

Extensive perianal pyoderma gangrenosum, diagnostic-therapeutic approach to a complicated patient. Case report and literature review

Extenso pioderma gangrenoso perianal: abordagem diagnóstico-terapêutica de um paciente complicado. Relato de caso e revisão da literatura

DOI: <http://www.dx.doi.org/10.5935/scd1984-8773.2022140211>

ABSTRACT

Background: Pyoderma gangrenosum is a rare neutrophilic dermatosis with very low incidence and varied clinical presentation associated with different comorbidities. It is also a diagnostic-therapeutic challenge. Clinical case: A 79-year-old woman presented 18 months of dermatosis evolution that began as a perianal pustule and progressed to a 20 cm in diameter ulcer. Due to her comorbidities, she received topic treatment with satisfactory evolution. Conclusions: Pyoderma gangrenosum is frequently associated with a systemic disease. Consequently, it must be approached from a systemic perspective with the support of a multidisciplinary team to provide the most appropriate treatment.

Keywords: Pyoderma gangrenosum, Skin diseases, Peptic ulcer hemorrhage, Hypothyroidism

RESUMO

Introdução: O pioderma gangrenoso é uma dermatose neutrofílica rara, de baixíssima incidência e apresentação clínica variada, associada a diversas comorbidades, também um desafio diagnóstico-terapêutico. **Caso clínico:** Paciente do sexo feminino, 79 anos, apresentava 18 meses de evolução da dermatose que se iniciou como pústula perianal e evoluiu para úlcera de 20 cm de diâmetro. Devido às suas comorbidades, recebeu tratamento tópico com evolução satisfatória. **Conclusões:** O pioderma gangrenoso está frequentemente associado a uma doença sistêmica. Consequentemente, deve ser abordado numa perspectiva sistêmica com o apoio de uma equipe multidisciplinar para fornecer o tratamento mais adequado.

Palavras-chave: Pioderma gangrenoso, Doenças cutâneas, Úlcera péptica, Dermatopatias

Case report

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Financial support: None

Conflict of interest: None

Submitted on: 04/01/2023

Approved on: 12/02/2023

How to cite this article:

Pérez-Campos LA, Gutiérrez-Ávila SA, Alcántara-Ramírez VD, Dávila-Rodríguez DO. Extensive perianal pyoderma gangrenosum, diagnostic-therapeutic approach to a complicated patient. Case report and literature review. Surg Cosmet Dermatol. 2023;15:e20230211.



BACKGROUND

Pyoderma gangrenosum is a chronic inflammatory neutrophilic dermatosis characterized by single or multiple painful ulcers. It has varied clinic presentations depending on the infiltrated regions,¹ and its approach continues to be an exclusion diagnosis.² Its incidence is 3–10 patients per one million worldwide.³

Its etiology is complex, multifactorial, and still poorly understood. It involves genetic interaction, environmental factors, immune dysregulation, altered neutrophil chemotaxis, and keratinocyte apoptosis with molecular patterns release associated with damage.⁴

Underlying systemic diseases are present in up to 77% of cases.⁵ Inflammatory bowel disease, rheumatoid arthritis, and hematological malignancies, among others, are the more frequently associated diseases.²

Five clinical variants make its diagnosis a challenge: classic (ulcerative), bullous, vegetative, pustular, and peristomal.⁶ Therefore, Delphi criteria with 86% sensitivity and 90% specificity (**Table 1**)⁷ and PARACELSUS score were recently defined to improve the diagnostic approach (**Table 2**).²

The pretibial area, peristomal skin, chest, hands, head, and neck are the primary skin location, and it is infrequent in the perianal area.⁸ Gulliver's sign can clinically evaluate their therapeutic response due to epithelial growth in the ulcer edge towards the center, leaving cribriform scars.⁹

Histopathology of early lesions classically shows deep suppurative, follicular-centric inflammation, dense neutrophilic infiltrates, and leukocytoclastic vasculitis. Then, the mixed inflammatory infiltrate predominates with neutrophils and epidermal ulceration. However, it is an inconsistent finding, not pathognomonic.¹⁰

Regarding treatment, currently, no drug has been approved by the Food and Drug Administration (FDA). Traditional

therapies include corticosteroids and other immunosuppressants, either local or systemic. Recently, biological therapies have become a trend.² Nevertheless, there is lacking of scientific evidence from large clinical trials that assess safety, efficacy, adverse events, and outcomes.

