

Pyoderma gangrenosum – a clinical manifestation of difficult diagnosis*

Pioderma Gangrenoso - apresentação clínica de difícil diagnóstico

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Abstract: Pyoderma gangrenosum is an uncommon ulcerative cutaneous dermatosis associated with a variety of systemic diseases including inflammatory bowel disease, arthritis, hematological malignancies, hepatitis and acquired immunodeficiency syndrome (AIDS). The pathogenesis of pyoderma gangrenosum remains unknown. Its diagnosis is usually based on clinical evidence and confirmed through a process of elimination of the other possible causes of cutaneous ulcers. This report describes a case of pyoderma gangrenosum with extensive ulceration that responded well to treatment.

Keywords: Diagnosis; Primary Treatment; Pyoderma gangrenosum

Resumo: Pioderma gangrenoso é uma dermatose cutânea ulcerativa incomum, associada a uma variedade de doenças sistêmicas, incluindo doença inflamatória intestinal, artrites, neoplasias hematológicas, hepatites e aids. A sua patogênese é desconhecida. O diagnóstico geralmente é baseado em evidências clínicas e confirmado com a exclusão das outras etiologias de lesões ulceradas cutâneas. Relatamos um caso de PG com ulcerações extensas com boa resposta ao tratamento.

Palavras-chave: Diagnóstico, Pioderma gangrenoso, Tratamento primário

Introduction

Pyoderma gangrenosum (PG) is an inflammatory, neutrophilic dermatosis of unknown etiology that affects principally adults of 20-50 years of age.¹ It was first described by Brusting et al. in 1930 in a patient with ulcerative colitis. PG is idiopathic in 25-50% of cases. In approximately 50% of cases, an association has been described with systemic diseases such as Crohn's disease, monoclonal gammopathies, seropositive arthritis, collagenoses, Behçet's disease, Wegener's granulomatosis and myeloproliferative and infectious diseases, principally hepatitis and acquired immunodeficiency syndrome (AIDS).²⁻⁴ Some patients with PG have abnormalities in cell and humoral immunity, with an increase in interleukin (IL) expression, particularly IL-8 and tumor necrosis

factor-alpha (TNF- α).⁵ Clinically, four variants exist: the ulcerative, bullous, vegetative and pustular forms. The most common variant is the ulcerative form, which begins with papules or nodules and rapidly progresses to ulcerated, painful lesions. In up to 25% of cases of PG, the appearance of new lesions may have been triggered by trauma such as insect bites, intravenous injections or biopsy, a phenomenon known as pathergy.^{6,7}

The present study reports on a case of extensive PG of difficult diagnosis in which an excellent response to treatment was achieved with corticoids, initially associated with clofazimine and dapsone and, later, with azathioprine.

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Case Report

The patient was a 34 year-old, single female with an ulcerated lesion on her face that had been present for a year, extending to the neck and the anterior and posterior thoracic region. At dermatological examination, ulcerated lesions with elevated borders and a base covered with seropurulent material were found on the face, neck and the upper portion of the anterior and posterior thoracic region (Figure 1). At the time of physical examination, differential diagnoses included PG, atypical mycobacteriosis and vasculitis.

The following supplementary tests were requested: full blood count, glucose, urea, creatinine, cholesterol, triglycerides, transaminases, alkaline phosphatase, gamma GT, uric acid, lactic dehydrogenase (LDH) and electrolyte levels, all of which were found to be within the normal range. Urinalysis was normal. Sputum smear was negative for acid-fast bacilli, chest x-ray was normal and two mycobacterium cultures were negative. VDRL and HIV testing was negative. Antinuclear factor (ANF), anti-double-stranded DNA antibodies, and C-reactive protein were also negative. Histology showed an edema in the papillary dermis with perivascular, lymphohistiocytic inflammatory infiltrate and neutrophilic polymorphonuclear leukocytes extending into the hypodermis (Figure 2). Wade and Grocott stains showed no parasitic structures.

