Case Report Annals of Dermatology 2022;34(3):212-215 • https://doi.org/10.5021/ad.2022.34.3.212

Bullous Variant of Pyoderma Gangrenosum in a Patient with Acute Myeloid Leukemia

Chang-Il Kwon[1], Gyeong-Won Lee[2], Chi-Yeon Kim[1,3]

[1]Department of Dermatology, Gyeongsang National University School of Medicine, [2]Division of Hematology-Oncology, Department of Internal Medicine, Gyeongsang Institute of Health Science, Gyeongsang National University Hospital, Gyeongsang National University School of Medicine, [3]Department of Dermatology and Gyeongsang Institute of Health Sciences, Gyeongsang National University Hospital, Gyeongsang National University School of Medicine, Jinju, Korea

Received May 7, 2020
Revised July 27, 2020
Accepted August 10, 2020

Corresponding Author
Chi-Yeon Kim
Department of Dermatology and Gyeongsang Institute of Health Sciences, Gyeongsang National University Hospital, Gyeongsang National University School of Medicine, 79 Gangnam-ro, Jinju 52727, Korea
Tel: +82-55-750-8187
Fax: +82-55-750-9244
E-mail: cykim@gnu.ac.kr
https://orcid.org/0000-0002-2306-8388

Unlike classic pyoderma gangrenosum (PG), the bullous variant of PG is typically represented by a painful erythematous papule, plaque, and superficial bulla that progress into the ulceration with bullous margin. Generally, bullous PG is most commonly associated with myeloproliferative disorders, such as acute myeloid leukemia (AML). Bullous PG in AML patients rarely occurs, but once it does, it suggests a poor clinical prognosis. Although many cases of classic PG in AML patients have been reported, bullous PG is relatively rare. Therefore, we present a case of bullous PG that developed in a patient with AML and was successfully treated with high-dose systemic steroids.

Keywords: Acute myeloid leukemia, Bullous pyoderma gangrenosum

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare ulcerating neutrophilic dermatosis[1]. Clinically, PG typically starts as a tender nodule, plaque, or sterile pustule. Over a course of days, it progresses to a sharply marginated ulcer with undermined violaceous borders and a surrounding erythematous zone[2]. The pathophysiology of PG remains poorly understood, although it is now believed to involve the loss of innate immune regulation and altered neutrophil chemotaxis[3-5]. The incidence of PG is not exactly known, but it occurs at the same frequency in both sexes and can appear at any age[6]. Generally, PG is idiopathic in 40% to 50% of the cases[1]. In the remainder, it is known to be associated with a wide variety of systemic diseases, such as ulcerative colitis, polyarthritis, regional enteritis, and hematologic malignancies[4]. The pathergy test positivity at a rate of 25% has been reported in the literature in PG patients and defined as the occurence of new lesions by trauma[7]. The presence of neutrophils in pathergic lesions of PG and other neutrophilic dermatoses such as ulcerative colitis, Crohn's disease, paraproteinemia or arthritis have been proposed as a reflection of altered neutrophilic function[7]. Depending on the clinical findings and the characteristics of the associated lesions, PG can be divided into four distinct subtypes: ulcerative, pustular, vegetative, and bullous[5,6]. The ulcerative type is mainly associated with inflammatory bowel disease (IBD) and arthritis. The pustular type is also related to IBD, and the vegetative type is often unrelated to a specific disease. However, bullous PG typically presents as a painful erythematous papule, plaque, and superficial bulla that evolve into an ulceration with a bluish bullous margin, and is most commonly associated with myeloproliferative disorders, such as acute myeloid leukemia (AML). Bullous PG rarely occurs in AML patients, but once it does, it suggests a poor clinical prognosis[6].

Therefore, we present a rare case of bullous PG that developed in a patient with AML successfully treated with high-dose systemic steroids.

CASE REPORT

A 67-year-old female patient was evaluated for a one-week history of a diffuse painful erythematous patch with superficial bulla that progressed into an ulceration with a bluish to grayish bullous border on the left shin, without any other involved lesions (Fig. 1). The size of the lesion was 8 cm in diameter and there was yellowish oozing with pain, itching, and a heating sensation. The patient was diagnosed with AML three months earlier by a bone marrow biopsy and was treated in the hematology-oncology department with systemic chemotherapy that included decitabine. Because the patient was immunosuppressed by systemic chemotherapy, we suspected an infection-associated disease, such as cellulitis and an abscess. Thereafter, systemic antibiotics were used sequentially for two weeks, but there was no clinical improvement of the lesion. There were negative results in blood culture and skin smear performed prior to administration of antibiotics. The pathergy test was also negative. For an accurate diagnosis, we performed a skin biopsy on the left shin and the histopathologic findings showed prominent spongiotic changes in the epidermis and dispersed neutrophilic and lymphocytic infiltration with fibrinoid necrosis in the dermis (Fig. 2). In addition, there were no atypical cells showing mitotic activity and no evidence of infection in the microbiological culture of the tissue and immunohistochemical tests, including periodic acid–Schiff (PAS) and Grocott's methenamine silver stain (GMS). Therefore, based on the clinical features and histopathologic findings, the patient was finally diagnosed with bullous PG. The patient was treated effectively with three weeks of high-dose systemic corticosteroids (initiated 1 mg/kg/day and tapered gradually to 0.2 mg/kg/day) and the lesion was improved and nearly covered by epithelium. The patient was observed for six months in the hematology-oncology department without any recurrence of the previous lesion or additional occurrence of extracutaneous manifestations. We received the patient's consent form about publishing all photographic materials.

