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CASE REPORT

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Pyoderma gangrenosum

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ABSTRACT

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis characterised by rapidly progressing, painful ulcers with undermined violaceous borders. It is frequently associated with systemic conditions such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and haematological disorders. Dysregulated immune responses, genetic predispositions, and inflammatory pathways contribute to its complex pathogenesis. A 68-year-old patient with seropositive RA presented with multiple painful ulcers on the scalp, trunk, and limbs. Histopathological examination revealed lymph-granulocytic infiltrates, collagen necrosis, and leukocytoclastic vasculitis. Laboratory tests demonstrated neutrophilia and elevated C-reactive protein levels. Initial treatment with methotrexate and corticosteroids yielded suboptimal results; however, the introduction of ciclosporin led to significant healing within four weeks. PG's clinical spectrum includes ulcerative, pustular, bullous, and vegetative subtypes, which are often triggered by minor trauma (pathergy). Differential diagnoses encompass vascular diseases, infections, malignancies, and other inflammatory conditions. Treatment typically involves immunosuppressive agents such as corticosteroids and ciclosporin, as well as biologic therapies targeting cytokines, including tumour necrosis factor-alpha (TNF-α), interleukin (IL)-1β, IL-17, and IL-23. Emerging targeted therapies and personalised approaches, tailored to disease severity and comorbidities, are increasingly recognised as essential for effective management. Timely diagnosis and appropriate treatment can prevent disease progression and improve clinical outcomes. Further research is imperative to establish standardised diagnostic criteria and optimise therapeutic strategies.

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Keywords: case report, pyoderma gangrenosum, neutrophilic dermatosis, ciclosporin

INTRODUCTION

Pyoderma gangrenosum (PG**)** is a rare, non-infectious neutrophilic dermatosis characterised by rapidly progressing, painful skin ulcers with undermined violaceous borders. The incidence of PG is estimated to range between 3 and 10 cases per million people per year [1]. The aetiology of PG remains unclear; however, it is frequently associated with systemic conditions such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and haematological disorders. Notably, the prevalence of RA among patients with PG is approximately 4.7%, compared to 1.5% in control subjects, indicating a more than threefold increase in the likelihood of developing PG for individuals with RA [2]. The pathogenesis is thought to involve dysregulation of the immune system, resulting in an abnormal neutrophilic response [3, 4]. Early recognition and appropriate management are crucial to prevent disease progression and reduce morbidity [5].

CASE REPORT

A 68-year-old male was admitted to the dermatology department with skin lesions characterised by rapidly evolving, painful ulcers with undermined borders and peripheral erythema located on the scalp, trunk, and upper and lower limbs (Fig. 1). Among the patient's comorbidities, seropositive rheumatoid arthritis was noted, a condition frequently associated with pyoderma gangrenosum. Histopathological examination revealed fragments of skin and subcutaneous tissue with epidermal ulceration, accompanied by intense lymph-granulocytic infiltrates, occasional histiocytic cells, and *foci* of collagen necrosis within the dermis. Numerous small blood vessels demonstrated features of leukocytoclastic vasculitis and fibrinoid necrosis of the vessel walls (Fig. 2). Tissue cultures did not show growth of bacteria, fungi, or mycobacteria. Laboratory investigations revealed neutrophilia (7,600/μL; reference range: 3,200–5,000/μL) and elevated C-reactive protein levels (8.6 mg/dL; reference

