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Case report

Pyoderma gangrenosum associated with rheumatoid arthritis: a case report

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ABSTRACT

Pyoderma gangrenosum is a chronic inflammatory dermatosis, which is associated with non-infectious systemic diseases such as rheumatoid arthritis and inflammatory bowel disease. It is more common in adults and may present with four distinct clinical forms, all leading to ulceration of the skin affected. Its diagnosis is clinical and demands exclusion of other causes. Treatment should be performed with local care and systemic therapy.

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Pioderma gangrenoso associado à artrite reumatoide: descrição de caso

RESUMO

Palavras-chave:

Pioderma gangrenoso
Dermatose neutrofilica
Artrite reumatoide

O pioderma gangrenoso é uma dermatose inflamatória crônica, que se associa a doenças sistêmicas como a artrite reumatoide. É mais comum em adultos e pode se apresentar com quatro formas clínicas, todas levando à ulceração da pele acometida. Seu diagnóstico é clínico e de exclusão. O tratamento deve ser realizado com cuidados locais e terapia sistêmica.

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Introduction

Pyoderma gangrenosum (PG) was first described over 70 years ago by Brunsting O'Larry.¹⁻³ This is a relatively infrequent, non-infectious, idiopathic, chronic, relapsing inflammatory dermatosis, with a local destructive character, usually associated

with other local or systemic diseases.⁴ It is more common in adults, but children can also be rarely affected.² The most affected age group is from 25 to 55 years old, and this disease is more common in women. The aetiology of PG is poorly understood, although it appears to be an immune-mediated cutaneous damage. Neutrophil dysfunction, especially defects in chemotaxis, has been suggested as a possible cause of PG.^{1,2,4}

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PG shows involvement predominantly of the lower limbs, but it may also affect the trunk, abdomen and face.² Clinically, the presence of hemorrhagic pustules, painful nodules or multiple vesicopustules are observed. These lesions evolve into destructive ulcers that grow centrifugally with slightly elevated, violaceous, sharply delineated, excavated edges presenting a necrotic center with presence of blood, pus and granulation tissue.^{2,3,5-7}

There are four different clinical forms of PG.^{4,8} The ulcerative form is the most frequent and corresponds to the classical clinical picture, usually associated with inflammatory bowel disease (IBD) and rheumatoid arthritis (RA). The pustular form is characterized by painful pustules with an erythematous halo, usually occurring in exacerbations of IBD.³ The bullous form presents with superficial hemorrhagic blisters that often leave scars, being associated with myeloproliferative disease. The vegetative form presents as a superficial, painless, solitary ulceration not associated with systemic disease.^{5,8} The histopathology is nonspecific, and a lymphocytic vasculitis is found at the erythematous edge of the lesion, besides the presence of polymorphonuclear-rich abscesses.^{5,6,8} Usually, the clinical diagnosis is obtained by exclusion.^{4,5,6}

RA is a systemic autoimmune inflammatory disease characterized by a chronic, symmetric and erosive polyarthritis, especially of small joints. Besides the joint picture, RA can present extra-articular symptoms, including cutaneous manifestations such as skin ulcers, rheumatoid nodules, vasculitis and PG necrotic lesions. Here we report a case of a patient with long-standing RA and poor adherence to treatment, who showed extensive necrotic ulcerated skin lesions characteristic of PG.

Description of the case

Patient with 40 years old, female, Caucasian, with a history of RA for 10 years. Two months ago was affected by erythematous nodules on her left thigh and buttock, which progressed to ulcerations and extensive ulcer formation with more than 10 cm in diameter. This clinical picture began shortly after her abruptly stopping the use of oral corticosteroids. The patient used disease-modifying drugs (DMDs) irregularly, discontinuing the use of methotrexate for about two years. On physical examination, well-delimited necrotic ulcerations with violaceous excavated edges and erythematous-violaceous halos were noted (Fig. 1). In addition, joint deformities compatible with ulnar deviation and swan neck and buttonhole fingers were seen. A skin biopsy revealed inflammation with neutrophilic vasculitis and fibrinoid necrosis of the vascular wall suggestive of PG (Fig. 2). Cultures for bacteria and fungi revealed no growth of microorganisms. Lab tests, including serology for hepatitis B, hepatitis C, anti-HIV and proteinogram were all normal, except by an increase in inflammatory markers and a high titre for rheumatoid factor. Radiological studies of hands and feet showed bone erosions in the proximal interphalangeal, metacarpophalangeal and metatarsophalangeal joints. The initial treatment was prednisone 1 mg/kg/day PO in divided doses at intervals of 8 hours, with methotrexate 10 mg/week PO that was rapidly stepped up to 25 mg/week SC. The patient underwent weekly reviews and



Fig. 1 – Ulcerated lesion with eritemato-violaceous excavated borders and center with necrotic areas on the front of the left thigh.

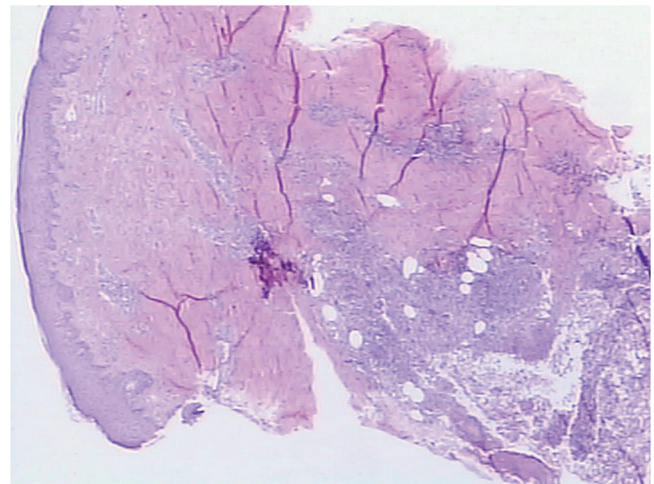


Fig. 2 – Skin biopsy of the lesion with neutrophilic vasculitis and fibrinoid necrosis (HE, 20x).

daily dressings, obtaining an excellent clinical outcome with resolution of the lesions in approximately 3 months (Fig. 3).