In view of the clinicopathological correlation and the exclusion of other diagnostic hypotheses, immunosuppressive therapy for PG was implemented. Initially, pulse therapy with intravenous methylprednisolone at a dose of 500 mg/day was used for three days, followed by 100 mg of prednisone orally, resulting in progressive regression of the lesions. In the initial phase, 100 mg/day of dapsone and 100 mg/day of clofazimine were associated. Later, these drugs were substituted by oral azathioprine at a total dose of 50 mg/day. During treatment, the patient developed an ulcerated lesion on the lower third of her left leg (Figures 3A and 3B), which healed completely following therapy (Figure 3C).

The patient has been in follow-up for PG as an outpatient for the past eighteen months, with complete remission of all the lesions. She is currently in use of prednisone at a dose of 20 mg/day and oral azathioprine at a dose of 50 mg/day. She has severe scarring with fibrotic strands, atrophy (Figures 4A, 4B and 4C) and ectropion in the lower left palpebral region (Figure 5).

Discussion

In cases of PG, the clinical and pathological findings and the evolution of the lesions are impor-

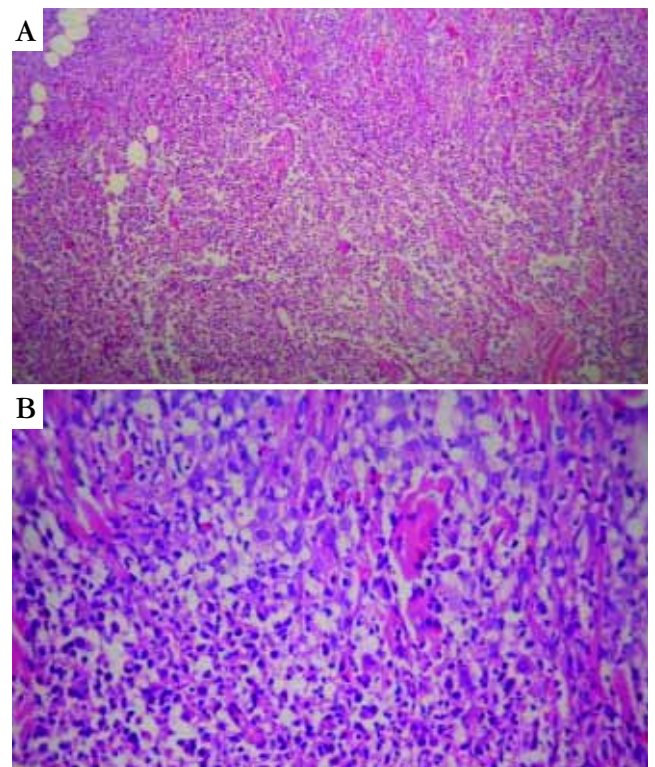
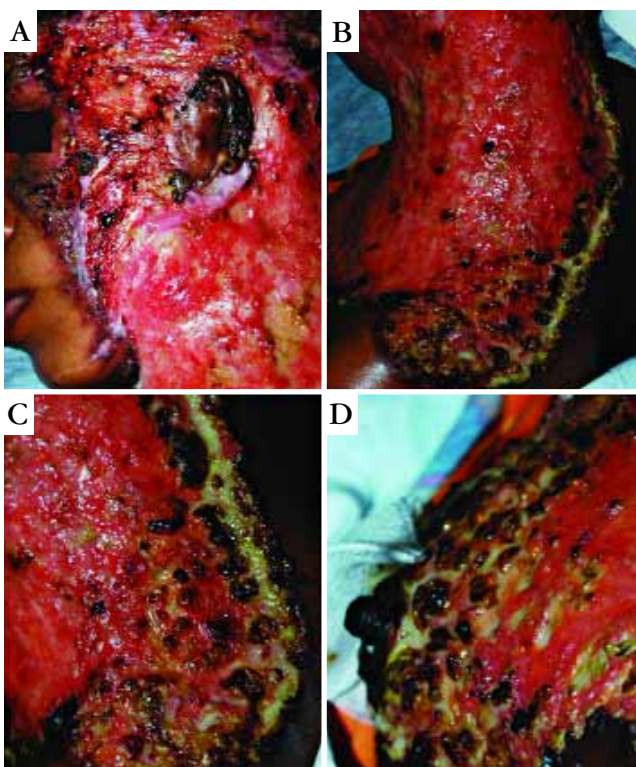


