SKIN

BRIEF ARTICLE

Upadacitinib for Pyoderma Gangrenosum: A Case Report and Review of Emerging Evidence

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare, ulcerative neutrophilic dermatosis characterized by painful, rapidly progressive skin ulcers, most commonly affecting the lower extremities. Management typically involves systemic corticosteroids and immunosuppressive agents, which often induce initial improvement but are frequently limited by adverse effects and high relapse rates upon tapering. These challenges highlight the limitations of conventional therapies and underscore the urgent need for effective steroid-sparing alternatives.
We report the case of a young man with PG refractory to corticosteroid tapering and adjunctive therapies, who achieved complete remission following initiation of upadacitinib, a selective oral Janus kinase 1 (JAK-1) inhibitor. Treatment resulted in a rapid clinical response, sustained ulcer closure, and allowed for corticosteroid dose reduction.

INTRODUCTION

Pyoderma gangrenosum is a painful ulcerating neutrophilic dermatosis characterized by a relapsing-remitting course.[1,2] Systemic corticosteroids yield rapid improvement and can serve as a diagnostic clue.[1,2] but prolonged use increases the risk of systemic adverse effects, highlighting the need for alternative treatments.

Upadacitinib, a selective JAK-1 inhibitor, approved for various rheumatologic conditions, inflammatory bowel disease, and atopic dermatitis, represents a promising new treatment.[3,4] We present the case of a young male diagnosed with PG that relapsed following oral steroid tapers but achieved complete remission with upadacitinib.

CASE REPORT

A 26-year-old Guatemalan man with a history of pigmented purpuric dermatosis managed with topical steroids, presented with multiple non-healing lower leg ulcers. Over two months, he developed three distinct ulcers: one following minor trauma on the left anterior lower leg, another at a biopsy site on the right anterior lower leg, and a third on the left medial lower leg. His family history was notable for pyoderma gangrenosum in his brother.

Examination revealed necrotic ulcers with ragged, undermined edges, violaceous borders, and purulent exudates on the left pretibial region (**Figure 1**), right medial tibial area, and left medial ankle. A biopsy of the