Pyoderma gangrenosum is a rare disease,^{3–4} which makes it challenging to conduct large clinical trials and observational studies with adequate statistical significance. Hence, observational studies such as case reports, case series, and trials in reference centers, among other strategies, become relevant¹¹ to evaluate the diagnostic-therapeutic approach, reporting their outcomes toward establishing records to provide the basis for future extended review development.

Therefore, we report a case of extensive perianal pyoderma gangrenosum in the presence of gastrointestinal bleeding secondary to duodenal ulcer and hypothyroidism, highlighting the importance of an individualized diagnostic-therapeutic approach based on comorbidities and clinical history.

Presentation of the case

A 79-year-old woman referred from the first level of care through a diagnosis of ulcer disease with a history of primary hypothyroidism, systemic arterial hypertension, acid peptic disease, hemorrhoidal disease, and bilateral knee osteoarthritis associated with the chronic use of nonsteroidal anti-inflammatory drugs for one year.

On physical examination, she presented a localized dermatosis in the perianal region consisting of a 20 cm approximately ulcer with undermined and erythematous-violaceous edges with fibrinous tissue associated. The condition started 18 months before the patient's admission with a pustule that progressed to a painful ulcer (**Figure 1**). She went to a dermatologist, who performed a skin biopsy, which reported leukocytoclastic vas-

TABLE 1: Delphi criteria. Positive by having the major criterion and 4 minors.⁷
The patient presents the major criterion and 5 minor criteria

Major criterion	
1.	Biopsy with neutrophilic infiltrate
Minor criteria	
1.	Exclusion of infection
2.	Pathergy
3.	Personal history of Inflammatory Bowel Disease or inflammatory arthritis
4.	History of papule, pustule, or vesicle that rapidly ulcerates within 4 days of appearing
5.	Peripheral erythema, undermining border, and tenderness at ulceration site
6.	Multiple ulcerations (at least one on anterior lower leg)
7.	Cribriform or "wrinkled paper" scar (s) at healed ulcer sites
8.	Decrease in ulcer size after immunosuppressive treatment

TABLE 2: PARACELSUS SCORE. Suggestive of Pyoderma=10 or more points. Venous ulcers = < 7 points.²
The patient has 13 points

P	Progressing disease (ulcer developing within 6 weeks). Mayor. 3 points
A	Assessment of relevant differential diagnoses. Mayor. 3 points
R	Reddish-violaceous wound margin. Mayor. 3 points
A	Amelioration (Alleviation) by immunosuppressant drugs. Minor. 2 points
C	Characteristically irregular (bizarre) ulcer shape. Minor. 2 points
E	Extreme pain >4/10 on visual analogue scale. Minor. 2 points
L	Localization of lesion at site of trauma (pathergy). Minor. 2 points
S	Suppurative inflammation in histopathology. Additional. 1 point
U	Undermined wound border. Additional. 1 point
S	Systemic disease associated. Additional. 1 point



FIGURE 1: Perianal ulcer characterized by irregular, violaceous, raised borders with a grainy background

culitis. (**Figure 2**) Upon admission to the hospital, the patient presented pale skin and low cardiac output data. She was admitted to the internal medicine service, protocolized, and treated by the endoscopy service for suspected inflammatory bowel disease. However, they observed digestive bleeding secondary to a duodenal ulcer.

Pyoderma gangrenosum treatment started based on a high-potency topical steroid (clobetasol) due to the contraindication of systemic therapy, and the patient demonstrated improvement of the condition.

After a 2-month follow-up, the patient did not present any recurrence, with a complete lesion healing after 30 days.