FIGURE 1 (A, B, C, D): Ulcerated lesions with raised borders and a base covered with seropurulent material, situated on the face, neck and upper anterior and posterior thoracic region

FIGURE 2 (A, B): Hematoxylin-eosin staining, magnification 200x. Edema in the papillary dermis with perivascular, lymphohistiocytic inflammatory infiltrate and neutrophilic polymorphonuclear leukocytes, extending into the hypodermis

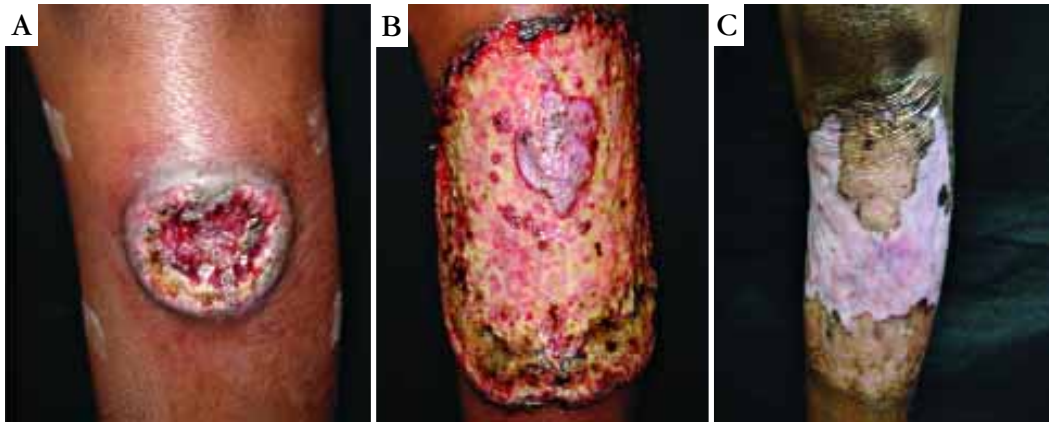


FIGURE 3 (A, B, C): Ulcerated lesion with rapid growth on the lower third of the left leg that developed following an insect bite. It healed completely following treatment

tant factors in reaching a diagnosis of the disease; however, the basis of a diagnosis of PG is the exclusion of other diseases, principally infectious and autoimmune diseases, neoplasias and even self-inflicted skin lesions. At histopathology, earlier PG lesions have a neutrophilic vascular pattern, sometimes with folliculocentric involvement, whereas more developed lesions show signs of necrosis and mononuclear infiltrate.⁸ Although nonspecific, the findings at histopathology contribute towards eliminating other differential diagnoses.

The treatment of choice for PG is oral or intravenous corticoids, with pulse therapy in some of the more severe cases. Cyclosporin, azathioprine, dapsone, clofazimine, thalidomide and mofetil mycophenolate have also been used.⁹ Recently, infliximab was used as an alternative treatment for PG.¹⁰ In 2004, Su et al.¹¹ proposed a set of primary and secondary diagnostic criteria for PG. The primary criteria included: the presence of a painful skin ulcer with regular borders and rapid progression, together with the exclusion of other causes of skin ulceration. Secondary criteria consisted of: a history suggestive of pathergy or the presence of cribriform scarring; an association with systemic diseases (inflammatory bowel disease, arthritis, IgA monoclonal gammopathy or neoplasia); a finding of sterile dermal neutrophilia and/or mixed

