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CASE REPORT

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Pyoderma Gangrenosum – a Challenging Diagnostic Approach

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ABSTRACT

Pyoderma gangrenosum (PG) is an infrequent, aseptic neutrophilic dermatosis that can be observed in patients with systemic diseases such as inflammatory bowel disease or rheumatic disorders.

Due to its rare entity, PG often constitutes a diagnostic enigma, as it simulates other skin disorders. Typically, it is displayed as painful, ulcerative lesions localized to the lower extremities. In our study, we present a case of a 67-year-old woman with recently diagnosed ulcerative colitis who presented with two painful ulcers, one on the left anterior tibia and the other one on the left subclavian area. Initially, their clinical image overlapped with skin abscess. However, taking into account patient's medical history, skin examination, sterile wound cultures and skin biopsy, the diagnosis of PG was established. The patient was completely recovered with high doses of corticosteroids, daily wound changes and surgical intervention involving loose wound edge approximation. In this study, we highlight that clinicians should always be aware of patient's medical history in such cases, in order to early diagnose PG and avoid inaccurate medical approaches which might have an impact on patients' quality of life.

Keywords: pyoderma gangrenosum, tibia, sternum, pathergy, suture.

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ABBREVIATIONS

PG: pyoderma gangrenosum
IBD: inflammatory bowel disease
MMF: mycophenolate mofetil
NPWT: negative pressure wound therapy
IVIG: intravenous immunoglobulin

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare inflammatory condition characterized by skin wounds and lesions. Mostly, this manifestation is detected as a large ulcer that comes from the continuous change in the initial small nodules with reddish appearance, often surrounded by bluish or greenish borders (1, 2).

PG is regarded as a rapidly progressive process that destroys the skin tissue and can even lead to necrosis of the affected area (3). This form, also known as ulcerative PG, is often described in the lower extremities or trunk. Other forms of pyoderma gangrenosum are bullous, pustular and vegetative (3).

Pain is a prominent feature in the affected area and the ulcers are exceptionally painful, frequently accompanying the clinical manifestations of any underlying disease. The most commonly associated conditions with PG are inflammatory bowel disease, other autoimmune diseases such as systemic sclerosis, systemic lupus erythematosus and some types of arthritis and hematologic malignancies. Consequently, PG is usually paired and associated with systemic diseases (4-6).

As far as the pathophysiology of pyoderma gangrenosum is concerned, underlying mechanisms have been suggested but the knowledge remains limited. Pyoderma gangrenosum belongs to the group of neutrophilic dermatoses (7, 8). In order to differentiate and exclude other clinical conditions that can mimic pyoderma gangrenosum, such as skin abscesses or other form of infections, malignancies or trauma, skin biopsies for analysis and wound cultures might be useful (8). Microscopic findings of pyoderma gangrenosum are non-specific. Taking into account a skin biopsy obtained from the peripheral borders will regularly reveal a perivascular infiltrate, filled with neutrophilic and lymphocytic cells and underlying edema of endothelial cells. When the ulcer is present, a diagnosis of neutrophilic dermatosis can be made based on the biopsy, with the distinction from other similar conditions being the negative results of wound cultures (8). In fact, no certain treatment guideline has been established for PG. Clinical manifestations guide the therapeutic targets, often considering any coexisting diseases. In cases of mild and localized disease, local treatment agents could be useful. However, in more severe and multifocal cases of PG, systemic steroids or immunosuppressive agents, such as cyclosporine, remain the main field of the therapeutic approach (9, 10).

