Revista Română de Reumatologie
Romanian Journal of Rheumatology

CASE REPORT

Double Trouble: Gout meets Pyoderma Gangrenosum in a relapsing storm

MADALINA-PUSA ROSU[1)], VALENTINA PETRICESCU[1)], CRISTIANA PREFAC[2)], ANCA URSU[3)], CONSTANTIN-IOAN BUSUIOC[4)], DENISA PREDETEANU[1)]

[1)] *Department of Rheumatology, "Sf. Maria" Clinical Hospital, Bucharest, Romania*
[2)] *Infectious Disease Department, "Sf. Maria" Clinical Hospital, Bucharest, Romania*
[3)] *Dermathology Department, "Sf. Maria" Clinical Hospital, Bucharest, Romania*
[4)] *Department of Pathology, "Sf. Maria" Clinical Hospital, Bucharest, Romania*

Abstract

Background: Pyoderma Gangrenosum (PG) is an uncommon neutrophilic skin condition often misdiagnosed as infectious skin ulceration. It's association with gout is extremely rare and may complicate the clinical picture, especially when systemic inflammatory response is present. Although cases of coexisting PG and gout have been reported, the association between these two conditions remains unexplored.

Case Presentation: A 40-year-old man with recurrent untreated gout presented with acute ankle arthritis, fever, and a painful ulcerative lesion. Laboratory tests showed leukocytosis, elevated C-reactive protein, and hyperuricemia. Initial cultures grew Streptococcus spp., and the patient was treated for cellulitis secondary to gout. Despite antibiotics, the lesion progressed rapidly, forming extensive necrotic ulcers. Autoimmune and infectious causes were excluded. Skin biopsy demonstrated neutrophilic infiltration and dermo-hypodermal necrosis, confirming PG. High-dose oral methylprednisolone (64 mg/day) led to rapid improvement and re-epithelialization within one week.

Conclusion: This case underscores the importance of considering PG in non-healing ulcers unresponsive to antibiotics in patients with gout. Both conditions share IL-1–driven neutrophilic inflammation, which may explain their coexistence. Early recognition, biopsy, and prompt corticosteroid therapy are critical to avoid unnecessary surgery and prevent tissue loss. Multidisciplinary management ensures timely diagnosis and optimal outcomes.

Keywords: pyoderma gangrenosum, gout, ulcer, neutrophilic dermatosis.

Introduction

PG is a non-infectious, inflammatory skin condition that belongs to a group of disorders called neutrophilic dermatoses. The most common form is classical PG, which makes up about 85% of cases [1,2]. It usually affects adults between 30 and 60 years old and occurs equally in men and women. Lesions most often appear on the lower legs. Around half of all PG cases are linked to an underlying systemic disease. Conditions that can look similar to PG include infections, leg ulcers, vasculitis, autoimmune diseases, cancer and injuries to the skin. Identifying any associated disease is important, because it can influence how serious the PG is and what kind of treatment is needed [3]. Diagnosing PG cand be difficult. There are no specific lab tests or biopsy findings that confirm it, so doctors usually diagnose it by rulling out other causes. Because of this, PG is often misdiagnosed and needs careful evaluation to look for other health conditions that might be involved.

Gout is a well-known inflammatory arthropaty caused by monosodium urate crystal deposition. Although PG is classically associated with systemic diseases, its occurrence in patients with gout is exceedingly rare. This unusual co-occurrence raises questions about potential shared inflammatory pathways or diagnostic pitfalls [4]. There have been a few individial case reports and small case series that mention patients having both PG and gout at the same time [5,6,7,8,9]. However, no large, controlled studies have yet examined whether there is a real connection between these two conditions. Because of this, the existing research does not provide a clear answer.

Case presentation

We present the case of a 40-years-old man with a past medical history of untreated recurrent gout (11 prior flares over the past 8 years), who presented in our hospital with acute arthritis of the left ankle, fever, chills, and a painful ulcerative skin lesion over the affected joint (Figure 1). The patient denies any urinary, digestive, or other associated symptoms. The iatrogenic hypothesis was ruled out due to lack of supporting data from the patient's medical history.