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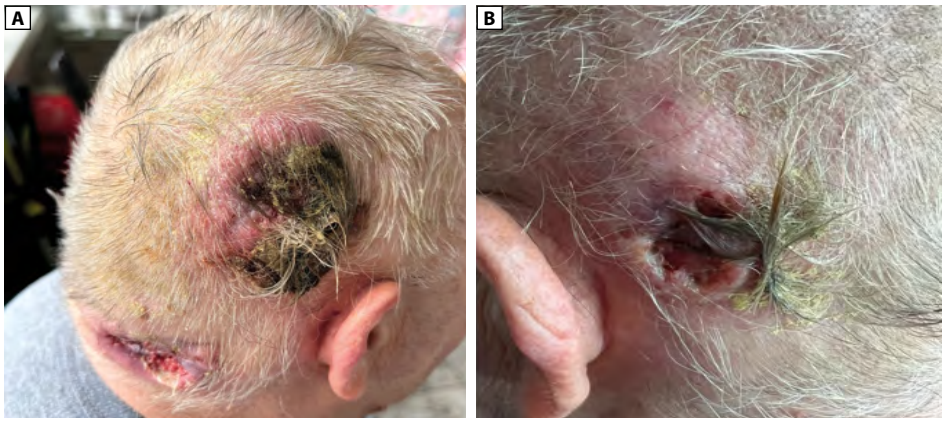

Figure 1A, B. Lesions on the scalp before diagnosis

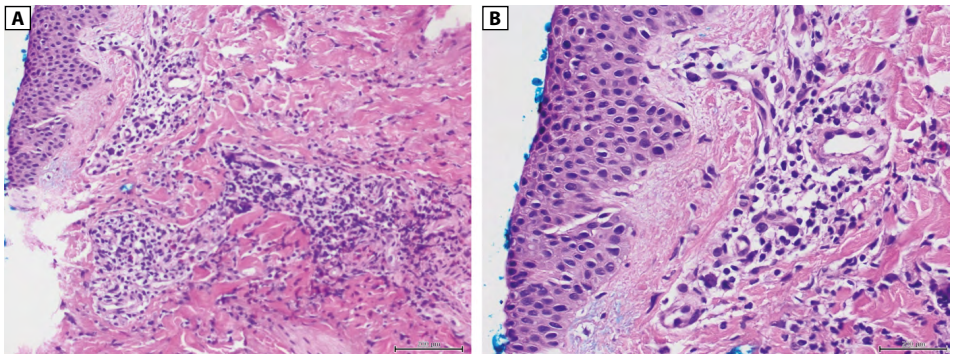

Figure 2A, B. Histopathology (× 200, H&E): inflammatory infiltrate (lymphocytes, neutrophils, histiocytes) in dermal vessels with lumen narrowing, endothelial destruction, and collagen degeneration

range, < 0.5 mg/dL). Antinuclear antibody levels were within normal limits. Based on clinical examination, the results of additional investigations, and the histopathological findings, a diagnosis of pyoderma gangrenosum was established. Methotrexate was administered at a weekly dose of 25 mg, in combination with systemic corticosteroid therapy using prednisolone at a daily dose of 40 mg (0.5 mg/kg body weight). The methotrexate therapy was continued for eight weeks. Due to a suboptimal clinical response to methotrexate, ciclosporin therapy was initiated at a daily dose of 5 mg/kg body weight, while steroid therapy was continued. After four weeks of therapy, significant improvement in the dermatological lesions was observed, with the majority of ulcers having healed (Fig. 3).

DISCUSSION

Pyoderma gangrenosum (PG) is a rare, debilitating inflammatory skin disease, clinically characterised by painful, rapidly evolving cutaneous ulcers with undermined, irregular, erythematous-violaceous edges [6].

It is classified among the neutrophilic dermatoses, a heterogeneous group of cutaneous inflammatory disorders defined by a sterile, predominantly neutrophilic infiltrate on histopathology [7].

Pyoderma gangrenosum is frequently associated with systemic diseases, including inflammatory bowel disease (IBD), arthritis, and haematological malignancies [8].

Few population-based studies have assessed the epidemiology of PG, and difficulties in accurate diagnosis may affect the precision of prevalence and incidence estimates. Among these, the largest study was a cross-sectional analysis conducted in the USA, employing a validated algorithm and data derived from Explorys, a cloud-based IBM platform for the analysis of longitudinal electronic health records. This study identified 1,971 individuals with PG within a database of over 31 million adult patients, reporting a prevalence of 58 cases per million adults. Similarly, a population-based study from the UK estimated the incidence of PG to be approximately six cases per million person-years [9].