The purpose of the current study was to present a case of a PG which was mimicking clinical manifestations of skin abscess and was initially treated accordingly. However, after cautious medical history acquisition, skin examination, wound cultures obtainment and skin biopsy, the diagnosis of PG was conducted. We also demonstrate the treatment process that was followed for the successful management of this autoinflammatory disorder. ❑

CASE PRESENTATION

A 67-year-old Caucasian woman presented to the emergency department of our Hospital in May 2022 with a large painful ulcerated lesion on her left anterior tibia. The lesion had appeared a few days earlier without any prior injury. She had a previous medical history of ulcerative colitis, which had been diagnosed four months ago and was being under control with daily doses of mesalazine 2 gr per os. Vital signs indicated a low-grade fever, tachycardia and normal blood pressure. Laboratory tests revealed the following results in her complete blood tests: leukocytosis (WBC 16.89), anemia (Hb/Hct 7.8/24.7), ESR 112, CRP 30.9). Physical examination showed a deep, itchy and painful sore with erythematous and violaceous undermined border on the left proximal tibia, with a size of 4 x 3 cm, located just below the knee joint and over the tibial tubercle. A smaller lesion sizing about 1 x 2 cm that resembled a purulent base was identified on the patient's sternum (left sternoclavicular area).

Initially, orthopedic and general surgeons were invited to evaluate the patient. The diagnosis of skin abscess due to cutaneous infection was made, followed by a thorough surgical debride-

ment of the lesions. Wound cultures were also taken. Patient was then referred to the internal medicine department because of anemia and the presence of inflammatory bowel disease. Upon admission to the internal medicine ward, empirical antibiotics (intravenous ciprofloxacin and clindamycin) and analgesics were administered, without significant amelioration. Blood and second wound cultures were collected but no culture managed to reveal any suspected microorganisms.

Considering the patient's medical history along with the clinical profile of both lesions and the negative result of wound cultures, a strong presumption of PG diagnosis was made. Further orthopedic consultation was requested and the retrieval of a skin biopsy was decided. A 5 mm skin sample was obtained from the laceration's edge and was sent to the histopathology department. The microscopic analysis revealed dense, neutrophilic infiltrate throughout the dermis, presence of giant cells, hyperkeratosis, hyperacanthosis, necrosis and ulceration of the overlying epidermis as observed in PG. No organisms were found. Therefore, the diagnosis of PG was confirmed.

Intravenous prednisolone 1 mg/kg was administered as initial treatment. Moreover, hepatitis virus panel revealed chronic hepatitis B infection; thus, concomitantly with prednisolone administration, antiviral therapy with tenofovir was added in order to prevent reactivation of the virus. Following the initiation of intravenous steroid therapy, the ulcers showed an encouraging response with improvement in their clinical presentation, while the patient reported a decrease in pain intensity. Daily wound changes of both lesions were performed using lukewarm sterile saline to reduce irritation and absorbent antibacterial dressings were applied to minimize bacterial colonization. The steroid therapy was gradually tapered over the subsequent days. However, after two weeks of intravenous administration of corticosteroids, the skin lesion over the tibial tubercle remained considerable, with exposed important tissue structures such as the distal patellar tendon and periosteum, prone to high risk of infection.

Herein, a decision was made to remove necrotic tissue and approximate the skin edges using three loose horizontal mattress size 2.0 nylon sutures. Daily routine dressing changes con-

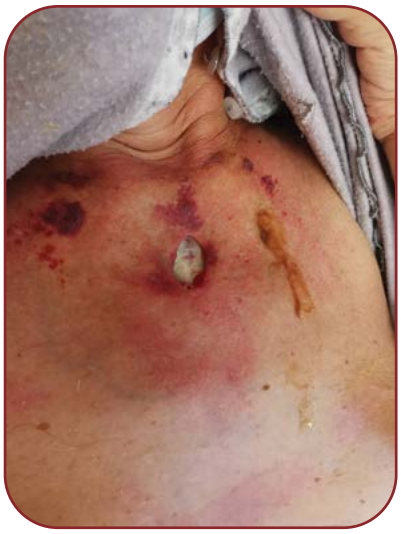

FIGURE 1. Ulcer of the sternum (left sternoclavicular area) upon admission after the initial debridement