Figure 1. *Swelling, warmth, redness of the left ankle*

Laboratory tests revealed leukocytosis 21.600 cells/µl, elevated inflammatory markers like C-reactive protein 375 mg/dl, ESR 53 mm/h, procalcitonin 2.7 ng/ml, and hyperuricemia 9 mg/dl. enal and liver functions were normal. Tumor markers were negative, with no evidence of malignancy on laboratory testing.

Ultrasound and Doppler US revealed subcutaneous edema in the distal third of the leg; no signs of superficial or deep venous thrombosis. Wound cultures were positive for Streptococcus spp., suggesting a secondary infection. Blood cultures were negative.

The ECG, chest X-ray and abdominal ultrasound revealed no notable abnormalities. No pathological findings were noted on the ankle X-ray (Figure 2 a,b).

Figure 2 a, b. *Lateral and anteriorposterior ankle X-ray*

Integrating clinical history, laboratory findings and multidisciplinary consultations (dermatology, infectious diseases, plastic surgery), we support the initial diagnosis of gout complicated by streptococcal cellulitis documented by positive culture. Thus, the patient received a combination of antibiotic therapy (ceftriaxone and vancomycin), colchicine and corticosteroids. During hospitalization, inflammatory markers decreased progressively and procalcitonin normalized by day 7, correlating with clinical improvement.

Upon discharge, the patient was advised to continue local wound care with betadine and to apply sterile dressings. Allopurinol therapy was initiated to manage elevated uric acid levels and prevent further gout attacks and an additional 7-day course of amoxicillin-clavulanic acid was prescribed.

Six days after discharge, the patient presented recurrent ankle swelling and pain, functional impairment, and an extensive ulceronecrotic lesion and for which he presented to the Department of Infectious Diseases (Figure 3).

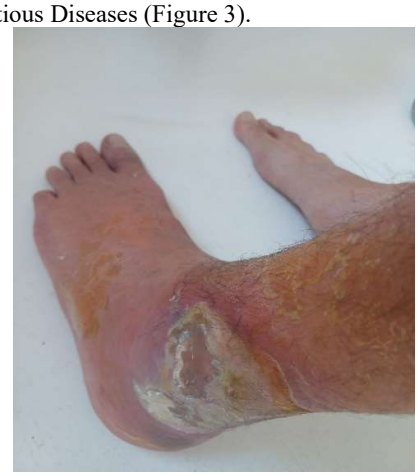

Figure 3. *Swollen ankle with an extensive ulceronecrotic lesion, surrounded by erythema and skin peeling*

A new panel of tests was ordered to exclude infectious causes, including HIV, Pseudomonas, Enterococcus, as well as rectal and nasal carriage screening. Hepatitis markers were negative.

The ankle CT showed diffuse demineralization of the bone segments, subchondral osteosclerosis and geodes, as well as periarticular fluid collections without periosteal reactions. MRI was recommended for further evaluation. The infectious disease specialists recommended a 4-week course of clindamycin treatment.

Despite treatment, the patient's clinical status deteriorated, with extension of the lesion. The ulcer expanded and deepened rapidly, indicating aggressive tissue involvement (Figure 4 a,b).

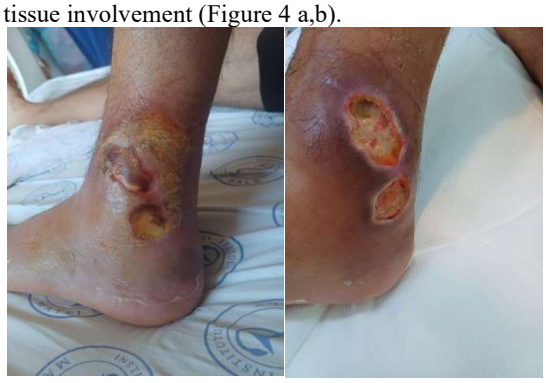

Figure 4 a, b. *Rapid progression, necrosis, and ulceration of the leg lesion with irregular erythematous-violaceus border*

Currently, laboratory analyses reveal no inflammatory syndrome; procalcitonin is negative. Additional autoimmune antibodies, such as rheumatoid factor, p-ANCA, c-ANCA, and ANA, were all negative, ruling out vasculitis and connective tissue disease.

