

CASE REPORT

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Genital pyoderma gangrenosum revealing Behçet's disease: a case report

Hassina Chicha, Said Taharboucht*, Nacera Tiboune, Nadia Touati and Ahcene Chibane

Abstract: Background: Pyoderma gangrenosum (PG) is a rare and chronic neutrophilic dermatosis. It is clinically characterized by aseptic ulcerations preferentially located in the lower limbs. Its location in the genital area is unusual and could be a source of diagnostic difficulties. In half of the cases, PG is associated with an underlying disease. The association with Behçet's disease is exceptional.

Case presentation: We report an original observation of a patient who presented a vulvar PG which revealed a Behçet's disease.

Conclusion: The distinction between these two pathologies was difficult because of the similarity of the cutaneous-mucous lesions on the one hand, and the absence of histological specificity of these two pathologies on the other hand.

Keywords: Pyoderma gangrenosum, Behcet's disease, Pathergy test, Neutrophilic dermatoses

Background

Pyoderma gangrenosum (PG) is a rare, chronic neutrophilic dermatosis of unknown origin, its clinical appearance is an ulcerative pustular lesions [1]. Approximately 50% of PG cases are associated with an underlying systemic illness, in particularly inflammatory bowel disease such as ulcerative colitis or Crohn's disease [1]. Its occurrence during Behçet's disease (BD) is unusual [1]. Indeed, PG is cited among the most exceptional dermatological manifestations of BD which, as a reminder, is currently considered to be vasculitis affecting vessels of variable diameter [2]. We report a particular observation of a vulvar and fistulizing pyoderma gangrenosum which revealed Behçet's disease.

Case presentation

A 42-year-old female patient hospitalized for a painful genital ulceration evolving for 4 months. She had received several courses of appropriate antibiotic therapy without any improvement. On dermatological examination she

had a purulent oozing and stinky ulceration measuring 10 cm, with ragged undermined edge, located at the level of the vulva with an extension to the perianal region. The margins were raised and purplish (Fig. 1). A pseudo folliculitis lesion was also found on the face (Fig. 2). Examination of the oral cavity revealed ulcers on the palate and tongue (Fig. 3). The patient reported the notion of recurrent oral aphthosis since 2 years. The pathergy test was strongly positive (Fig. 4). Ophthalmologic examination showed a bilateral intermediate and posterior uveitis associated with a strong Tyndall effect.

The diagnosis of BD was retained based on international criteria for Behçet's disease (Table 1) [3]. Bacteriological samples and repeated cultures of the ulceration were sterile. The laboratory examination objectified anemia at 9.9 g/dl microcytic, hypochromic with an inflammatory syndrome (increased erythrocyte sedimentation and C-reactive protein (CRP at 93 mg/l). The search for antinuclear and anti-DNA antibodies was negative, the Hepatitis B, C, HIV, and Syphilis viral serologies were negative. The chest X-ray and abdominal ultrasound were normal. Pelvic MRI found an anovaginal fistula with significant inflammatory changes in the anal margin and on the sphincter. The punch biopsy

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Fig. 1 The genital ulceration of the vulva with an extension to the perianal region before treatment



Fig. 2 A pseudo folliculitis on the left cheek

of ulcer showed neutrophilic infiltration without fibrin deposition or necrotic changes in vessel wall. Based on the clinical and histological finding, our case was diagnosed as genital ulcerative PG, which occurred during the exacerbation of BD and treated with colchicine at 1 mg per day, combined with corticosteroids at a rate of 0.5 mg/kg per day of prednisolone. Genital ulcer markedly healed, and oral aphthosis rapidly improved after one week of treatment with a normalization of CRP (Fig. 5). Because of the severe ocular involvement of the posterior segment, treatment with azathioprine at a rate of 100 mg/day combined with Infliximab at a rate of 5 mg/kg was initiated. The outcome was favorable with clinical and biological remission maintained with a follow-up of 6 months.

Discussion

The observation that we are reporting is unprecedented because of PG, which is a rare idiopathic inflammatory disease moreover localized on the genital sphere, and its equally rare association with Behcet's disease. PG was revealing a BD in our patient.

In its typical form, the PG is characterized by one or many sterile painful ulcers, with a purulent base, raised

and undermined purplish edges; it has a rapid extension and a chronic evolution. There are several clinical forms, but the appearance is often suggestive of a subacute or a chronic infection, paradoxically, there is no lymphangitis or adenopathy. The pain is variable, it can sometimes be very intense [4]. The initial search for microorganisms is always negative but secondary infection occurs frequently [4]. The lower limbs constitute the preferred site of the PG. Other locations can be observed in particular on the buttocks, the cephalic extremity, and more rarely the anal and genital region [1]. The latter can be a source of diagnostic and therapeutic delay, which was the case with the patient.

PG is associated with systemic disease in approximately 50 to 78% of patients [5]. Inflammatory bowel disease, arthritis, and hematologic disease are the most common pathologic associations [5].

The association between PG and BD is rare. Since, the first case of Munro and Cox in 1988 [6], only 16 cases of PG associated with BD have been reported in the literature [6–21]. In the majority of these observations, PG is diagnosed after the associated disease [15]. Nevertheless, it can precede the onset, or be the telltale sign of an underlying disease [5].



Fig. 3 Oral aphthosis on the palette

Table 1 The international criteria for Behcet's disease scoring system . Point Score System : Scoring ≥ 4 indicates Behcet's diagnosis) [3]

Sign/symptom	Points
Ocular lesions	2
Genital aphthosis	2
Oral aphthosis	2
Skin lesions	1
Neurological manifestations	1
Vascular manifestations	1
Positive pathergy test	1



Fig. 5 Improvement of the genital ulceration after a week of treatment by corticosteroïdes



Fig. 4 The strongly positive pathergy test

In the present case, genital ulcerative PG developed concurrently with an exacerbation of BD. We report the third case of PG in the literature, showing mucosal ulcers associated with BD [8, 17].