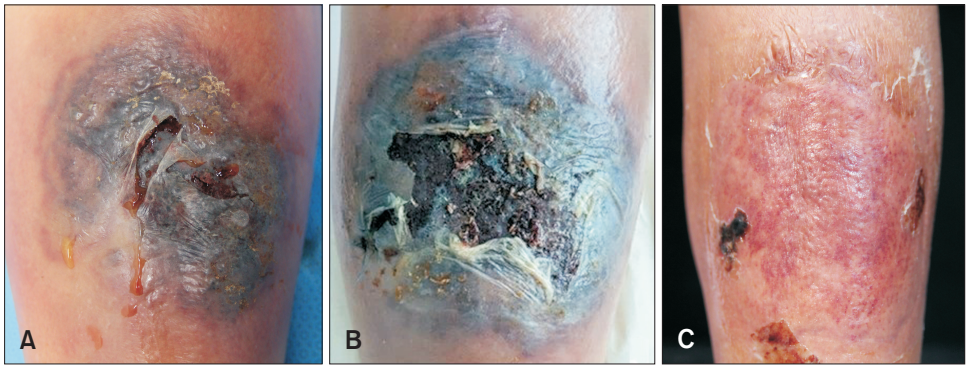

Fig. 1. (A) The diffuse erythematous swollen patch with bulla involving the left shin. (B) The unimproved lesion after two weeks of systemic antibiotic treatment. (C) The improved lesion after three weeks of systemic steroid treatment.

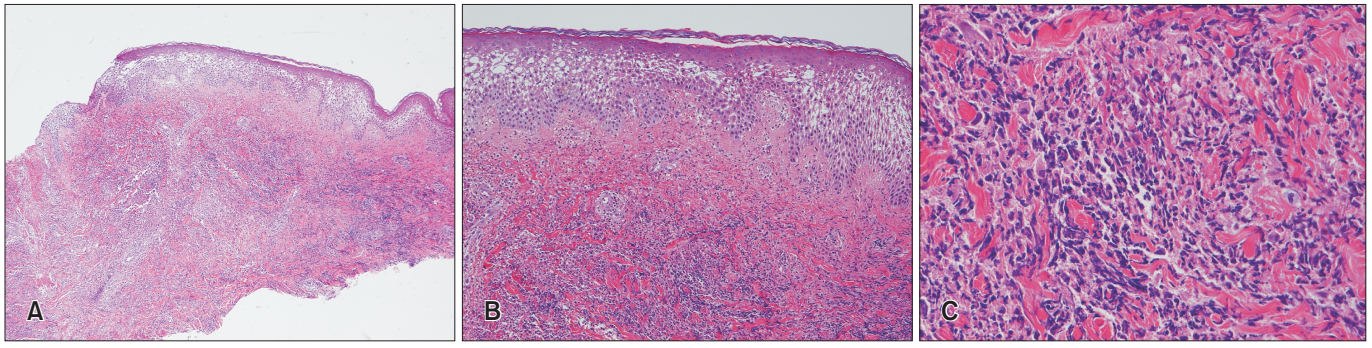

Fig. 2. Microscopic features of pyoderma gangrenosum on the left shin. (A) Prominent spongiotic change in the epidermis (H&E, ×40). (B) Dispersed neutrophilic and lymphocytic infiltration with fibrinoid necrosis in the dermis (H&E, ×100). (C) Closed view (H&E, ×400).

DISCUSSION

PG is a rare sterile neutrophilic dermatosis[1]. The etiology of this disease has not been clearly determined, but aberrant immune responses and unidentified factors are thought to be involved[8]. The effect of AML on PG is also unclear, but it is thought that chemotherapy can impair wound healing in patients with AML[9,10].

Bullous PG typically presents as a nodule and a non-ulcerated erythematous patch with bulla that progress to a superficial ulcer surrounded by a hemorrhagic and bullous border[11]. The clinical features helping to differentiate bullous PG from classic PG are hemorrhagic bulla at the onset and superficial ulceration with a bluish to gray bullous margin, unlike the deep ulcerative and penetrating lesions mainly seen in classical PG[11]. Although there is no specific histological feature of bullous PG, massive neutrophilic infiltration throughout the dermis with intra- or sub-epidermal edema is often found[6]. Because PG often presents similar to an infectious disease, proper diagnosis can be delayed. In addition, delayed wound healing due to misdiagnosis increases the risk of infection and adverse effects, such as drug eruption owing to the continuous use of systemic antibiotics. Therefore, an infection-related disease must be differentially diagnosed initially[2]. Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, can be differentiated from PG by showing the lack of vasculitis and the abrupt onset of dermatosis without ulcerations[12].