The delayed wound healing and rapid progression of the lesion, despite comprehensive treatment efforts, caused significant challenges for the medical team. A skin biopsy was performed and histopathological examination revealed neutrophilic infiltration, polymorphic inflammatory elements, vascular changes, and dermo-hypodermic necrosis (Figure 5).

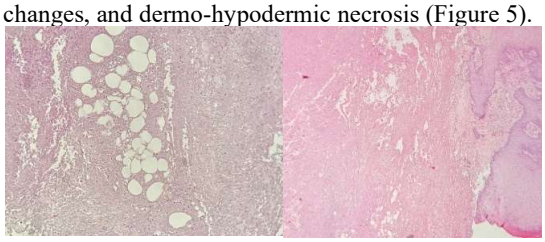

Figure 5. *HP exam – Hyperplastic epidermis with scattered neutrophils in the dermis (HE)*

Furthermore, to rule out other causes of ulceration, an MRI of the left ankle indicated a 7 cm irregular necrotic and suppurative lesion in the subcutaneous adipose tissue on the lateral and posterolateral side of the ankle as seen in Figure 6. There is also diffuse subcutaneous edema, with no signs of osteonecrosis/bone abscess or synovitis or tenosynovitis.

Figure 6. *MRI of the left ankle showing necrotic and suppurative lesion in the subcutaneous adipose tissue*

Following all data, a diagnosis of PG was reached, and the patient received 64 mg of oral methylprednisolone daily. Notably, the patient's condition improved within one week of initiating treatment. The lesion stopped progressing and showed early signs of re-epithelization at the margins (Figure 7).

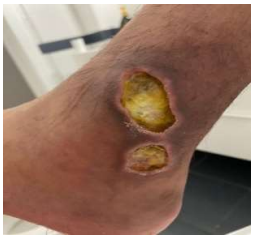

Figure 7. *Evolution of the lesion after 7 days of corticosteroid therapy*

The images below illustrate the progression of the lesion from its initial presentation to one week after starting corticosteroid therapy (Figure 8).

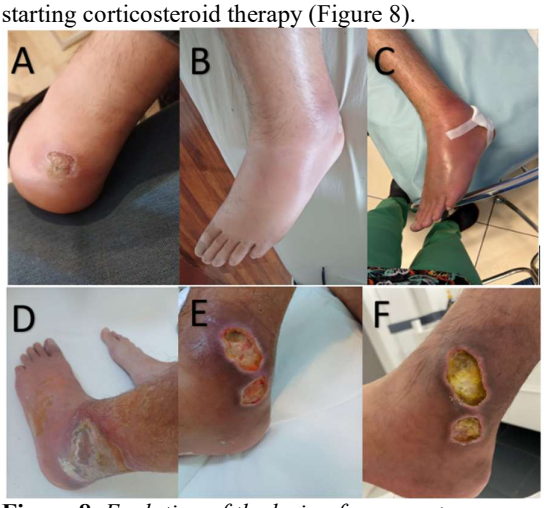

Figure 8. *Evolution of the lesion from onset*

Discussions

PG remains a complex and challenging entity both diagnostically and therapeutically. Its variable presentation, unpredictable course, and association with multiple systemic diseases make it a difficult diagnostic even for experienced clinicians. The coexistence of PG with gout, as illustrated in this case, is exceptionally rare, and the interplay between these two inflammatory conditions raises intriguing questions regarding shared immunopathogenic mechanisms, diagnostic pitfalls, and therapeutic approaches.

