Pyoderma gangrenosum: a challenge to the rheumatologist

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ABSTRACT

Pyoderma gangrenosum (PG) is a necrotizing neutrophilic dermatosis, a condition with polymorphonuclear infiltrates, which is non-infective, non neoplastic and has no primary vasculitis. It may be idiopathic or associated with a systemic disorder. It is characterized by painful ulcers with undermined edge, of variable depth and size. The legs are most commonly affected but other parts of the skin and mucous membranes may also be involved. The course can be mild or malignant, chronic or relapsing, and has a remarkable morbidity. The pathogenesis is unknown. In 50 to 70% of the patients, PG is associated with underlying systemic diseases such as inflammatory bowel disease, myeloproliferative disorders, hematological or malignancies; it can appear in isolated form. This is a report of two patients with PG and arthritis which intends to show the importance, for rheumatologists, of considering this dermatosis, since articular complaints are present in 37% of the PG patients.

Keywords: pyoderma gangrenosum, arthritis, skin ulcer.

INTRODUCTION

Pyoderma gangrenosum (PG) is part of the neutrophilic dermatoses spectrum, processes that have in common the infiltration of polimorphonuclear leukocytes into skin, subcutaneous tissue and other organs; its character is noninfectious and without primary vasculitis.[1]

Two patients with pyoderma gangrenosum and associated arthritis are presented; they are followed up at the Rheumatology and Dermatology services at Hospital das Clínicas/UFMG.

CASE REPORT

Case 1: LSG, male, currently aged 16. In October, 2001, he presented a case history with daily fever (up to 40°C), occurrence of subcutaneous, erythematous and painful nodes in his legs, arthritis in his elbows and ankles, and no morning rigidity.

He was followed up at Hospital das Clínicas/UFMG since July 2002. From August 2002 to March 2007, he presented four relapses, with manifestations such as erythematous nodes, vesicles that developed into ulcers or small ulcerated wounds since the beginning. Episodes were treated with plasters, oral corticoid and antibiotics. In May 2007 new painful and deep ulcers appeared in his right leg, which were much larger and deeper than the others, which rapidly coalesced. Without other manifestations. The pyoderma gangrenosum diagnosis was considered and confirmed by the dermatology team. Prednisone 1 mg/kg/day was initiated with an excellent response, following a gradual reduction until complete suspension in March 2008

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and the introduction of methotrexate (10 mg/week). In June 2008 he had recurrence of wounds, with readjustment of drugs and good response. Today, he does not have any skin wounds or arthritis.

Relevant exams are shown below: (Nov/2001) normochromic/normocytic anemia; C-reactive protein:69.5 mg/dL; erythrocyte sedimentation rate: 90 mm/h; negative ANA/rheumatoid factor; (April/2003) PPD: non-reactor: x-ray (chest): normal; (Aug/2004) mycobacterium in sputum, in ear lobes and elbows: negative; protein electrophoresis: normal: hepatitis B and C serology: negative; (Apr/2003) biopsy of the node with inflammatory infiltrated formed by eosinophil and neutrophil polymorphonuclear in deep skin and subcutaneously, interstitial edema and congestion; (Mar/2006) haemoglobin electrophoresis: AA; ANCA, anticardiolipin/ lupus anticoagulant: negative; (Mar/2007) skin biopsy – dermal edema with lymphocytary and hystiocitary inflammatory infiltrate predominating in the perivascular and neutrophil polymorphonuclear areas and reaching hypodermis without signs of neoplasia or specific microorganisms.

Case 2: SSF, female, 22 years old, hospitalized on February 1, 2007, presenting fever, arthralgia in her knees and ankles and several ulcers in her legs with a month of development. At admission, she presented regular general status, was pale, eupneic, thin. blood pressure: 110x70 mmHg, heart rate: 110 bpm, normal heart and pulmonary auscultation and palpable spleen at 2 cm from the left lower rib cage border. There were ulcers spread in her legs, with necrotic background and some purulent secretion, as well as high and irregular edge and hyperaemia. There was no arthritis. Three years before, she presented a lighter similar case history, which was treated with prednisone and dapsone and had developed satisfactorily. There were no inflammatory bowel disease-specific or autoimmune disease-specific clinical manifestations. She maintained fever, despite using several antibiotic schemes. Relevant exams are shown below: Rheumatoid factor, lupus anticoagulant and anticardiolipins, ANCA and cryoglobulin: negative; ANA + 1/1280 (fine speckled, negative fractioned); hand/wrist X-Ray: Normal; transtoracic ecocardiogram: normal; abdome TC: Hypodense images and increasing spleen; serology for hepatitis B, C and HIV: negative; aspirate culture of spleen collection: negative; myelogram and biopsy of bone marrow: normal. Skin biopsy: she presented light, infiltrated, inflammatory lymphohistiocytic, with some neutrophils and plasmocytes in the perivascular areas in dermis and dense inflammatory lymphohistiocytic infiltrate, and large number of polymorphonuclear in hypodermis. Research on fungi and bacteria was negative.

Treatment for primary PG started with prednisone 60 mg/ day and cyclosporine 150 mg/day with total disappearance of lesions and improvement of the systemic symptoms. The prednisone dose was gradually reduced until suspension and cyclosporine kept at 200 mg/day. Image examinations showed volume reduction in the spleen images. Today, she is asymptomatic.

