

Refractory Pyoderma Gangrenosum: Stabilized on Colchicine and Tumor Necrosis Factor (TNF) Inhibitor

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Abstract

Pyoderma gangrenosum (PG) is a rare ulcerative, painful inflammatory skin condition that is categorized among neutrophilic dermatoses. We report an otherwise healthy female who initially presented to a dermatology clinic with erythematous nodules and pustules scattered over her legs and thigh, which progressed later to multiple painful ulcers. Upon further investigation, it was diagnosed as idiopathic PG. Prednisone was an initial mainstay of treatment. While tapering, mycophenolate mofetil was started as adjunctive therapy but failed to maintain remission. A tumor necrosis factor inhibitor was initiated alongside colchicine with a significant clinical response.

Categories: Dermatology

Keywords: tumor necrosis factor alpha (tnf- α), mycophenolate mofetil, colchicine, refractory, pyoderma gangrenosum

Introduction

Pyoderma gangrenosum (PG) is an ulcerative inflammatory cutaneous disease frequently presenting as an inflammatory papule or pustule that evolves into a painful ulcer with a violaceous, eroded margin and a purulent floor. Additionally, PG may manifest with bullous, vegetative, peristomal, or extracutaneous lesions [1]. PG is an uncommon condition with an incidence between three and 10 per million individuals yearly [2]. The etiology, pathophysiology, and optimal treatment remain unclear. Therefore, variable laboratory and histopathologic data necessitate clinicopathologic correlation for diagnosis [3].

As PG is considered an inflammatory process, systemic corticosteroid therapy is the first-line therapy. Unfortunately, there is a 40% risk of relapse after complete remission [2]. Consequently, tapering corticosteroids with a steroid-sparing agent have been shown to prevent relapse [4]. Colchicine has been shown to be effective in treating neutrophilic dermatoses, such as Sweet syndrome and Behcet's disease, making it a valuable option for controlling PG [2].

After achieving remission on systemic corticosteroids but failing to respond to mycophenolate mofetil, we report a patient who was successfully stabilized on a combination of adalimumab and colchicine. To our knowledge, this is the first case in the published literature to report disease control on this treatment protocol.

Case Presentation

A 42-year-old, previously healthy female presented to the dermatology clinic with erythematous nodules and pustules scattered over her legs and thighs. We presumed it was furunculosis, for which she was given antibiotics. One week later, it progressed to painful ulcers. Physical examination revealed multiple tender ulceration involving the legs bilaterally. She denied any skin trauma. The ulcerations were deep into fat with violaceous undermined borders, edematous and erythematous surrounding skin, and fibrinoid and purulence exudate at the bases, as seen in Figures 1A, 1B. Histopathologic examination revealed neutrophilic dermatosis with ulceration. Systemic evaluation of the patient did not reveal any systemic symptoms, including gastrointestinal symptoms and arthralgias, and did not suffer from any of the conditions noted to be associated with PG.

How to cite this article

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FIGURE 1: The clinical presentation of pyoderma gangrenosum

(a) Erythematous nodules with small ulcers bilaterally. (b) Ulcers have progressed over the weeks.

Oral prednisone 60 mg daily was started for three weeks. After initial improvement, mycophenolate mofetil 3 g per day was added. Prednisone tapering was attempted twice, resulting in moderate to severe flaring of her disease. Therefore, mycophenolate mofetil was discontinued because of suboptimal response. After a verbal agreement, the patient began receiving adalimumab at 40 mg every two weeks with significant improvement. Prednisone was tapered over six weeks and then discontinued. Milder relapse was noticed as small painful nodules, intralesional triamcinolone 10mg/mL was received, and adalimumab was adjusted to 40mg per week with significant improvement. However, after improvement for two months, another mild relapse was noticed. Colchicine 2.4 mg/day, divided into two doses, was initiated. After three weeks, clear improvement and sustained remission were observed. The combination of adalimumab and colchicine proved effective. At her last follow-up after four months of therapy, lesions had improved and healed with a

cribriform scar as seen in Figure 2.