PG is classified within the spectrum of neutrophilic dermatoses—conditions characterized by sterile neutrophilic infiltration of the skin without identifiable infectious etiology [1,2]. Its estimated annual incidence ranges between 3 and 10 cases per million individuals, but true prevalence may be higher due to underdiagnosis and misclassification as infectious or vascular ulcers [3]. The disease often manifests between the third and fifth decades of life and shows no significant sex predilection, consistent with the age of the patient in the present case. Approximately 50% of PG cases are associated with systemic comorbidities such as inflammatory bowel disease, rheumatoid arthritis, hematologic malignancies, or autoimmune disorders [4]. However, its co-occurrence with gout is exceedingly uncommon and poorly characterized.

The rarity of PG–gout coexistence warrants special attention because the diagnostic overlap can lead to delayed or inappropriate management. In the present case, the initial clinical suspicion of cellulitis secondary to gouty arthritis was plausible, given the acute inflammation, fever, elevated inflammatory markers, and positive wound culture. However, the failure to respond to broad-spectrum antibiotics and rapid ulcer progression necessitated reconsideration of the diagnosis. This clinical trajectory underscores the

importance of maintaining a high index of suspicion for PG, particularly when ulcerative lesions worsen despite adequate antimicrobial therapy.

Although gout and PG are traditionally viewed as distinct entities—one being a crystal-induced arthritis and the other an idiopathic neutrophilic dermatosis—emerging evidence suggests potential immunological overlap. Both diseases are mediated by dysregulated neutrophil activity and cytokine-driven inflammation.

In gout, monosodium urate (MSU) crystals activate the NLRP3 inflammasome within macrophages, leading to the release of interleukin-1β (IL-1β), a pivotal cytokine that recruits and activates neutrophils [10]. Similarly, IL-1β plays a central role in PG pathogenesis, promoting neutrophil chemotaxis and activation within the dermis [11]. Elevated levels of IL-1, IL-8, TNF-α, and IL-17 have been identified in PG lesions, mirroring the cytokine milieu seen in acute gout flares [12]. This parallel inflammatory signature suggests that shared innate immune dysregulation may underlie the simultaneous occurrence of these disorders.

Neutrophil extracellular traps (NETs) have been implicated in the propagation of inflammation in both PG and gout. NET formation, while an essential antimicrobial mechanism, contributes to tissue injury and chronic inflammation when dysregulated. MSU crystals are potent inducers of NETosis, and similar neutrophil activation patterns have been observed in PG lesions [13]. The persistence of NETs in skin ulcers may perpetuate tissue destruction, providing a mechanistic explanation for the refractory ulceration observed in our patient despite infection control.

The diagnostic journey in this case exemplifies one challenge in clinical dermatology—the differentiation of PG from infectious or vascular ulcers. PG is a diagnosis of exclusion, as there is no pathognomonic histological or serological test. The clinical presentation typically involves a painful pustule or nodule that rapidly ulcerates, developing a necrotic base and violaceous undermined borders. However, early lesions may closely resemble cellulitis, abscess, or necrotizing infection, leading to inappropriate surgical debridement or antibiotic use [14].

The misdiagnosis rate of PG has been reported to exceed 30%, often resulting in unnecessary surgical procedures that exacerbate pathergy—the phenomenon wherein minor trauma induces new lesions or aggravates existing ones. In our patient, the initial positive wound culture for Streptococcus spp. and elevated procalcitonin levels confounded the diagnosis, suggesting secondary infection rather than primary PG. This case highlights the diagnostic complexity when infectious and inflammatory processes coexist.

Biopsy remains essential for confirmation, although histopathological findings are nonspecific. Typical features include epidermal ulceration, dermal edema, and dense neutrophilic infiltration, sometimes with leukocytoclastic vasculitis. The biopsy in this case revealed neutrophilic dermal infiltration with necrosis—findings compatible with PG and consistent with literature descriptions [15]. The absence of microorganisms on special stains and lack of vasculitic features supported the noninfectious inflammatory nature of the lesion.