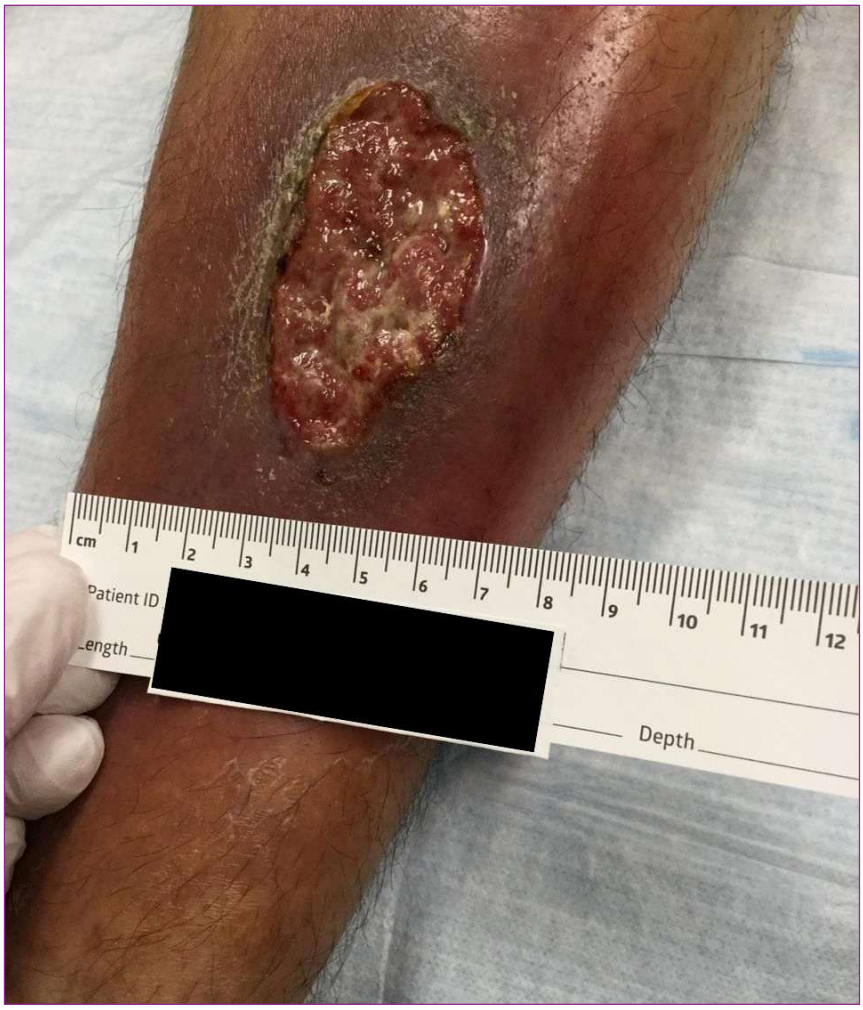

Figure 1. Necrotic ulcer on the left anterior tibia.

left pretibial ulcer showed nonspecific ulceration with fibrinoid necrosis and neutrophilic debris. Laboratory workup revealed elevated C-reactive protein level (22.0 mg/L) and erythrocyte sedimentation rate (31 mm/hr), and an antinuclear antibody (ANA) titer of 1:320 (speckled pattern).

The patient had no evidence of inflammatory bowel disease, inflammatory arthritis, malignancy, hematologic disorders, or lupus. An extensive autoimmune, hematologic, and infectious workup was unremarkable. Vascular evaluation for venous insufficiency led to left great saphenous vein stripping, which did not alter ulcer progression.

Pyoderma gangrenosum was diagnosed based on the PARACELSUS scoring (16 points), Delphi consensus criteria, and exclusion of alternative diagnoses.[1–3,6]

Initial treatment included oral prednisone at 1 mg/kg (60 mg daily), tapered over four months, along with topical clobetasol and wound care. While all three ulcers improved, none fully closed. The patient was transitioned to dapsone and intralesional corticosteroid injections, leading to complete closure of two ulcers and partial improvement of the left anterior tibial ulcer. However, injections were discontinued due to steroid-

induced skin atrophy, which triggered a disease flare.

Systemic corticosteroids were resumed and continued for 18 months alongside dapsone. However, each tapering attempt triggered a flare, requiring dosage escalation. The course was further complicated by recurrent wound-associated cellulitis requiring antibiotics and iatrogenic corticosteroid-induced Cushing's syndrome.

In February 2024, the ulcer continued to worsen despite the patient being on prednisone 40 mg daily. Upadacitinib 15 mg daily was initiated. Eight months later, the ulcer had fully healed, leaving only a depressed scar, while prednisone was progressively tapered to 7 mg daily (**Figure 2A**). At twelve months, the ulcer remained closed, and prednisone was reduced to 2 mg daily, with plans for complete discontinuation (**Figure 2B**).

DISCUSSION

The patient was diagnosed with the most common ulcerative subtype of PG, often triggered by minor trauma, a phenomenon known as "pathergy".[1,2,5] PG is frequently associated with inflammatory bowel disease (IBD), inflammatory arthritides, or hematologic malignancies, though it can also be idiopathic.[1,2,5] A genetic component has been suggested, with syndromic forms described.[1,2] In this case, both the patient and

