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CASE REPORT

The great mimicker: A case report of an extensive pyoderma gangrenosum in a 39-year-old Filipino female treated with systemic corticosteroids and antibiotics

Camille Joyce J. Crisostomo, MD, DPDS,[1] Niña A. Gabaton, MD, FPDS[1]

ABSTRACT

INTRODUCTION Pyoderma gangrenosum (PG) is a rare inflammatory disease with unknown etiology. Ulcerative PG presents with a rapidly enlarging painful ulcer with erythematous and undermined border often misdiagnosed as infection, vascular disorder, malignancy, and other inflammatory disease. Hence, this poses a diagnostic challenge for clinicians leading to a delay in the management and significant morbidity. The treatment of PG is equally challenging due to the rarity of the disease and the scarcity of clinical trials. Currently, there are no clinical practice guidelines for the management of PG.

CASE REPORT Our patient presented with multiple large ulcers with erythematous and undermined borders over the chest, abdomen, and the lower back. Cribriform scars and contractures were noted as well. She underwent several sessions of surgical debridement and was given different broad-spectrum antibiotics with noted worsening of the lesions. Due to extensive involvement of the disease, her quality of life has been significantly affected. A diagnosis of PG was made after the biopsy showed predominantly neutrophilic infiltrate. Prednisone 1mg/kg/day and clobetasol propionate ointment were initiated with significant decrease in pain and size of the ulcers after one month of therapy. Doxycycline was used as an adjunct therapy with excellent response.

CONCLUSION Pyoderma gangrenosum is a rare, debilitating disease that remains a diagnostic dilemma. The worsening of ulcers despite surgical debridement and antibiotics is a clue that should prompt clinicians to consider PG. This case highlights the important role of dermatology in individuals who present with non-healing chronic ulcers because as seen in this case, not all ulcers are just ulcers.

KEYWORDS pyoderma gangrenosum, neutrophilic dermatosis, ulcers

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare, chronic inflammatory disease with an estimated incidence of 3-10 cases per million of the population per year.[1] It is classified under the group of neutrophilic dermatoses. Although the etiology is still unknown, abnormalities of the immune system have been suggested to play a role in the pathogenesis of the disease.[2]

The classic or ulcerative PG begins as papules, pustules, or nodules rapidly progressing to ulcers with violaceous and undermined borders commonly affecting the lower extremities. This is accompanied by significant pain that is usually out of proportion to the appearance of the lesion.[3] Despite these distinctive features, the diagnosis of pyoderma gangrenosum remains challenging due to lack of a specific laboratory test. In addition, several other diseases can mimic the presentation of PG leading to misdiagnosis.

The scarcity of research trials for pyoderma gangrenosum is due to the low incidence of the disease. Hence, evidence-based therapeutic guidelines for PG are still currently lacking, making it difficult to manage this disease.

Herein we report a case of an extensive pyoderma gangrenosum initially diagnosed as an infection and was managed several times with surgical debridement and broad-spectrum antibiotics with worsening of the condition. The patient was treated with oral prednisone and doxycycline with excellent response.

CASE SUMMARY

This is a case of a 39-year-old Filipino female who presented with a 3-year history of rapidly enlarging painful ulcers on the chest, abdomen and back. The lesions would begin as

[1]Department of Dermatology, Southern Philippines Medical Center, J. P. Laurel Ave., Bajada, Davao City, Philippines

Corresponding author
Camille Joyce J. Crisostomo, MD, DPDS
cjcrisostomo11@gmail.com

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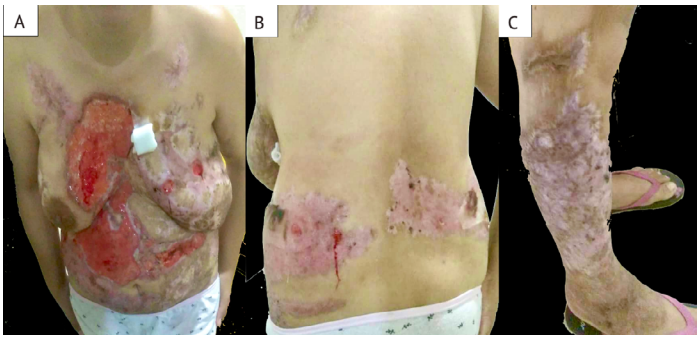

Figure 1. A. Multiple, well-defined ulcers surrounded by erythematous, undermined borders over the chest (largest measuring 18 cm x 10 cm), abdomen (15 cm x 10 cm and 9 cm x 2.5 cm), and the B. lower back (1 cm x 1 cm). C. Cribriform scars on the right lower leg.

a papule with central suppuration, which would rupture spontaneously evolving to a very painful ulcer. At the onset of the initial lesion on the abdomen three (3) years prior to consult, the patient immediately sought consult in a private hospital and was prescribed with clindamycin with no apparent improvement. During the interim, there was development of new lesions on the chest, right leg, back, and left arm. The patient sought consult with internists and surgeons at different hospitals where wound cultures taken at different times revealed different bacterial species including *Pseudomonas*, *Morganella*, and *Staphylococcus*. Despite antibiotic coverage for these organisms and a series of surgical debridements, there was no apparent improvement of the ulcers leading to an impaired quality of life.