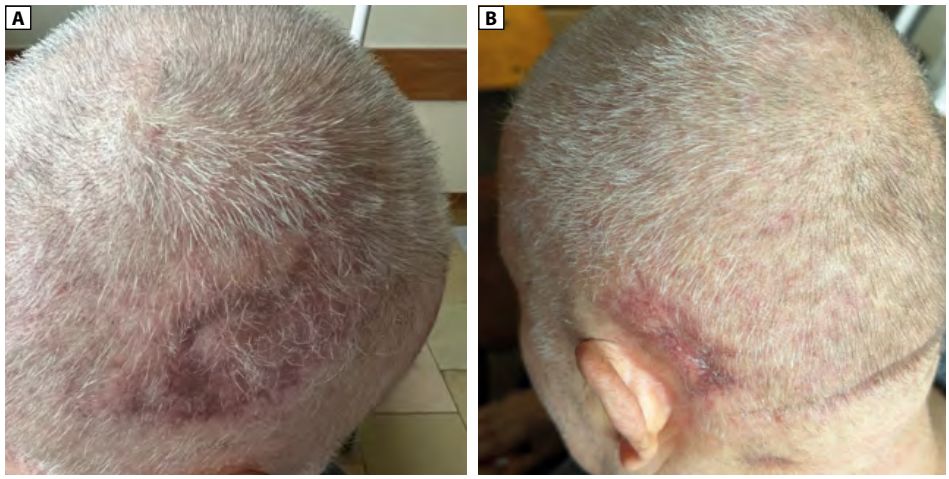

Figure 3A, B. Lesions within the scalp during treatment

The pathophysiology of pyoderma gangrenosum (PG) is complex and not fully understood, involving multiple pathways that contribute to its diverse clinical manifestations. Dysregulation of the innate immune system, including abnormal neutrophil chemotaxis, migration, and function, has been implicated. PG is recognised as a neutrophilic dermatosis, typified by aseptic neutrophilic infiltration and systemic inflammation. It is commonly associated with inflammatory disorders such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and haematological conditions, including acute myeloid leukaemia (AML). Research highlights clonal T-cell expansion and links to neutropenia or leukocyte adhesion deficiencies.

Genetic factors are also thought to play a significant role. PG shares genetic similarities with IBD, including *loci* such as *IL8RA* and mutations in *PSTPIP1*. This mutation, associated with syndromes such as PAPA (pyogenic arthritis, pyoderma gangrenosum, and acne) and PASH (pyoderma gangrenosum, acne, and hidradenitis suppurativa), enhances pyrin binding, leading to inflammasome activation and increased interleukin (IL)-1β production, which drives neutrophilic infiltration. Additional genetic abnormalities, such as mutations in JAK2 (linked to cytokine signalling) and methylenetetrahydrofolate reductase (implicated in coagulation and ulceration), have been reported.

Tumour necrosis factor-alpha (TNF-α) plays a pivotal role in inflammatory processes, including those observed in PG. As noted in studies on multiple sclerosis (MS), elevated plasma TNF-α levels correlate with disease activity and may serve as a biomarker of inflammation. In fact, TNF-α is central to mediating the inflammatory response in several immune-mediated diseases, including PG, where it triggers the recruitment of immune cells and stimulates the production of pro-inflammatory cytokines. Elevated TNF-α levels have been linked to increased disease activity and could potentially reflect the extent of tissue damage [10, 11]. Furthermore, studies suggest that TNF-α may contribute to the pathogenesis of PG by fostering systemic inflammation, which is also a hallmark of conditions such as rheumatoid arthritis and inflammatory bowel disease.

Additionally, GM-CSF has been suggested to facilitate neutrophil adhesion and inflammation, potentially linking PG with TNF-responsive diseases. These findings underscore the intricate interplay between genetic predispositions, immune dysregulation, and inflammatory pathways in the pathogenesis of PG [12].