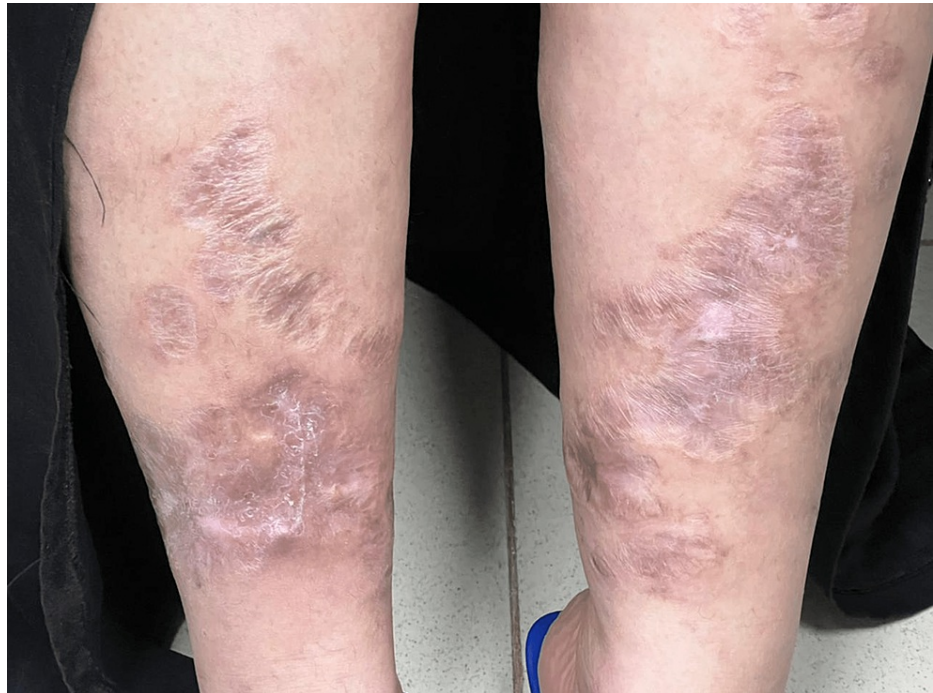


FIGURE 2: Healed pyoderma gangrenosum

Discussion

PG was first described in 1908 as a “geometric phagedena” and was later redefined as PG in 1930. PG is a misnomer; it is neither an infectious nor gangrenous condition [5]. The etiology of PG remains uncertain in the literature; however, neutrophilic dysfunction, genetic variation, and dysregulation of the immune system are postulated as contributing factors to the pathogenesis of PG. Hence, it can be associated with systemic diseases like inflammatory bowel disease, arthritis, and hematological disorders, sometimes leading to choosing one medication over the other [6,7]. Treatment of PG remains challenging, and, to date, no guidelines have been established [2,8].

PG is considered an autoimmune disease; corticosteroids are the initial therapy to induce remission, but they carry a risk of adverse effects in the long term. Therefore, Mycophenolate mofetil (MMF) was a favorable steroid-sparing agent in refractory PG, as reported in the literature, with 84.6% of patients responding to the treatment [9]. Another literature review reported the results of multiple case series totaling 63 patients treated with MMF. The result shows that 93% of patients improved on MMF, with five patients achieving complete remission [10]. Surprisingly, our patient had several moderate-to-severe relapses when prednisone was tapered.

TNF- α inhibitors showed a promising result in treating PG. A review of case reports and series conducted in 2019 demonstrates that adalimumab has a success rate of 90%. Moreover, in some cases, other immunosuppressive medications were substituted with adalimumab due to inadequate clinical response [11]. Accordingly, MMF was substituted with adalimumab showing a remarkable clinical response with milder relapses after the steroid was tapered. During relapses, intralesional triamcinolone was injected into the ulcer periphery circumferentially, as it is effective in limited disease [12].

Colchicine is proposed to be a treatment option as an antineutrophilic agent in PG [2]. In the literature, only two case reports were treated initially with systemic steroids and then stabilized on colchicine alone, which was well-tolerated except for one patient who reported mild diarrhea. Furthermore, colchicine has a lower adverse effect on long-term use than MMF [13,14]. For our patients, we use colchicine in combination with adalimumab as it works effectively in stabilizing refractory PG.

Conclusions

In conclusion, the choice of therapy is individual to each patient and is based on their response as well as their association with other systemic diseases. To add to the current literature, we proposed that both colchicine and adalimumab could be excellent adjunctive therapeutic options besides corticosteroids in the treatment of refractory PG. Additional studies on a larger scale are required to determine the most effective

course of treatment for PG.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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