Past medical history was unremarkable. There was no intake of any medications nor any trauma over the area prior to the onset of the lesions. Physical examination revealed multiple, well-defined, ulcers with a base containing purulent discharge surrounded by erythematous, undermined borders over the chest, abdomen, and the lower back (Figure 1A-B). There were three (3) chest ulcers, two (2) abdominal ulcers, and a small ulcer on the lower back, ranging from 1-18 cm in size. Cribriform scars with fibrotic strands and contractures were noted on the chest, abdomen, back, left arm, gluteal area extending to the left thigh, and right leg (Figure 1C).

Blood investigations showed anemia, neutrophilia, and elevated ESR. No atypical cells or blasts were seen on peripheral blood smear but neutrophilic leukocytosis was noted. Wedge incision biopsy was done on the ulcer edge. Histopathology revealed a mildly acanthotic and spongiotic epidermis overlying a dermis with superficial edema and diffuse predominantly neutrophilic inflammatory infiltrate (Figure 2A-C). Another section showed foci of epidermal necrosis (Figure 2D). These are findings consistent with a neutrophilic dermatosis.

Based on the clinical and histopathologic findings, a diagnosis of pyoderma gangrenosum (PG) was made. The patient was started on prednisone at a dose of 1 mg/kg/day, clobetasol propionate ointment over the periphery of the ulcers, and hydrocolloid dressing for wound care. There was a significant decrease in the size of the ulcers with formation of granulation tissue after one (1) month of treatment while some ulcers healed with cribriform scarring (Figure 3A). Doxycycline 100 mg twice daily was given as an adjunct treatment. Complete control of the condition was achieved on the fourth month (Figure 3B) for which oral prednisone and doxycycline were gradually tapered and discontinued on the sixth month of treatment. By this time, the majority of the patient's ulcers had completely healed (Figure 3C). Patient is still in remission four

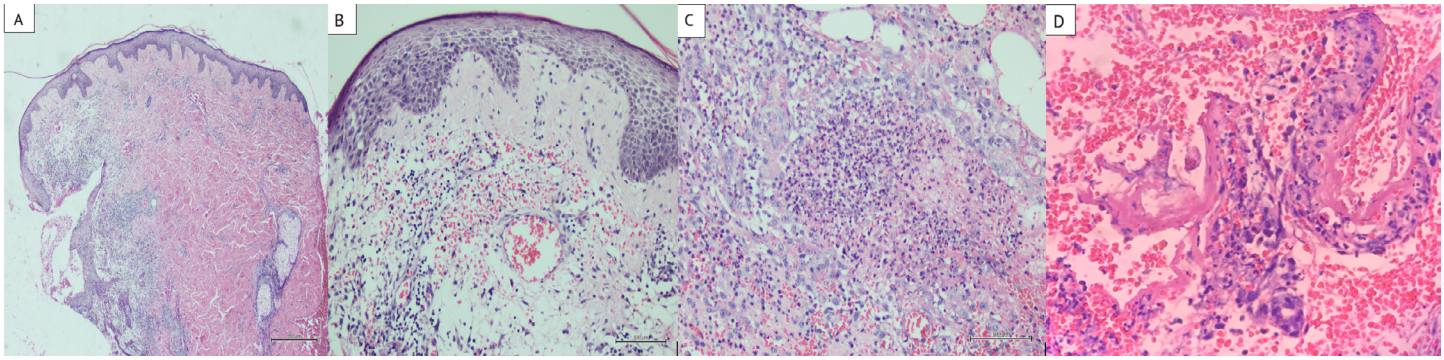

Figure 2. A. Scanning view (H&E; 4x) of the biopsy of the ulcer edge. B. There's a superficial dermal edema (H&E; 40x) and C. diffuse predominantly neutrophilic infiltrates (H&E; 40x). D. Foci of epidermal necrosis was noted in another section (H&E; 40x).

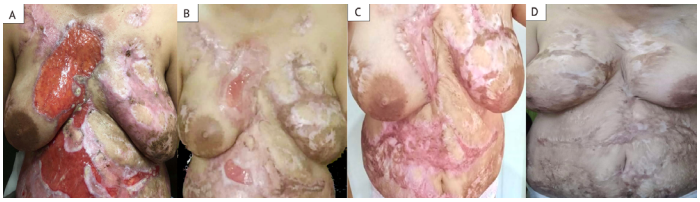

Figure 3. A. After 1 month of treatment, there was a decrease in the size of the ulcers. B. At 4 months, the majority of the ulcers have healed. C. No ulcers but with cribriform scarring 6 months after treatment. D. Complete remission 4 years after treatment.