Thus, PG management is rapid suppression of inflammation to prevent further tissue loss. Systemic corticosteroids, administered at doses of 0.5–1 mg/kg/day, remain first-line therapy and are effective in up to half of patients [16]. In our case, initiation of oral methylprednisolone 64 mg/day led to a marked improvement within one week, demonstrating both diagnostic confirmation and therapeutic efficacy. This rapid response underscores the importance of early immunosuppression once infection is excluded.

Cyclosporine, an alternative first-line agent, has shown equivalent efficacy to corticosteroids in randomized trials, particularly for patients with contraindications to steroids or refractory disease. Other immunomodulators such as azathioprine, methotrexate, and mycophenolate mofetil have been used as steroid-sparing agents [17]. More recently, biologic therapies targeting TNF-α, IL-1, IL-17, and IL-23 pathways have shown promise, particularly in refractory or associated systemic disease [18,19].

Given the shared IL-1–driven mechanisms between gout and PG, IL-1 inhibitors such as anakinra and canakinumab may hold particular therapeutic relevance for patients presenting with both conditions. Indeed, case reports have demonstrated resolution of refractory PG in patients treated with IL-1 blockade [20]. However, due to the rarity of coexistent disease, evidence remains anecdotal, and systematic evaluation is needed.

Furthermore, optimal wound care is critical in PG to support healing and prevent secondary infection. The TIME (Tissue, Infection, Moisture, Edge) framework provides a structured approach to wound management [21]. In our patient, sterile dressings and topical antiseptics such as povidone-iodine were used alongside systemic therapy, yielding progressive re-epithelialization. Surgical intervention should generally be avoided due to the risk of pathergy, although gentle debridement of necrotic tissue may be considered under adequate immunosuppression.

Successful management of PG, especially in complex cases such as this one, requires a multidisciplinary approach involving dermatology, rheumatology, infectious disease, and pathology teams. This collaborative model ensures comprehensive evaluation, timely diagnosis, and integrated therapy, reducing the risk of diagnostic delay or inappropriate intervention.

The question remains whether gout and PG coexist by coincidence or share a causal link. Epidemiologic evidence is sparse but suggestive. A population-based case-control study by Kridin et al. [4] reported a modest but statistically significant association between gout and PG, with an adjusted odds ratio indicating increased risk of PG among gout patients. However, due to the rarity of PG, even large-scale datasets yield limited absolute numbers, and causality cannot be inferred.

Potentially, chronic hyperuricemia and crystal-induced inflammation may serve as triggers for neutrophil priming and systemic immune activation, thereby lowering the threshold for PG development in genetically predisposed individuals. Additionally, recurrent gout flares lead to repeated corticosteroid exposure, which can alter immune homeostasis and paradoxically contribute to inflammatory dysregulation. In our case, the patient's long history of untreated recurrent gout may have created a persistent proinflammatory milieu, setting the stage for PG onset during a particularly intense flare.

Conversely, it is plausible that PG-induced systemic inflammation could exacerbate gout flares by promoting hyperuricemia and inflammatory stress. Therefore, a bidirectional relationship cannot be excluded. Future research should focus on cytokine profiling and genetic studies to elucidate whether gout constitutes a true predisposing factor or merely a coincidental comorbidity.

Diagnostic delay in PG is a major determinant of prognosis. Recent multicenter studies demonstrate that delayed diagnosis correlates with prolonged healing time, increased healthcare utilization, and higher rates of complications, including limb loss [22]. Haddadin et al. [23] reported that each month of diagnostic delay increased median healing time by up to 25%. In our case, the interval between initial presentation and definitive diagnosis was several weeks, during which the lesion expanded despite aggressive antimicrobial therapy. This highlights the critical importance of early recognition and prompt immunosuppressive treatment once infectious etiologies have been excluded.

Beyond its physical manifestations, PG imposes substantial psychological and quality-of-life burdens. Chronic pain, functional impairment, and visible disfigurement contribute to anxiety, depression, and social withdrawal [24]. In the presented case, the lesion's location on a weight-bearing joint further limited mobility and independence. Comprehensive care should thus incorporate psychological support and rehabilitation measures alongside medical therapy.