Classical PG typically presents as an extremely painful erythematous lesion that rapidly progresses to a blistered or necrotic ulcer. The lesion often features a ragged, undermined edge with a violaceous or erythematous border. Although the lower legs are the most commonly affected site, PG can occur at any body location. The condition may be triggered by minor trauma, a phenomenon known as "pathergy" [13].

Within the disease spectrum, four subtypes of PG are recognised: ulcerative, pustular, bullous, and vegetative. Additional variants include postsurgical (postoperative) and peristomal PG (Tab. 1) [9]. Currently, no standardised diagnostic criteria for PG exist; however, the proposed criteria are summarised in Table 2 [14].

In the differential diagnosis of PG, other causes of cutaneous ulcers must be considered. These include arterial and venous disease, haematological conditions (*e.g.*, sickle cell disease, cryoglobulinaemia, antiphospholipid syndrome), vascular occlusion, vasculitis, infections, calciphylaxis, drug-induced ulceration, primary or metastatic tumours, hypertension-associated ulcers (Martorell ulcer), and inflammatory disorders such as cutaneous Crohn's disease [13].

Table 1. Clinical variants of pyoderma gangrenosum

Variant	Clinical presentation	Common locations	Histopathology	Reported associated systemic diseases
Ulcerative	Painful inflammatory nodules or pustules rapidly progressing to necrotic ulcers with violaceous undermined edges and surrounding erythema	Anterior lower extremities, trauma sites	Findings vary by location and lesion stage. Edge biopsies show neutrophils, perivascular lymphocytic infiltrates, and dermal oedema. Central biopsies reveal neutrophilic infiltrate, fibrin deposition, thrombosis, and red blood cell extravasation	IBD, haematological malignancies, rheumatoid arthritis, seronegative arthritis, monoclonal gammopathy
Bullous	Rapidly forming painful bullae that may progress to erosion or ulcer	Face, upper extremities	Subcorneal, subepidermal, or intra-epidermal bullae with dermal neutrophilic infiltrates and microabscesses. Negative or non-specific immunofluorescence helps exclude immunobullous diseases	Myeloproliferative disorders (*e.g.*, acute myeloid leukaemia), IBD
Pustular	Symmetrical pustules with erythematous borders	Legs, trunk	Subcorneal, subepidermal, or intra-epidermal bullae with dermal neutrophilic infiltrates and microabscesses. Immunofluorescence is negative or non-specific	IBD
Vegetative	Mildly painful, slow-growing, non-purulent, superficial ulcers with non-undermined, less violaceous edges. Rapidly responds to therapy	Trunk	Palisading granulomatous reaction (mononuclear cells surrounding central necrosis) with neutrophilic abscesses and sinus tracts	None
Peristomal	Papules eroding into ulcers with undermined edges, often difficult to differentiate from other peristomal lesions	Adjacent to stoma	Dermal neutrophilic infiltrates with granulation tissue	IBD, enteric malignancy, connective tissue disease, monoclonal gammopathy
Postoperative	Erythema at surgical sites, followed by wound dehiscence or coalescing ulcers. Pain exceeds expected levels based on examination	Surgical sites	Dermal oedema and neutrophilic infiltrates	Common after abdominal or breast surgery

IBD — inflammatory bowel disease

In an updated literature review on established and emerging pharmacological treatments conducted by Maronese et al. [6], several medications were highlighted as potential therapies for PG. These include:

- **Classical immunosuppressive and immunomodulating agents**: corticosteroids, ciclosporin, methotrexate, mycophenolate mofetil, azathioprine, tacrolimus, dapsone, colchicine, thalidomide, intravenous immunoglobulin, and granulocyte and monocyte adsorption apheresis.
- **Biologics**: anti-TNF-α (infliximab, adalimumab, etanercept, certolizumab pegol, golimumab), anti-IL-1β (anakinra, canakinumab, gevokizumab), anti-IL-17A (secukinumab), IL-17RA (brodalumab), IL-17A/F (ixekizumab), anti-p40 subunit of IL-12 and IL-23 (ustekinumab), p19 subunit of IL-23 (guselkumab, risankizumab), anti-C5a (vilobelimab), anti-IL-6R (tocilizumab), anti-CD3 (visilizumab), anti-CD20 (rituximab), and anti-α4β7 integrin (vedolizumab).
- **Small molecules**: apremilast, tofacitinib, ruxolitinib, and baricitinib [6, 15].