Discussion

About 50% of cases of PG occur concomitantly with other disease, particularly IBD, RA, myeloproliferative diseases, hepatitis B and C, acquired immunodeficiency syndrome (AIDS), systemic lupus erythematosus, psoriasis and reactive arthropathies.^{1,3,4,9} The other 50% of cases of PG occur in isolation.^{1,4,5,8} The association with RA can occur in up to 37% of patients with PG and its appearance is more common after the onset of arthritis. Usually, patients with PG are positive for rheumatoid factor, and a common radiographic finding is the presence of erosions. RA affects women twice as often as men, and its incidence increases with age. When this disease involves other organs, the morbidity and disease severity are



Fig. 3 – Completely healed lesion, after 11 months of treatment, on the front of the left thigh.

more expressive, which may reduce the life expectancy in five to 10 years. The diagnosis depends on a combination of a number of clinical symptoms and signs, and on laboratory and radiographic findings. The patient described had RA for 10 years and pursued an irregular treatment, which precipitated the development of lesions of PG.

Some diagnostic criteria for PG have been proposed, but until now with no validation. The criteria of Su et al. (2004) are divided into major (rapid progression of a painful ulcer with irregular and violaceous edges and with exclusion of other causes of cutaneous ulcers) and minor (history suggestive of pathergy, systemic diseases associated with PG, histopathology findings of sterile dermal neutrophilia, inflammatory infiltrate and lymphocytic vasculitis, and rapid response to treatment with corticosteroids) criteria.^{2,3,7} The diagnosis would be established with two major criteria and one minor criterion.⁹ The patient cited in this report had, as major criteria, the fast progression of a painful ulcer with irregular and violaceous edges and the exclusion of other causes of cutaneous ulcers; and, as minor criteria, diseases associated with systemic PG, histopathology presenting sterile dermal neutrophilia, inflammatory infiltrate and lymphocytic vasculitis, and a fast response to treatment with corticosteroids. It should be mandatory to obtain cultures for fungi and bacteria and routine haematological and biochemical workup.⁷ The clinical and pathological findings and the evolution of the lesions of PG are important for the establishment of the diagnosis, but its basis is the exclusion of other diseases, especially infectious diseases, autoimmune disorders and malignancies.

The histopathology findings are not specific to PG and have variable aspects, depending on the biopsy site and duration of the disease, but it is essential to exclude other diagnoses.² The differential diagnoses are vascular occlusions, stasis, vasculitis, malignancies, infections, aggression by physical agents,

drug skin eruptions, cutaneous Crohn's disease and ulcerated necrobiosis lipoidica.²

The evolution of PG is often chronic, with frequent recurrences, sometimes related to traumatic processes (pathergy phenomenon).^{3,5} Pathergy is defined as the development of a new inflammatory lesion in the trauma area. Even when minimal, the occurrence of trauma in a condition of pathergy may be followed by a progressive destruction of healthy skin. This phenomenon has been reported in 25% of patients with PG.

The management of PG includes topical care and local and systemic therapy. Daily wet dressings with petrolatum (to prevent trauma to the underlying tissue during removal) and infection control are essential for treatment of the ulcers. Surgical debridement should be avoided.² Cultures of secretions may be positive for bacterial infection, but usually this results only in tissue colonization.⁷ Topical therapy is useful in some cases and the successful use of tacrolimus, pimecrolimus and potent topical corticosteroids have been reported.^{2,3} Initially, the systemic care consists of high doses of corticosteroids (1-2 mg/kg), aiming a quick response.⁸ The clinical improvement may take months; in some patients, immunomodulatory or immunosuppressive drugs must be added.⁹ The most commonly used medications are clofazimine, dapsone, thalidomide, methotrexate, cyclosporine, azathioprine, cyclophosphamide and mycophenolate mofetil.^{1,2,4-8} Generally, these drugs are administered in association with corticosteroids, to reduce their dose and also in an attempt to control refractory cases.^{1,7} In refractory cases of PG, biological agents, such as anti-TNF alpha and fusion proteins, are used.⁷ Recently, reports have been published demonstrating that in patients with neutrophilic dermatosis, an overproduction of TNF-alpha occurs. This is a proinflammatory cytokine which, together with IL-6, is associated with idiopathic forms of PG. With early institution of an aggressive treatment, one can decrease pain and prevent extensive scarring.⁵ In the literature, it was suggested that the severity of the associated disease is a factor that influences the prognosis of PG. In most cases, the effective treatment of the associated disease leads to improvement or complete remission of PG.

Interestingly, although the global treatment of RA has evolved over the last decades, the prevalence of extra-articular manifestations has remained relatively constant. It is known that patients with PG in association with RA are more refractory to treatment than patients without arthritis.² In this study, we present a case of PG associated with RA and triggered by an irregular treatment of the latter condition. We also demonstrate the severity of PG injuries and the optimal response after the implementation of treatment with corticosteroids and RA-modifying drugs.

Conflicts of interest

The authors declare no conflicts of interest.

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