The rarity of PG–gout coexistence poses challenges to drawing definitive conclusions from single case reports. Nevertheless, such cases are invaluable for generating hypotheses and guiding future studies. Large-scale population-based analyses and mechanistic research are needed to clarify whether common inflammatory pathways mediate this association. Future work should explore cytokine profiles, inflammasome activation markers, and genetic polymorphisms shared between the two diseases. Moreover, prospective registries of neutrophilic dermatoses could help identify subtle associations and therapeutic responses across overlapping autoinflammatory conditions.

Conclusions

Thus, the present case report emphasizes the need for early recognition and diagnosis of PG and involves a young patient with no known comorbidities, who experienced more than 10 untreated gout attacks. The clinical course was complicated by the development of pyoderma gangrenosum, which significantly challenged the differential diagnosis. The frequent gout flares and early-onset disease (<40 years) are recognized as poor prognostic factors and showed treatment resistance and poorer outcomes. Delayed diagnosis significantly worsens prognosis, raising the risk of limb loss or death. Although the initial presentation was not suggestive for PG, the diagnosis was confirmed after exhaustive diagnostic workup. Early biopsy and collaboration between specialties are key to avoid unnecessary surgical procedures and to ensure prompt appropriate therapy.

In summary, the coexistence of pyoderma gangrenosum and gout, though rare, provides a unique window into the shared mechanisms of neutrophilic and autoinflammatory diseases. Both disorders are driven by innate immune dysregulation, characterized by excessive neutrophil activation, cytokine release, and tissue destruction. Clinically, their overlap can obscure diagnosis and delay effective treatment.

Conflicts of Interest: The authors declare no conflicts of interest.

Informed Consent: The patient provided written informed consent. The identity of the patient has been kept anonymous in accordance with ethical standards.

References

[1] George C, Deroide F, Rustin M. Pyoderma gangrenosum - a guide to diagnosis and management. Clin Med (Lond). 2019 May;19(3):224-228. doi: 10.7861/clinmedicine.19-3-224. PMID: 31092515; PMCID: PMC6542232.

[2] Ahronowitz I, Harp J, Shinkai K. Etiology and management of pyoderma gangrenosum: a comprehensive review. Am J Clin Dermatol. 2012 Jun 1;13(3):191-211. doi: 10.2165/11595240-000000000-00000. PMID: 22356259.

[3] Hasselmann, D.O.; Bens, G.; Tilgen et al. Pyoderma gangrenosum: Clinical presentation and outcome in 18 cases and review of the literature. J. Dtsch. Dermatol. Ges. 2007, 5, 560–564.

[4] Kridin, K.; Ludwig, R.J.; Tzur Bitan et al. Is Gout Associated with Pyoderma Gangrenosum? A Population-Based Case-Control Study. J. Clin. Med. 2020, 9, 1626. https://doi.org/10.3390/jcm9061626.

[5] Cabalag, M.S.; Wasiak, J.; Lim, S.W et al. Inpatient Management of Pyoderma Gangrenosum: Treatments, Outcomes, and Clinical Implications. Ann. Plast. Surg. 2015. [Google Scholar] [CrossRef]

[6] Vallerand, I.A.; Hardin, J. Ustekinumab for the treatment of recalcitrant pyoderma gangrenosum: A case report. SAGE Open Med. Case Reports 019, 7. [Google Scholar] [CrossRef]

[7] Ye, M.J.; Ye, J.M. Pyoderma gangrenosum: A review of clinical features and outcomes of 23 cases requiring inpatient management. Dermatol. Res. Pract. 2014. [Google Scholar] [CrossRef] [Green Version]

[8] A case of generalized atypical pyoderma gangrenosum mimicking Sweet syndrome Journal of the American Academy of Dermatology, Volume 68, Issue 4, AB39.