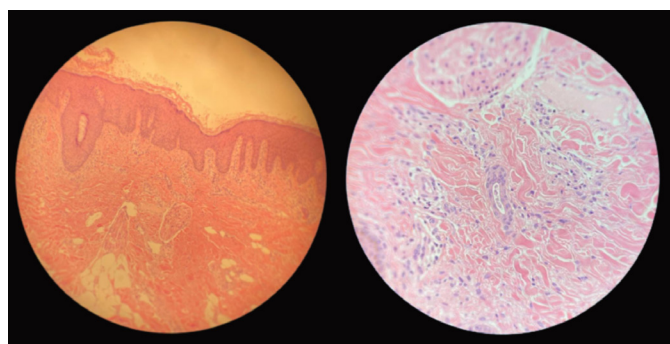


FIGURE 2: Skin biopsy showing the epidermis with lamellar horny layer, horny plugs, moderate irregular acanthosis, dermis with vessels with fibrinoid degeneration in its wall, surrounded and invaded by neutrophils, moderate and diffuse infiltrate between collagen fibers by lymphocytes, histiocytes, epithelioid cells, and neutrophils

DISCUSSION

The researchers present a diagnostic-therapeutic approach to rare pyoderma gangrenosum location associated with comorbidities. Based on the Delphi and PARACELSUS scores, we established the diagnosis, which is currently internationally accepted, generating homogeneity when reporting the results and reducing the diagnostic-therapeutic approach. However, future studies of greater statistical relevance are required.

The association with hypothyroidism and pyoderma gangrenosum is new in the medical literature, and it was recently added to its list of systemic associations. Thus, it should receive special attention in future reviews since it is relevant to the disease pathophysiology and its relationship with the decrease in collagen and hydroxyproline in wounds during the inflammatory and the proliferative phase, we emphasize the maintenance of endocrinological control to improve healing conditions.¹¹

Therefore, we emphasize maintaining endocrinological control to improve healing conditions. However, more scientific evidence should be available regarding relationships and clinical results.

Regarding treatment, in localized forms, topical therapy has shown an excellent response.¹² A prospective study assessed topical tacrolimus 0.03% and clobetasol 0.05% and observed that 44.8% of individuals presented a response at six months, 33% required systemic treatment, and 15% had recurrent disease.¹³ We opted for clobetasol only, considering that steroids increase the risk of bleeding or perforation in hospitalized patients,¹⁴ and we observed improvement of the lesion in a 3-month follow-up.

Recently, in an updated literature review, the researchers proposed a treatment algorithm based on evidence-based medicine.¹⁵ The study points out that an ulcer ≥ 3 cm, ≥ 3 lesions, or $\geq 5\%$ body surface involvement is classified as a mild disease and proposes that these patients receive treatment for pain and topical therapy, leaving the systemic therapy for those with moderate or severe disease or with a contraindication for this treatment, as is the case of the presented patient.

Finally, no international guidelines assess the results in patients with comorbidities contraindicating the use of systemic and biological therapies. Thus, it justifies the topical treatment, and the clinical result was favorable. The preceding may form the basis for future reviews and research projects focused on topical therapy in a complicated patient with a contraindication to systemic treatment.

This article has well-established limitations, as it is a case report, so the results presented here should be considered carefully. However, the researchers adequate the paper to international guidelines (CARE), thus increasing its internal validity. On the other hand, using this resource acquires epidemiological relevance in rare diseases such as this case.¹¹

CONCLUSION

Pyoderma gangrenosum is a neutrophilic dermatosis with a diagnostic-therapeutic challenge, notwithstanding that there are few clinical studies due to the low prevalence of the disease, leading to the limited information or little statistical relevance on the clinical outcome and response to treatment. On the other hand, the literature still has not reported pyoderma gangrenosum in the perianal area in the presence of multiple comorbidities. The recent standardization of diagnostic criteria is a tool that can facilitate timely diagnosis and treatment to avoid the risk of developing squamous cell carcinoma.¹⁶

It is frequently associated with a systemic disease, so it must be approached from a systemic perspective with the support of a multidisciplinary team to provide the best treatment.

Patient perspective: “During my hospitalization, multiple specialties assessed each of my diseases to give appropriate and individualized treatment to my case. I went to several doctors for more than a year; however, it was not until this last hospitalization that I improved. ●

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