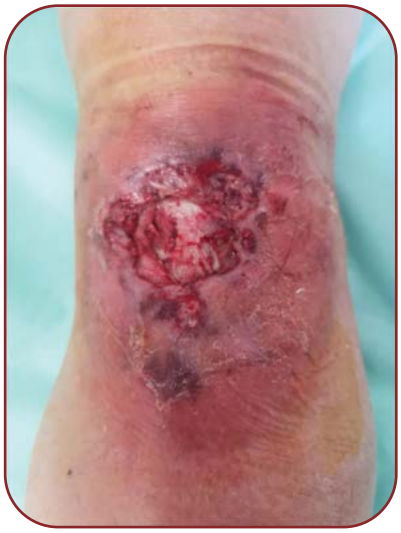

FIGURE 2. Ulcer of the left anterior proximal tibia upon admission after the initial debridement. The exudative wound base is surrounded by an undermined border and peripheral erythema

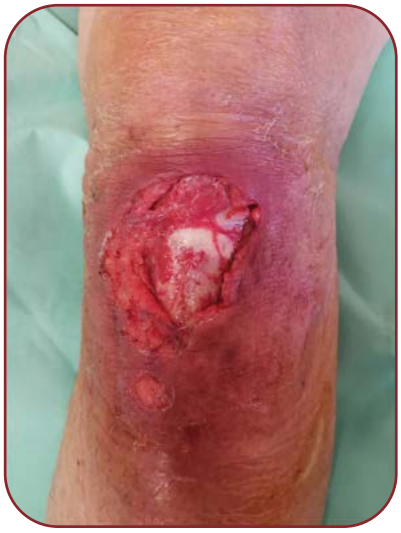

FIGURE 3. Ulcer after one week following debridement. Clinical deterioration of the ulcer and exposure of important tissues (distal patellar tendon and periosteum) can be observed

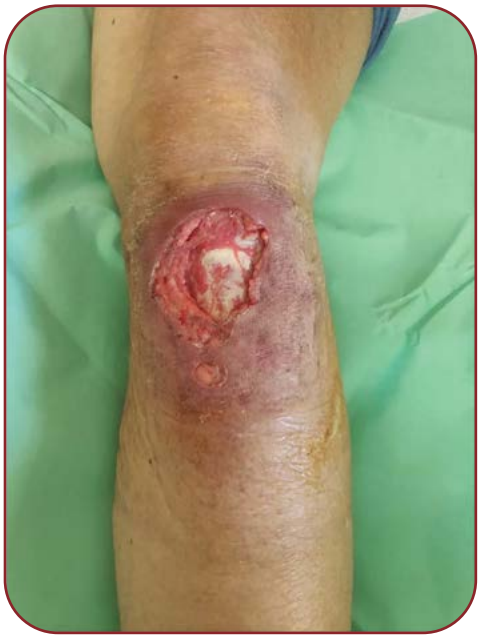

FIGURE 4. Ulcer after two weeks of corticosteroid therapy and daily wound changes. The peripheral erythema has been resolved

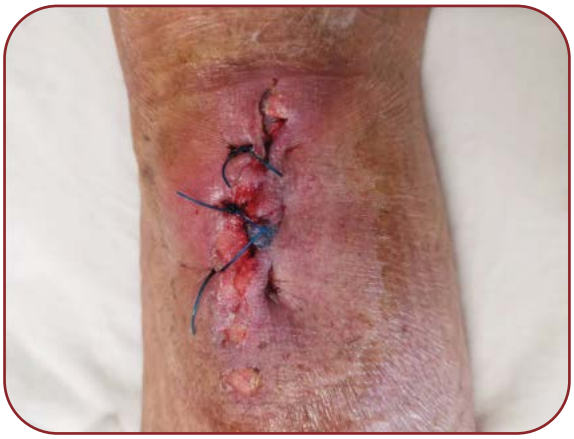

FIGURE 5. Approximation of skin edges with three loose horizontal mattress size 2.0 nylon sutures