[9] Kaler J, Sheffield S, Thway M, et al Pyoderma Gangrenosum as a Presenting Feature of Undifferentiated Spondyloarthropathy with Erosive Inflammatory Arthritis. Case Rep Rheumatol. 2020 Mar

26;2020:1848562. doi: 10.1155/2020/1848562. PMID: 32274238; PMCID: PMC7136808.
[10] So A, Martinon F. Inflammation in gout: mechanisms and therapeutic targets. Nat Rev Rheumatol. 2017;13(11):639–647.
[11] Maverakis E, Marzano AV, Le ST, et al. Pyoderma gangrenosum. Nat Rev Dis Primers. 2020;6(1):81. [DOI] [PubMed] [Google Scholar][Ref list]
[12] Maronese CA, Pimentel MA, Li MM et al. Pyoderma gangrenosum: an updated literature review on established and emerging pharmacological treatments. Am J Clin Dermatol. 2022;23(5):615–634. [DOI] [PMC free article] [PubMed] [Google Scholar][Ref list]
[13] Schauer C, Janko C, Munoz LE, et al. Aggregated neutrophil extracellular traps limit inflammation by degrading cytokines and chemokines. Nat Med. 2014;20(5):511–517.
[14] Pereira N, Brites MM, Goncalo M, et al. Pyoderma gangrenosum a review of 24 cases observed over 10 years. Int J Dermatol. 2013;52(8):938–945. doi: 10.1111/j.1365-4632.2011.05451.x. [DOI] [PubMed] [Google Scholar][Ref list]
[15] Chakiri R, Baybay H, Hatimi A et al. Clinical and histological patterns and treatment of pyoderma gangrenosum. Pan Afr Med J. 2020 Jun 2;36:59. doi: 10.11604/pamj.2020.36.59.12329. PMID: 32733629; PMCID: PMC7371440.
[16] Brooklyn T, Dunnill MG, Probert CS. Diagnosis and treatment of pyoderma gangrenosum. BMJ. 2006;333(7560):181–184.
[17] Ormerod AD, Thomas KS, Craig FE, et al. Comparison of the two most commonly used treatments for pyoderma gangrenosum: results of the STOP GAP randomised controlled trial. BMJ. 2015;350:h2958.
[18] Brooklyn TN, Dunnill MG, Shetty A, et al. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. Gut. 2006;55(4):505–509.
[19] Ortega-Loayza AG, Nugent WH, Lucero OM, et al. Biologic therapy in pyoderma gangrenosum: a systematic review. J Am Acad Dermatol. 2020;82(5):1323–1331.
[20] Kolios AG, Yawalkar N, Anliker MD. Successful treatment of pyoderma gangrenosum with the interleukin-1 receptor antagonist anakinra: a case report. Br J Dermatol. 2015;172(3):824–826.
[21] Schultz GS, Sibbald RG, Falanga V, et al. Wound bed preparation: a systematic approach to wound management. Wound Repair Regen. 2003;11(Suppl 1):S1–S28
[22] Erduran F, Adışen E, Hayran Y, et al. Analysis of clinical characteristics and factors affecting treatment responses in patients with pyoderma gangrenosum: a multicenter study of 239 patients. An Bras Dermatol. 2024 Nov-Dec;99(6):815-825. doi: 10.1016/j.abd.2024.02.002. Epub 2024 May 11. PMID: 38735817; PMCID: PMC11551399.
[23] Haddadin OM, Erickson KM, Latour E, et al. Impact of delay of diagnosis of pyoderma gangrenosum on healing outcomes and health care utilization: A prospective cohort study. J Am Acad Dermatol. 2024 Dec;91(6):1274-1277. doi: 10.1016/j.jaad.2024.08.038. Epub 2024 Aug 24. PMID: 39187020.
[24] Reichrath J, Bens G, Bonowitz A, et al. Treatment recommendations for pyoderma gangrenosum: an evidence-based review of the literature based on more than 350 patients. J Am Acad Dermatol. 2005;53(2):273–283.

Corresponding author

Madalina Pusa Rosu, Department of Rheumatology, "Sfanta Maria" Clinical Hospital, Bucharest, Romania, email: madalina.duna@yahoo.com

Received: 16.08.2025

Accepted: 28.09.2025