Behcet's disease was described by Hulusi Behcet as a multisystem inflammatory disease [22]. Currently, it is classified in the category of vasculitis affecting vessels of variable diameter [2].

Although oral ulceration, genital ulceration, and eye disease are the classic triad of manifestations, the cardiovascular, gastrointestinal, musculoskeletal, and central nervous systems can also be affected [3].

In BD, multiple cutaneous lesions such as erythema nodosum, folliculitis, and pustules are seen, but PG is very rare [15].

The patient was diagnosed as Behcet's disease according to the criteria of the "International Study Group for Behcet's disease" [3]. She presented one major criteria (recurrent oral aphthosis) and three minor criteria (very suggestive ocular involvement, a presence of cutaneous pathergy and pseudo folliculitis lesions). The diagnosis of genital PG was based on the presence of two major

criteria (appearance of the ulceration, exclusion of other causes of infectious or vascular skin ulcerations) and four minor criteria [23, 24] (positive pathergy reaction, rapid therapeutic response to systemic corticosteroid therapy, presence of a predominantly neutrophilic inflammatory infiltrate on histology, and association with BD) (Table 2).

It is sometimes difficult to distinguish between clinical manifestations of BD and PG in the same patient. Both BD and PG belong to the category of the neutrophilic dermatoses in which primary pustular lesions occur and neither of them has a characteristic histological appearance [15].

Indeed, at the onset stage and during the pustulo-ulcerative form of PG, the resemblance to skin lesions of BD is possible, and the pathergy test can be positive in both conditions [1].

The term pathergy refers to the occurrence of skin lesions following minimal trauma, and is used to assess excessive irritability of the skin in inflammatory diseases [23].

Its positivity in these two pathologies reflects the presence of an exaggerated inflammatory reaction. Histologically, this aberrant reaction leads to a release of cytokines responsible for a perivascular infiltrate and the accumulation of neutrophils at the site of the reaction [25].

Likewise, ulcerative lesions of the mouth and genital area can be seen in both diseases [19]. On the other hand, the frequency of mucosal ulcers and their clinical appearance are completely different [19].

Orogenital ulcers are commonly seen in BD, whereas rarely seen in PG. In BD, genital ulcers are similar in appearance to oral ulcers and can sometimes cause scar formation, and tend to be small and round, with well-circumscribed margins, an erythematous halo and a yellow-grey floor. In PG, ulcers of the genital mucosa appear similar to those of skin, which are comprised of a burrowing ulcers with irregular margins and a ragged purple overhanging edges. Rapid local destruction may occur in PG [19]. Thus, the clinical features of mucosal ulcers are different to some degree between the two diseases.

However, there is a histopathological distinction between PG and BD. The two pathologies are characterized by a neutrophilic vascular reaction [15].

In PG, vascular involvement ranges from none to fibroid necrosis, and in most cases a neutrophilic infiltrate is present with limited vascular damage [19]. Conversely, in BD, mononuclear cell vasculitis with variable fibrin deposition or leukocytoclastic vasculitis is usually found [19].

BD has been associated with other neutrophilic dermatoses such as Sweet's syndrome and neutrophilic eccrine hidradenitis [1]. This suggests the presence of a clinical and histological overlap between BD and neutrophilic dermatoses. These overlaps could constitute the clinical expression of two autoinflammatory diseases in whose genetic component remains to be determined [1]. However, the true etiopathogenic link between these two conditions is not yet fully understood.

The activity of PG is chronic, and closely related to the activity of associated diseases [15].

Treatment of PG is usually based on systemic corticosteroid therapy alone or in combination with thalidomide or Dapsone [1]. In cases of corticosteroid-resistant PGs, the use of other immunosuppressants, such as tacrolimus, cyclosporin and mycophenolate mofetil, and azathioprine, may be effective. Currently, anti-TNF α are a promising treatment for refractory PG [1]. These therapeutic agents are used to treat both PG and BD [4].

The prognosis of PG depends on the associated disease and the severity of the clinical form of PG [1].

In this patient, the evolution of PG and oral aphthosis were favorable from the start of corticosteroid treatment. The use of immunosuppressive therapy combined with TNF inhibitors was justified by the presence of severe ocular involvement of the posterior segment.

Conclusion

The observation that we report is illustrated by both a rare localization of a PG (genital sphere), and its exceptional association with Behçet's disease. The coexistence of these two conditions could be a source of diagnostic

Table 2 PG diagnostic criteria [23, 24]

PG is retained: 2 major criteria + at least 2 minor criteria

Major criteria

- A sterile pustule or cutaneous ulcer with undermining purplish border.
- Other causes of cutaneous ulceration are excluded.

Minor criteria

- Histology: Demonstrating neutrophilic infiltrate and vasculitis.
- Associated with compatible systemic disease.
- A treatment response to immunosuppressive medication and absence of response to the classical treatment of ulcers.
- A phenomenon of pathergy
- A pain with a visual analog scale (+ 4).

difficulties. The treatment and prognosis of PG are conditioned by the severity of the visceral involvement of BD.

Abbreviations

PG: Pyoderma gangrenosum; BD: Behcet's disease; CRP: Reactive protein.

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S.T contributed to the writing of the article, its correction and the management of the patient. N.T, N.T and A.C contributed to the care of the patient in the department. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

We obtained verbal consent from the patient. Our patient is illiterate.

Competing interests

The authors declare that they have no competing interests.

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