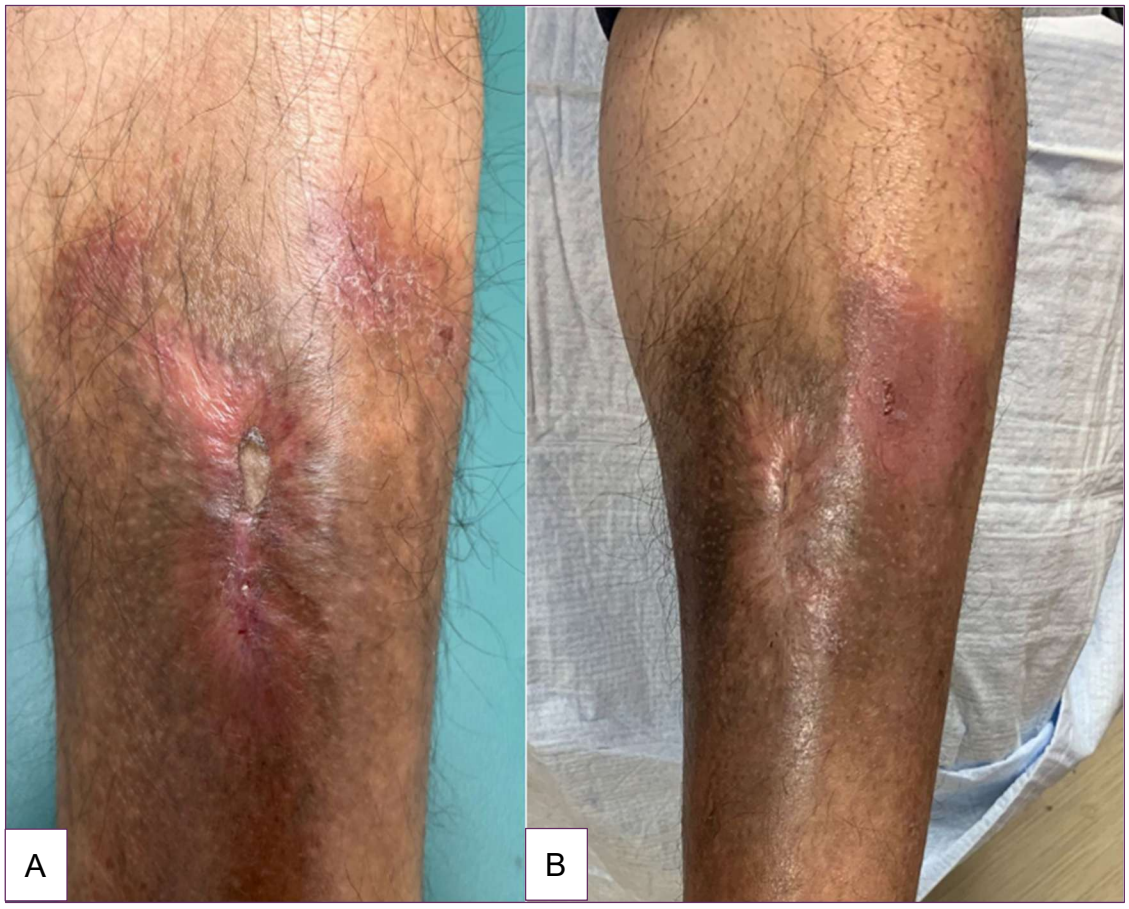

Figure 2. (A) Healed left anterior tibial PG ulcer with a depressed scar at 8 months follow up (B) left anterior tibial PG ulcer remains healed at 12 months follow up

his brother, who also had PG, tested positive for ANA; however, neither exhibited features of a rheumatologic condition or known PG-associated syndrome.

Diagnosis of PG remains challenging, as histopathology is nonspecific and primarily excludes other causes of ulceration.[1,2,5] Typical findings include a neutrophilic infiltrate.[1] While no universally accepted criteria exist, diagnostic tools such as PARACELSUS score and Delphi consensus guidelines have been proposed.[1,5]

Management is equally complex due to unclear pathogenesis, though immune dysregulation and elevated proinflammatory and neutrophil chemotactic factors are likely implicated.[1,2] Therapy is guided by disease severity and progression, incorporating wound care, topical and intralesional corticosteroids, and systemic immunosuppressants in severe and refractory cases.[1,2] However, due to its relapsing nature, achieving sustained healing remains a challenge.[1,2]

Recent studies implicate the Janus kinase/signal transduction and activator of transcription (JAK/STAT) signaling pathway in PG pathogenesis, with increased expression demonstrated in affected skin via immunohistochemistry.[1,2,4,6] Targeting this pathway has emerged as a potential therapeutic strategy.[1,2,4]

Nonselective JAK inhibitors have shown promising results.[1,4,6] We reviewed twelve cases of the selective JAK-1 inhibitor upadacitinib, including our own, for the treatment of PG (**Table 1**). Complete healing was reported as early as 6 weeks, with average follow-up ranging from 12 to 24 weeks. Our case had the longest follow-up of 12 months with sustained remission. Over half of the cases involved concurrent use of systemic corticosteroids or other immunosuppressants; however upadacitinib initiation allowed corticosteroids tapering.

