Delayed diagnosis of bullous pyoderma gangrenosum with acute myelogenous leukemia

S Sener, G Sarac, N Altunisik, Y Bayindir

Department of Dermatology, Inönü University, Department of Dermatology, Malatya State Hospital, Department of Infectious Disease, School of Medicine, Inönü University, Malatya, Turkey

Abstract
Pyoderma gangrenosum (PG) is a rare, but serious neutrophilic dermatosis characterized by recurrent painful cutaneous ulcerations. It is commonly associated with inflammatory bowel disease, rheumatoid arthritis, and hematological malignancies. Because laboratory evaluations and histologic features of PG are nonspecific, diagnosis is based on the clinical features of the ulcer and requires exclusion of other conditions that cause such ulceration. The disease responds to glucocorticoids, immunosuppressives, and anti-inflammatory drugs. We present a 30-year-old man with acute myelogenous leukemia (subtype M5) and bullous PG. Treatment with high-dose prednisolone was successful.

Key words: Acute myelogenous leukemia, bullous pyoderma gangrenosum, leukemia and pyoderma gangrenosum

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Introduction
Pyoderma gangrenosum (PG) is a neutrophilic ulcerative disease of the skin with distinctive characteristics. Lesions begin as tender nodules, papulopustules, or vesicles that spontaneously ulcerate and progress to painful ulcers. The ulcer edge is often bluish in color, raised, undermined and the surrounding skin is erythematous. Any area of the body can be involved, for example, lower extremities, buttocks, abdomen, and face. Other than classical PG, recognized clinical variants of PG include the pustular, vegetative, bullous or atypical and peristomal entities. They differ based on their clinical morphology, site, and associated diseases. Bullous PG is a superficial variant that affects the upper limbs and face. Dermatopathology is not pathognomonic and shows a dermal neutrophilic infiltration.

Case Report
A 30-year-old male was admitted to the Department of Infectious Diseases with 1–7 cm large multiple tenders, erythematous plaques affecting the anterior and posterior trunk and arms. He had 2 years history of an acute myeloid leukemia and 1 year history of chemotherapy treatment. Subsequently, he developed fever and constitutional symptoms. On laboratory investigation, white blood cells were 23,500/ml, C-reactive protein was 380 mg/L, and erythrocyte sedimentation rate (ESR) was 110 mm/h. Renal and liver function tests were within normal limits and bacterial culture from the surface of the lesion was negative. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

sterile. These were initially diagnosed as infective, and flucloxacillin was commenced. On the following days, despite antibiotic escalation, the lesions developed into large, exquisitely tender, concentric plaques with well-demarcated, violaceous, serpiginous borders and central necrosis and bullae [Figure 1]. The patient was referred to the Dermatology Department. The skin biopsy taken from a nodulobullous lesion revealed a spongiotic epidermis with a dermis showing dense polymorfonuclear and lymphocytic infiltration. Histopathologic examination also revealed a moderate perivascular infiltrate consisting mainly of neutrophils and lymphocytes without the involvement of leukemic cells. Bullous PG was diagnosed on clinical and histopathologic grounds by the dermatology consultant. The patient was treated with intravenous prednisolone 100 mg/day. Rapid epithelialization was observed within 2 weeks of treatment [Figure 2]. The dose of prednisolone was gradually decreased to 20 mg/day and used as maintenance therapy for 3 months. The complete improvement was achieved in 6 months. The patient has been followed up for approximately 1 year. There were no side effects observed during the treatment, and in addition, no new lesions developed at the follow-up period.

Discussion

PG is an unusual ulcerative disease of the skin with distinctive clinical characteristics first described in 1930.[1] It may be classified as a neutrophilic dermatosis, as it exhibits intense dermal inflammatory infiltrates composed of neutrophils with little evidence of primary vasculitis.[2]

It has classical presentations (ulcerative) and some variants (pustular, bullous–atypical, vegetative, and peristomal).[1] Bullous PG is an atypical, more superficial variant and has the strongest association with myeloid malignancies. In contrast with the classical form, atypical bullous PG presents as bullous areas that spread rapidly in a concentric pattern and may break down to form superficial ulcers. The raised and undermined borders of the ulcers are relatively subdued bluish-gray in color, in sharp contrast with the much brighter violaceous border usually associated with classical PG.[3,4] Upper limbs and face tend to be affected more than lower limbs. Lesions can be single or multiple, more rapidly progressive than classical form and occur at any age in either sex.[5]

Bullous PG may precede, occur concurrently with, or follow the diagnosis of malignancy.[5] Pathergy (lesions developing at sites of recent trauma) is commonly observed, so surgery or debridement are contraindicated. This dermatosis often presents with fever, elevated ESR, and other general symptoms.[1] Exact pathogenesis is unknown, although defective immune mechanisms, i.e. T-cell imbalance or failure of phagocytosis by monocytes have been implicated in many cases.[7]

Definitive diagnosis of PG is based mainly on clinical findings and exclusion of infectious or neoplastic disorders because laboratory evaluations and histologic features of PG are nonspecific.[1]

PG is a potentially lethal disease with a mortality rate of up to 30% in some series. Poor prognostic indicators are male sex, old age at onset, and bullous PG specifically when associated with malignant hematological disorders.[8]

There is no specific and uniformly effective therapy for PG. In patients with underlying disease, therapy should be directed not only to PG but also and primarily to the systemic disorder. Local or topical treatment such as wet-to-dry dressings, limb elevation, rest, topical agents, or intralesional corticosteroid or cyclosporine injections may be tried in milder forms and those not associated with systemic disease. Systemic therapies administered in the treatment of PG have included minocycline, dapsone, glucocorticoids, cyclosporine, azathioprine, tacrolimus, and hyperbaric oxygen.[9]

In this case, local wound care and high-dose systemic corticosteroid therapy made a dramatic recovery.
Conclusion

PG should be included in the differential diagnosis of cutaneous lesions developing in patients with acute myelogenous leukemia. Misdiagnosis of early lesions as infective in origin is a common pitfall. However, early recognition of PG is important, because prompt administration of glucocorticoids or other immunosuppressive agents can lead to a dramatic resolution.

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Conflicts of interest
There are no conflicts of interest.

References