Herpetic infection in a patient with pyoderma gangrenosum and chronic myeloid leukaemia

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Summary

Pyoderma gangrenosum is a neutrophilic dermatosis that can be idiopathic or associated with other conditions such as hematologic malignancies. Both diseases require the use of immunosuppressive therapies that predispose patients to opportunistic infections, that sometimes have atypical presentation. We describe a case of genital pyoderma gangrenosum complicated by herpes simplex virus infection in a 69-year-old woman with chronic myeloid leukaemia.

KEY WORDS: herpes simplex virus; pyoderma gangrenosum; chronic myeloid leukaemia.

Introduction

Pyoderma gangrenosum (PG) is a clinical entity within the field of neutrophilic dermatoses. In approximately 50% of cases, PG is idiopathic and involves only the skin. The other cases are antecedent, coincident or subsequent to another condition. The most common associations are inflammatory bowel disease, arthritis (seronegative arthritis, spondylitis of inflammatory bowel disease, rheumatoid arthritis), and haematologic diseases (1). These conditions often require the use of immunosuppressive therapies, that increase the risk of developing herpes simplex virus (HSV) infection. We describe a case of HSV infection associated with PG in a woman with chronic myeloid leukaemia (CML).

Case report

A 69-year-old Caucasian woman presented with extremely painful lesions, appeared 8 months before. Her background medical history included CML treated with chlorambucil, chronic smoking-related obstructive airways disease and hypothyroidism requiring hormone replacement therapy. Cutaneous examination revealed multiple superficial ulcers that tended towards confluence (6 cm in diameter), with circular, well-demarcated, undermined purple-red borders, involving the sacral region, the medial part of the gluteal area, the perineum and the external genitalia. Small non-inflammatory vesicles were distinguished on the ulcer margins (Figure 1). Laboratory investigation revealed a slight hypochromic anemia and leukocytosis, consistent with the diagnosis of CML, but with higher values than previous controls (WBC: 118.20 x 10³/μl). Low serum iron and albumin, high erythrocyte sedimentation rate and fibrinogen were also detected. Venereal Disease Research Laboratory test, HIV test, anti-neutrophilic cytoplasmic, antinuclear and anti-DNA antibodies, rheumatoid factor, Lupus Erythematosus test and cryoglobulins were all negative. The culture of the skin lesion swabs was negative for fungal infection and positive for Proteus and Escherichia coli, but antibiotic treatment slightly improved the ulcer aspect. Chest X-ray report was consistent with patient’s smoke history and related disease. Abdominal echography was normal and no gas-
Pyoderma gangrenosum and herpetic infection

Herpes viruses are among the most common opportunistic pathogens infecting patients with neoplastic diseases. HSV infection is common in patients receiving anti-tumor cytotoxic therapy and often results from reactivation of latent virus during treatment-induced immunosuppression. Typical, self-limited orolabial or genital lesions do not always require laboratory diagnosis, but HSV may have an atypical presentation in cancer patients (2). HSV infections among immunocompromised patients are typically more invasive, slower to heal, associated with long viral shedding, and sometimes disseminated. Mucocutaneous HSV disease in patient with hematological malignancies often mimics other pathogens, such as Candida, or treatment-induced mucositis. In case of CML, a herpetic infection can be responsible for mucocutaneous blisters which developed into chronic ulcers mimicking a dermatological blistering disease (3).

The association between PG and herpetic infection could be explained by the use of high-dose immunosuppressive treatment for PG, that predisposes patients to opportunistic infections. In our case the HSV infection appeared before the begin of therapy for PG, but the patient was under chlorambucil for her leukaemia. It has been suggested that the prolonged course of PG should be linked to defects in the shutdown of the neutrophil oxidative burst and in the resolution of neutrophilia (4). However, neutrophils play also a role in immune protection of the vaginal mucosa, limiting and clearing HSV-2 vaginal infections (5).

Literature rarely reports PG and HSV in association. The first case dates from 1979, when Wahba et al. described a patient with chronic lymphatic leukemia and HSV-2 isolated from genital PG. In that instance, Authors recommended to carefully research viruses in patients with PG and impaired immunity or hematological malignancy, mainly if face or genital area are involved (6). Furthermore, in 2005, Tay et al. reported the case of a man with resistant PG complicated by HSV-1 infection, whose late recognition led to the ulcer progression (7).

Along with cases of PG complicated by HSV infection, literature also reports cases of HSV involving the genital area misdiagnosed as PG, particularly in immunocompromised patients. Brown et al. described a patient with chronic lymphocytic leukemia, treated with oral corticosteroids, who presented chronic perianal ulcerations due to atypical HSV infection, but that was referred for evaluation and treatment of recalcitrant PG (8). Moreover, Kumar et al. reported the case of a female infected with HIV who presented with a non-healing painful ulcer in the left hand due to HSV infection; the primary occurrence of PG misdiagnosis, in that occasion, resulted in inappropriate immunosuppressive treatment that prompted an increase in ulcer size, the appearance of perianal vesicles and prolonged patient’s discomfort (9). Since our patient was already treated with chlorambucil for her CML, we decided to start the antiviral therapy to control the HSV infection, prior to start an immunosuppressive drug for PG management. We chose to start cyclosporine treatment for PG, because, in case of a theoretical presence of residual HSV infection, steroids, the first-line therapy for PG, should decrease the virus clearance. The circumstance that the antiviral therapy alone was not able to produce the ulcers disappearance and the clinical response to cyclosporine may be due to the use of high-dose immunosuppressive treatment for PG, that predisposes patients to opportunistic infections.

Discussion

Figure 2 - Pyoderma lesions after 4 weeks of cyclosporine treatment.
Cyclosporine was convincing that our suspected diagnosis of PG as primary etiology was correct.

In conclusion, the diagnosis of HSV and/or PG is not always simple: HSV infection can simulate PG in immunocompromised patients, the bullous variant of PG is linked to haematologic neoplastic diseases, the herpetic infection and PG can coexist in patients with chronic myeloid leukaemia.

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**References**