Table 1. Summary of cases of pyoderma gangrenosum treated with upadacitinib, including our case.

Article	Associated Condition	Sex/Age (Years)	Disorder Duration Prior to Initiation of Upadacitinib	Previous Treatment	Upadacitinib		
					Treatment	Concomitant Therapies	Outcome
Kooybaran et al[12] (2022)	RA	F/50	3 months	Anakinra, SCS	15 mg daily	SCS 80 mg daily, tapered to 9 mg daily at 22 weeks	Improvement at 14 weeks, persisted at 22 weeks

Van Eycken et al[6] (2023)	Spondyloarthritis	F/65	<1 year, relapsing and remitting before treatment with upadacitinib	Tacrolimus, SCS, colchicine, cyclosporine,	15 mg daily	SCS ≥10 mg daily, tapered to 3 mg daily at 24 weeks	Improvement at 6 weeks, complete remission at 12 weeks, persistent remission at 24 weeks
Dos Santos at al[11] (2023)	RA	F/45	4 months	SCS, dapsone	15 mg daily	NR	Improved at 25 days, complete regression after 6 weeks
Tanida et al[7] (2023)	UC	F/44	<1 month	SCS	45 mg daily, decreased to 30 mg daily after 10 days due to anemia	SCS 30 mg daily (tapered off over 1.5 months), GMA (10 sessions)	Healing with re-epithelization at 10 weeks, stable healing at 3 months
Mendolaro at al[10] (2024)	Crohn's disease	F/59	NR	SCS, infliximab	45 mg daily	NR	Significant improvement and almost complete healing at 6 weeks
Prieto Jimenez et al[9] (2024)	UC	F/40	NR	NR	45 mg daily for 8 weeks induction dose, 30 mg daily maintenance dose	NR	Significant healing at 7 weeks, resolution after 6 months
Park et al[5] (2024)	UC	F/62	1 year	SCS, cyclosporine, infliximab, topical triamcinolone	30 mg daily renally dosed, increased to 45 mg daily for 8 weeks induction dose, 30 mg daily maintenance dose	NR	Significant healing after 3 months

Melgosa Ramos et al[8] (2024)	IBD	M/45	1 year	SCS, methotrexate, cyclosporine, adalimumab	15 mg daily	Adalimumab 40 mg weekly, SCS 20 mg daily	Significant improvement after 26 weeks
	Mammoplasty	F/26	1 year	SCS, methotrexate, cyclosporine, adalimumab	15 mg daily for 1 month, then 30 mg daily	Adalimumab 40 mg weekly, SCS 20 mg daily	Significant improvement after 16 weeks
	RA	F/62	5 years	SCS, methotrexate, cyclosporine, adalimumab, golimumab	30 mg daily	SCS 75 mg daily	Significant improvement after 16 weeks
	Cocaine abuse	M/50	10 years	SCS, methotrexate, azathioprine, cyclosporine, adalimumab, certolizumab, infliximab	30 mg daily	No	Significant improvement after 12 weeks
The present study (2025)	None	M/26	2.5 years	SCS, topical clobetasol, dapsone, intralesional CS injections	15 mg daily	SCS 35 mg daily, tapered to 2 mg daily over 1 year	Fully healed at 34 weeks, remained closed at 12 months

Abbreviations: F, female; M, male; NR, not reported; SCS, systemic corticosteroids; CS, corticosteroid; RA, rheumatoid arthritis; UC, ulcerative colitis; GMA, granulocyte and monocyte adsorptive apheresis; IBD, inflammatory bowel disease.

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