DISCUSSION

In the first patient, the recidivating and episodic feature of the cutaneous and articular case history, additionally to non-common ulcers, required a long term follow-up and long propedeutics until clinical confirmation of PG diagnosis. There were

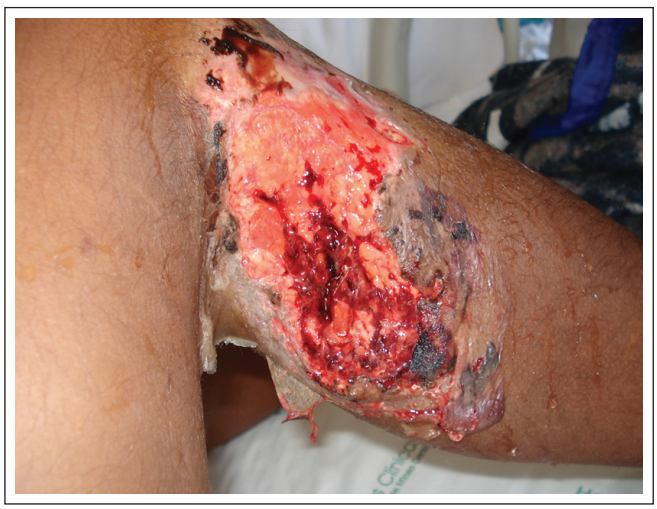

Figure 1. Ulcerated lesion in patient of case 1.

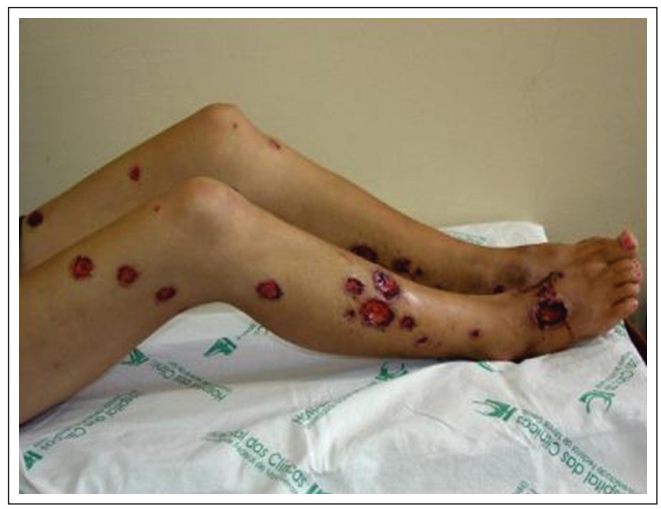

Figure 2. Ulcerated lesions in the lower limbs, patient of case 2.

no criteria to diagnose an associated inflammatory articular disease during the follow-up years. Methotrexate was chosen due to the impossibility of the family to afford cyclosporine and a stricter follow-up. The patient presented as case 2, additionally to a more chronic case history of ulcers and arthritis, had wounds in her spleen that motivated specific propedeutics to exclude infection and neoplasia. The improvement with an immunosuppressive treatment confirmed that it was an extracutaneous manifestation of pyoderma.

PG is a painful ulcerative disease, which develops with exacerbations and remissions and may progress and endanger joints. The incidence peak ranges from 20 to 50 years old; women are the most affected. Cases in children and teenagers reach 4% of the total number, and general incidence is estimated to be 3-10 cases/million of inhabitants/year.[2]

Approximately 50 to 70% of the patients have a baseline disease, such as inflammatory bowel disease, rheumatic disease, hematologic disease or malignity.[1] Association with PAPA syndrome (pyogenic arthritis, pyoderma gangrenosum and acne) was also described.[3]

Pathogenesis is poorly known, and there may be a neutrophil dysfunction causing metabolic oscillation and abnormal transit of neutrophils.[4] No immunologic defect common to all cases has been described.[5]

In the beginning, nodes or painful sterile pustules occur, which then develop with central ulceration. The classic ulcer is extensive, with infiltrated borders, erythematous-violaceous, undermined, with necrotic background and granulation tissue. They are deep and reach dermis and the subcutaneous tissue. Ulcers may be single or multiple, are more frequent in lower limbs and may be found in any other part of the body. Almost 30% of the patients present previous trauma caused by a wound (pathergy). Polypoid or bullous forms may rarely occur.[2,5]

Some patients present fever, illness and myalgias. Neutrophil sterile infiltrates may be found in other organs.[1,2] Arthritis is found in 37% of the cases and presents a variable pattern: classic rheumatoid, asymmetry of legs, and monoarthritis of the big joints have already been described.[3,6]

Secretion cultures, histology study for removing malignity, vasculitis and fungi, micobacteria or parasite infections are indicated. The histopathology study is not always conclusive for diagnosis, since changes may be uncertain and vary according to the lesion stage. Inflammatory cell infiltration in shorter vessel wall may occur; systemic vasculitis should be exluded. If granulomas are found, infectious diseases may be excluded. Typical histological findings include suppurative neutrophil inflammation in the epidermis and dermis with tissue necrosis, vascular reaction with lymphocyte perivascular infiltrate, usually without concurrent vascular fibrinoid necrosis.[5,7]

Criteria for PG diagnosis include major and minor criteria, and ulceration is an essential factor, after excluding other possible causes.[4]

In the disseminated or rapid course disease that does not present a baseline disease, first therapy options are corticoid, cyclosporine associated or not associated with prednisone and venous pulse therapy with methylprednisolone. Other immunosuppressors are reported in case of unsuccess, and refractory ulcers are not uncommon. Powerful and permanent analgesia is important.[5] Surgery will be indicated only to remove necrotic matter, because of patergy which makes lesions worse.[8]

CONCLUSION

PG is presented as one of the challenges in the differential diagnosis of diseases with muscle and skeleton complaints. Knowing the clinical presentation, diagnosis and differential diagnosis of this disease may help rheumatologists in organizing their clinical thinking and in choosing the treatment adopted.

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