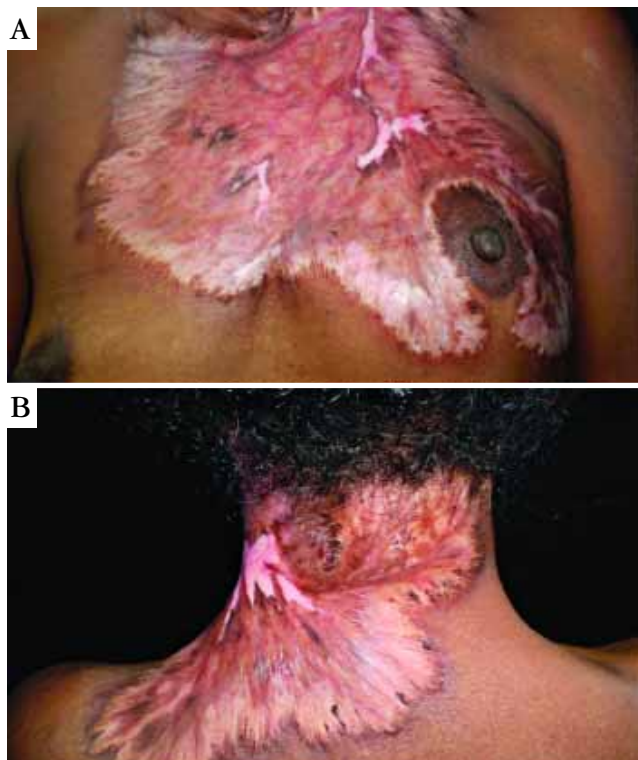


FIGURE 4 (A, B): Scarring of the lesions following treatment



FIGURE 5: Cicatricial ectropion

inflammatory infiltrate and/or lymphocytic vasculitis at histopathology and a rapid response to systemic corticotherapy. The presence of the two primary criteria plus one of the secondary criteria establishes a diagnosis of PG.

Although the etiology of PG is not yet completely understood, many investigators refer to an associa-

tion with systemic diseases. In the patient in question, all the tests requested were normal, suggesting that PG was probably of idiopathic etiology. This case has some peculiarities: an extremely extensive clinical presentation of difficult diagnosis, the presence of pathergy even during treatment with immunosuppressors, good therapeutic response and unsightly scarring that will be difficult to correct surgically. □

REFERENCES

1. Ruocco E, Sangiuliano S, Gravina AG, Miranda A, Nicoletti G. Pyoderma gangrenosum: an updated review. *J Eur Acad Dermatol Venereol.* 2009;23:1008-17.
2. Ravic-Nikolic A, Milicic V, Ristic G, Jovovic-Dagovic B. Pyoderma gangrenosum associated with Sjögren syndrome. *Eur J Dermatol.* 2009;19:392-3.
3. Futaki K, Komine M, Hosoda S, Hirashima M, Yokokura H, Yamada T, et al. Pyoderma gangrenosum associated with Takayasu arteritis without typical symptoms. *Eur J Dermatol.* 2009;19:266-7.
4. Yamanaka K, Kuniyuki S, Maekawa N, Yoshida Y, Teshima H. Pyoderma gangrenosum with myelodysplastic syndrome treated with analogous bone marrow transplantation. *Acta Derm Venereol.* 2009;89:105-6.
5. Batista MD, Fernandes RL, Rocha MAD, Ikino JK, Pinheiro RF, Chauffaille MLLF, et al. Pioderma gangrenoso bolhoso e síndrome mielodisplásica. *An Bras Dermatol.* 2006; 81(Supl 3): S309-12.
6. Powell FC, Su WP, Perry HO. Pyoderma gangrenosum: classification and management. *J Am Acad Dermatol.* 1996;34:395-409.
7. Costa IMC, Nogueira LCS. Pioderma gangrenoso e artrite reumatóide. Relato de Caso. *An Bras Dermatol.* 2005;80:81-2.
8. Souza CS, Chiossi MPV, Takada MH, Foss NT, Roselino AMF. Pioderma gangrenoso: casuística e revisão aspectos clínicos, laboratoriais e terapêuticos. *An Bras Dermatol.* 1999;74:465-72.
9. Eaton PA, Callen JP. Mycophenolate mofetil as therapy for pyoderma gangrenosum. *Arch Dermatol.* 2009;145:781-5.
10. Chow RKP, Ho VC. Treatment of pyoderma gangrenosum. *J Am Acad Dermatol.* 1996;34:1047-60.
11. Su WP, Davis MD, Weenig RH, Powell FC, Perry HO. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. *Int J Dermatol.* 2004;43: 790-800.

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