(4) years after treatment (Figure 3D).

DISCUSSION

Pyoderma gangrenosum (PG) remains a diagnosis of exclusion despite the several proposed diagnostic criteria in the literature. The clinical presentation commonly mimics other diseases including infections, vasculopathies, malignancies, and other inflammatory disorders.[3] Infectious differential diagnoses that can mimic PG include atypical mycobacteria, cutaneous tuberculosis, cutaneous leishmaniasis, ecthyma gangrenosum, and other deep fungal infections. The histopathologic findings do not confirm the diagnosis but rather aid in excluding the other differential diagnoses.

There are several subtypes of PG depending on the clinical presentation and morphology. The most common type is the ulcerative or the classic PG, which presents initially with a solitary or multiple pustules or nodules that rapidly ulcerate with a violaceous and undermined border. This type commonly affects the lower extremities and is frequently associated with arthritis, inflammatory bowel disease, monoclonal gammopathy, and malignancy.[3] A large case series of PG revealed that 77.7% of the lesions present on the leg, with the remaining involving the trunk (11.7%), peristomal site (8.7%), upper extremities (8.7%) , and head and neck (7.8%).[4] Another study by Pereira et al., revealed that out of 17 patients with ulcerative PG, 13 patients had involvement of the lower limbs (76%) while the remaining four (4) had abdominal lesions (23.5%).[5]

The most recent diagnostic criteria of PG based on a Delphi Consensus of International Experts in 2018 include a major criterion which is a biopsy finding of ulcer edge demonstrating a neutrophilic infiltrate and eight (8) minor criteria which include the following: (1) exclusion of infection, (2) pathergy, (3) history of inflammatory bowel disease or inflammatory arthritis, (4) history of papule, pustule or vesicle ulcerating within four (4) days, (5) peripheral erythema, undermining border, and tenderness at ulceration site, (6) multiple ulcerations, at least one (1) on an anterior lower leg, (7) cribriform or "wrinkled paper" scar(s) at healed ulcer sites; and (8) decreased ulcer size within one (1) month of initiating immunosuppressive medication. To make a diagnosis of PG, a patient must meet the major criterion and four (4) out of eight (8) minor criteria. These are the only diagnostic criteria that makes PG not a diagnosis of exclusion and has been reported to have a sensitivity and specificity of 86% and 90%, respectively.[6] The patient fulfilled the major criterion and five (5) out of eight (8) minor criteria. Hence, the diagnosis of ulcerative pyoderma gangrenosum (PG).

The management of PG is likewise difficult due to the lack of clinical practice guidelines. Treatment is based on the severity of the disease, as well as patient response. In mild PG, local therapy such as intralesional or topical high-potency corticosteroids and topical calcineurin inhibitors may be adequate. A mainstay of treatment for PG is oral corticosteroids. Prednisone 1 to 2 mg/kg/day is often used to induce remission of the disease with gradual tapering and addition of steroid-sparing agents. Similar efficacy is seen with cyclosporine given as a monotherapy or in combination with other therapies. Other adjunctive treatment modalities include minocycline, dapsone, methotrexate, mycophenolate mofetil, cyclophosphamide, and thalidomide.[7] Antibiotics, such as doxycycline, can also be used due to its anti-inflammatory and antimicrobial effect.[8] One patient with partial immunoglobulin A deficiency who was diagnosed with PG on the leg was treated with prednisolone 40 mg and doxycycline 100 mg once daily for three (3) months with complete resolution of lesion.[9] Another case of a female patient with superficial granulomatous pyoderma gangrenosum, who was initially given systemic immunosuppressives but eventually developed complications, responded well with oral doxycycline.[10] Combination therapy should be tailored based on the response of the patient.[7] In this case, there was a significant improvement with a decrease in size of the ulcers after one (1) month of initiating treatment with oral prednisone and clobetasol propionate ointment. Doxycycline was used as an adjunct therapy in our patient with excellent response.

In conclusion, pyoderma gangrenosum (PG) is a rare, debilitating disease that often remains a diagnostic dilemma. The diagnosis of PG can be extremely challenging. However, the important clues that supported the diagnosis of PG likely were non-response to both broad-spectrum antibiotics and surgical debridement. Histopathologic findings are

confirmatory. Doxycycline, a treatment adjunct used for its anti-inflammatory properties, can be used in patients with PG to lessen the possible long-term side effects of corticosteroids. A timely referral to a dermatologist is vital to prevent further delays in the diagnosis and management of PG, as well as to avoid long-term scarring and sequelae of the disease that can significantly affect the patient's quality of life. This case highlights the important role of dermatology in individuals who present with non-healing chronic ulcers because as seen in this case, not all ulcers are just ulcers.

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