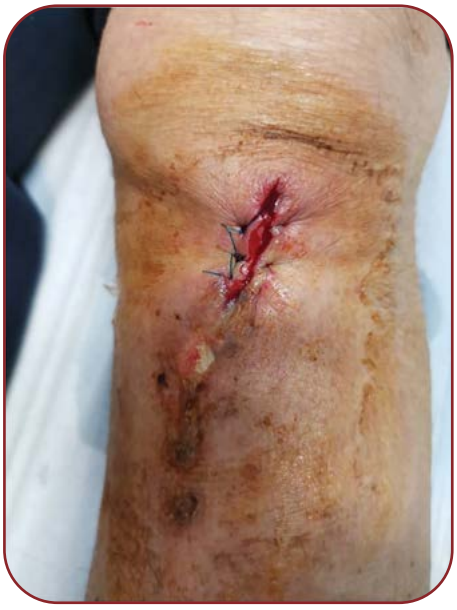

FIGURE 6. Ulcer after four weeks following the initial treatment

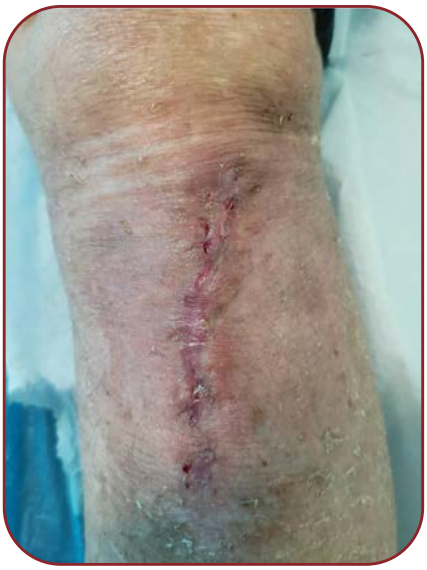

FIGURE 7. A complete healing of the lesion after six weeks following the initial treatment

tinued. The discharge treatment plan included administration of methylprednisolone 16 mg *per* os daily and re-evaluation in a gastroenterology clinic. After fifteen days, the ulcer displayed a remarkable improvement and nylon sutures were removed. After one month, the laceration on the tibia had been completely healed, while the ulcer on patient's sternum had also been healed by secondary intention and the patient had returned to her daily activities. ❑

DISCUSSION

Not only the diagnosis but also the treatment of PG might be demanding. Despite its characteristic clinical appearance, there are several other ulcerative conditions that can be its mimickers, leading to potential diagnostic errors. In this particular case, the clinical manifestation resembled a cutaneous infection with the appearance of an abscess-like lesion in the tibia and was referred for orthopedic consultation. Orthopedic surgeons rarely come across the clinical entity of PG in the emergency department. Therefore, it was primarily misdiagnosed, whereas surgical debridement and drainage that followed led soon to wound aggravation.

Pyoderma gangrenosum is a rare autoinflammatory skin disorder which falls into the category of neutrophilic dermatoses, mostly presenting as an extra-intestinal manifestation in patients with underlying IBD. While PG can make its appearance in any age group, several studies suggest that more frequently, it might be observed in the

mid-40s (8, 11). The differential diagnosis of PG includes vascular occlusion or stasis, cutaneous involvement of a malignancy, primary cutaneous infections, vasculitis, drug-induced disorders, exogenous tissue injury, hypertension (Martorell ulcer), calciphylaxis and other inflammatory disorders (12, 13). Hence, PG is considered as a diagnosis of exclusion.

Currently, there are no established, evaluated or validated diagnostic criteria to confirm the possible existence of PG. Su *et al* proposed a diagnostic framework, that includes four minor and two major criteria (12). The PARACELSUS score is another diagnostic tool that can be specifically used for the differential diagnosis with venous leg ulcers, based on major, minor and additional criteria, with a total score of 10 points or above, highly indicative of PG diagnosis (14). In addition, Marevakis *et al* proposed an enhanced diagnostic framework using one major criterion-biopsy of ulcer edge demonstrating neutrophilic infiltrate-and eight minor criteria which are based on certain factors (15).