CONCLUSIONS

Pyoderma gangrenosum (PG) remains a challenging condition due to its rarity, complex pathophysiology, and lack of standardized diagnostic criteria. It is often associated with systemic diseases such as rheumatoid arthritis, inflammatory bowel disease, and haematological disorders, which necessitates a multidisciplinary approach to diagnosis and management. This case highlights the importance of considering PG in patients presenting with rapidly progressing painful ulcers, particularly those with known systemic conditions.

Histopathological examination and laboratory findings, coupled with clinical evaluation, are essential for accurate diagnosis. Despite the initial suboptimal response to conventional therapies such as corticosteroids and methotrexate, the use of ciclosporin proved effective, emphasizing the need for tailored therapeutic strategies based on individual patient profiles and disease severity.

Emerging therapies targeting specific inflammatory pathways offer hope for more effective and personalized management of PG. Future research should focus on

Table 2. Comparison of diagnostic criteria for pyoderma gangrenosum

Criteria by Su et al. (2004)	PARACELSUS Score (2018)	Delphi consensus (2018)
Diagnosed as PG when both major criteria and two or more of the minor criteria are fulfilled	The following items are scored, and the possibility of PG is judged to be high when the total score is ≥ 10	Diagnosed as PG when the major item and four or more of the minor items are fulfilled
Major criteria	**Major items (3 points each)**	**Major items**
• Rapidly progressing painful necrotising ulcer with an irregular-shaped purplish-red, undermined margin • Exclusion of other diseases that may cause skin ulcers	• Progressive course • Exclusion of other diseases	• Evidence of neutrophil infiltration in biopsy specimens from the ulcer margin • Reddish or bluish-purple wound margin
Minor criteria	**Secondary items (2 points each)**	**Minor items**
• History of ulcer formation after slight trauma or cribriform scar • Systemic diseases related to PG • Histopathology showing sterile neutrophilic infiltration (*e.g.*, mixed inflammation, lymphocytic angiitis) • Prompt improvement with systemic steroids	• Improvement of symptoms with immunosuppressive therapy • Characteristic irregular ulcer • Extreme pain (VAS > 4) • Localised pathergy	• Exclusion of infection • Pathergy (ulcer formation at the site of trauma) • Association with IBD or inflammatory arthropathy • Ulceration within 4 days of papule, pustule, or blister appearance
	Additional items (1 point each)	
	• Histologically demonstrated purulent inflammation • Undermined wound margin • Association with systemic disease	
Clinical findings		
• Ulcer with surrounding erythema, undermined margins, and tenderness • Cribriform or wrinkled scar post-healing		• At least one ulcer on the anterior lower leg • Cribriform or wrinkled scar post-healing

IBD — inflammatory bowel disease; PG — pyoderma gangrenosum; VAS — visual analogue scale for pain

establishing standardized diagnostic criteria, identifying biomarkers for early detection, and developing evidence-based guidelines for treatment. Prompt recognition and appropriate intervention can significantly improve patient outcomes, underscoring the critical role of collaborative care in managing this complex and debilitating condition.

Article information and declarations

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Author contributions

Writing: original draft, data curation, conceptualization — MGR, KK; supervision — VKJ, AG; preparing and assessment of histopathology examination — MKO. All authors contributed to the article and approved the submitted version. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis. No medical writing or editorial assistance was received in the preparation of this manuscript.

Conflict of interest

The authors declare no conflicts of interest.

Ethics statement

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Supplementary material

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