL has been linked to several infectious agents that induce cells of the innate immune response, including macrophages and keratinocytes to secrete cytokines such as IL-8.[9] Recently it was shown that levels of IL-8 are significantly and constitutively elevated in the serum of CTCL patients,[10] suggesting for the first time that dysregulation of innate immune responses may be important in CTCL disease pathogenesis.

We hypothesize that in some cases, engagement of toll-like receptors on keratinocytes and other innate immune cells may lead to generation of a specific immunologic profile in CTCL lesions with IL-8 overproduction directly in the tumor microenvironment. In this case, continuous overproduction of IL-8 by perhaps an infectious etiology could have led to neutrophil accumulation and formation of PG. Our hypothesis may also explain why our patient responded well to antibiotics and not to steroid therapy.

In the patient with CTCL and new-onset enlarging painful ulcerations, the differential diagnosis of ulcerated CTCL, infection, and pyoderma gangrenosum has critical therapeutic importance for survival.

REFERENCES

1. Ahronowitz I, Harp J, Shinkai K. Etiology and management of pyoderma gangrenosum. *Am J Clin Dermatol*. 2012;13:191-211.
2. Hussain W, Layton A, Baxter K, Scott D. Pyoderma gangrenosum preceding the onset of cutaneous T-cell lymphoma. *Clin Exp Dermatol*. 2006;31:284-286.
3. Salameh F, Barzilai A, Baum S, Trau H. Mycosis fungoides and CD30+ cutaneous T-cell lymphoma simulating pyoderma gangrenosum in a patient with ulcerative colitis. *J Dermatol Case Rep*. 2009;3:30-33.
4. Carbia SG, Hochman A, Chain M, et al. Mycosis fungoides presenting with extensive pyoderma gangrenosum-like ulcers. *J Eur Acad Dermatol Venereol*. 2002;16:401-404.
5. Ho KK, Browne A, Fitzgibbons J, Carney D, Powell FC. Mycosis fungoides bullosa simulating pyoderma gangrenosum. *Br J Dermatol*. 2000;142:124-127.
6. Ahronowitz I, Harp J, Shinkai K. Etiology and management of pyoderma gangrenosum: a comprehensive review. *Am J Clin Dermatol*. 2012;13:191-211.
7. Oka M, Berking C, Nesbit M, et al. Interleukin-8 overexpression is present in pyoderma gangrenosum ulcers and leads to ulcer formation in human skin xenografts. *Lab Invest*. 2000;80:595-604.
8. Tensen CP, Vermeer MH, van der Stoop PM, et al. Epidermal interferon-gamma inducible protein-10 (IP-10) and monokine induced by gamma-interferon (Mig) but not IL-8 mRNA expression is associated with epidermotropism in cutaneous T cell lymphomas. *J Invest Dermatol*. 1998;111:222-226.
9. Mirvish ED, Pomerantz RG, Geskin LJ. Infectious agents in cutaneous T-cell lymphoma. *J Am Acad Dermatol*. 2011;64:423-431.
10. Geskin LJ, Akilov OE, Lin Y, Lokshin AE. Distinct age-matched serum biomarker profiles in patients with cutaneous T-cell lymphoma. *Exp Dermatol*. 2014;23:598-600.