However, none of these diagnostic algorithms have been widely adopted so far, rendering PG a real diagnostic odyssey. Generally, the diagnosis of PG relies on clinical history, histopathology, clinical manifestation and assessment, exclusion of other causes of skin ulceration and resolution pattern. There is no diagnostic gold standard, and the clinical suspicion of PG should be seriously taken into consideration when managing ulcers in order to offer the best therapeutic option (16).

In general, there is no consensus guideline for treatment of PG. Mostly, it is based on clinical experience and continues to rely on immunosuppressive agents as the main cornerstone. The combined routine wound care along with the use of local or systemic immunosuppressant agents remains the central component of treatment (17). Local therapy includes regular wound care with dressings and compression or even use of topical corticosteroids and calcineurin inhibitors (16). In certain cases, depending on the size and location of the wound, treatment may involve autologous skin grafts, allogeneic skin grafts, xenograft skin grafts, negative pressure wound therapy (NPWT) and free flap grafts (16).

Systemic therapy consists of oral or intravenous corticosteroids usually prednisolone (0.5-1 mg/kg/day). Systemic corticosteroids should be attempted as first-line therapy, but complete remission is achieved in no more than 40% of cases. The combination of corticosteroids with immunosuppressive/immunomodulatory adjuvants, with the most common agent being cyclosporine may be considered as the most appropriate therapy for PG, especially multifocal (18). Other systemic treatment options with varying clinical responses and success include methotrexate (preferred in patients with PG and concomitant neoplasm, where cyclosporine and other immunosuppressants are contraindicated), mycophenolate mofetil (MMF), azathioprine, tacrolimus, dapsone, colchicine (limited cases), thalidomide (primary or idiopathic PG when other treatments fail) and intravenous immunoglobulin (IVIG) (17).

The use of biological agents introduced a new era in managing PG, with a shift towards the use of anti-tumor necrosis factor drugs (*e.g.*, infliximab, adalimumab, etanercept, golimumab and certolizumab), antiinterleukin (IL)-12/IL-23 drugs (*e.g.*, ustekinumab), anti-IL-23 drugs (*e.g.*, tildrakizumab), a receptor antagonist (*e.g.*, anakinra); IL-1β antagonists (*e.g.*, canakinumab and gevokizumab), anti-IL-6 receptors (*e.g.*, tocilizumab), anti-IL-17 drugs (*e.g.*, secukinumab), and JAK-STAT inhibitors (*e.g.*, tofacitinib and ruxolitinib) as second-line therapies with great potential and good clinical responses (19).

In our case, due to the large wound expanse, exposure of essential tissue structures and high risk of infection, as the patient was on prednisone for about two weeks, the mobilization and approximation of skin edges with sutures was designated. This approach allowed for complete wound healing without inducing pathergy. Similarly, Hasan *et al* chose a similar treatment for a genital PG, accomplishing loose wound closure with a horizontal mattress technique in order to protect the exposed testicle (20). ❑

CONCLUSIONS

Pyoderma gangrenosum remains a field of interest, often challenging to diagnose and treat. It is important for clinicians across various specialties to consider PG in their differential diagnosis when encountering patients with skin lesions or ulcers. A plethora of conditions simulates PG, and its diagnosis is not based on validated criteria. Hence, its diagnosis is often delayed or

missed. As performed in our case, we emphasize the importance of obtaining a detailed patient history and collecting wound cultures in patients initially suspected of having a soft tissue infection. Furthermore, in cases where skin integrity is compromised, leaving underlying tissues exposed and thus prone to possible infection, an alternative therapeutic pathway that involves using corticosteroids as first-line therapy in combination with loose wound suturing, can demonstrate excellent results. ❑

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Informed consent: We undersign, certificate that we have the written consent of the identifiable person in order to describe the cases in this scientific paper.

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