In treatment, PG typically requires multiple approaches to reduce inflammation and achieve wound healing. Local wound care with topical and systemic therapy has been the mainstay treatment[13]. Although there is no reported treatment of choice for bullous PG, it typically responds to management for the hematologic malignancy disorder and systemic chemotherapy often results in lesion improvement[4]. However, in refractory cases, systemic treatment similar to classical PG that includes corticosteroids, cyclosporine, azathioprine, and tacrolimus can be administered[4].

Generally, PG lesions are associated with malignant diseases in approximately 7% of the cases and among them, the association with AML is the most right[14]. Moreover, in the case of a malignancy associated with PG, approximately one-half to two-thirds of the patients have lesions consistent with bullous PG[14]. Bullous PG found in relation to a hematologic malignancy such as AML usually suggests a poor clinical prognosis and about 75% of the patients expire from the underlying malignant disorder within one year of the skin lesion appearance[14]. Moreover, it is known that if bullous PG occurs in patients with a previously stable non-malignant hematologic disease, it may cause malignant transformation of the existing disease[15].

In conclusion, unlike classic PG that occurs in various diseases, such as ulcerative colitis, diverticulitis, rheumatologic conditions, and malignancies, bullous PG characteristically occurs in patients with hematologic disorders and in this case, the clinical prognosis is poor[10]. Bullous PG may precede, occur concurrently, or be diagnosed after a malignancy[6]. However, because skin lesions can appear as the only symptom of an underlying hematologic malignancy and delayed treatment may result in more unfavorable results for the patients, it is important to quickly differentiate it from other infectious diseases. Therefore, dermatologists should be aware of bullous PG and further evaluations should be done properly, including peripheral blood smears and a bone marrow biopsy.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

None.

ORCID

Chang-Il Kwon, https://orcid.org/0000-0002-3952-3023
Gyeong-Won Lee, https://orcid.org/0000-0002-1781-2262
Chi-Yeon Kim, https://orcid.org/0000-0002-2306-8388

REFERENCES

1. Wollina U. Pyoderma gangrenosum--a review. Orphanet J Rare Dis 2007;2:19.
2. Brooklyn T, Dunnill G, Probert C. Diagnosis and treatment of pyoderma gangrenosum. BMJ 2006;333:181-184.
3. Braswell SF, Kostopoulos TC, Ortega-Loayza AG. Pathophysiology of pyoderma gangrenosum (PG): an updated review. J Am Acad Dermatol 2015;73:691-698.
4. Jacobs P, Palmer S, Gordon-Smith EC. Pyoderma gangrenosum in

myelodysplasia and acute leukaemia. Postgrad Med J 1985;61:689-694.
5. Ahronowitz I, Harp J, Shinkai K. Etiology and management of pyoderma gangrenosum: a comprehensive review. Am J Clin Dermatol 2012;13:191-211.
6. Fox LP, Geyer AS, Husain S, Grossman ME. Bullous pyoderma gangrenosum as the presenting sign of fatal acute myelogenous leukemia. Leuk Lymphoma 2006;47:147-150.
7. Su WP, Davis MD, Weenig RH, Powell FC, Perry HO. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. Int J Dermatol 2004;43:790-800.
8. Callen JP, Jackson JM. Pyoderma gangrenosum: an update. Rheum Dis Clin North Am 2007;33:787-802.
9. Shore RN. Pyoderma gangrenosum, defective neutrophil chemotaxis, and leukemia. Arch Dermatol 1976;112:1792-1793.
10. van de Kerkhof PC, de Vaan GA, Holland R. Pyoderma gangrenosum in acute myeloid leukaemia during immunosuppression. Eur J Pediatr 1988;148:34-36.
11. Crow KD, Bowers RE. Bullous haemorrhagic ulceration, a variant of pyoderma gangrenosum. Trans St Johns Hosp Dermatol Soc 1974;60:142-151.
12. Ajili F, Souissi A, Bougrine F, Boussetta N, Abdelhafidh NB, Sayhi S, et al. Coexistence of pyoderma gangrenosum and sweet's syndrome in a patient with ulcerative colitis. Pan Afr Med J 2015;21:151.
13. Miller J, Yentzer BA, Clark A, Jorizzo JL, Feldman SR. Pyoderma gangrenosum: a review and update on new therapies. J Am Acad Dermatol 2010;62:646-654.
14. Duguid CM, O'Loughlin S, Otridge B, Powell FC. Paraneoplastic pyoderma gangrenosum. Australas J Dermatol 1993;34:17-22.
15. Ho KK, Otridge BW, Vandenberg E, Powell FC. Pyoderma gangrenosum, polycythemia rubra vera, and the development of leukemia. J Am Acad Dermatol 1992;27(5 Pt 2):804-808.