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Perianal herpetic ulcer with rapid spreading: a sign of acquired immunodeficiency syndrome (AIDS)

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Abstract

Perianal skin lesions are present in a significant portion of dermatology patients. It is therefore important for every dermatologist to be familiar with a wide range of differential diagnoses and to treat the underlying cause in a timely manner. Here we present the case of a 24-year-old male with perianal ulceration due to a newly diagnosed herpes simplex virus infection. After a 5-month period of stability, the ulcer suddenly started to spread. Importantly, a concomitant previously unrecognized stage 4 HIV (acquired immunodeficiency syndrome) was discovered. Our case supports the view that the appearance and/or rapid progression of perianal herpetic lesions or ulcers could correlate with conversion of HIV into acquired immunodeficiency syndrome. Consideration of this fact could be beneficial when patients with perianal lesions are managed. In addition, all patients with infectious perianal lesions should be screened for sexually transmitted diseases so as not to miss underlying concomitant infections such as HIV.

Keywords: perianal ulcer, perianal lesions, HSV, HPV, HIV, AIDS

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Introduction

Perianal skin lesions present a frequent reason for referral to a dermatologist, and therefore dermatologists should be familiar with a wide spectrum of differential diagnoses. The differential diagnosis of perianal lesions is listed in Table 1 (1–3). Due to receptive anal intercourse, perianal lesions are especially common in men that have sex with men (MSM) (4).

Perianal skin lesions may present as papules, nonspecific erythema, vesicles, vegetations, ulcers, or necrosis. Perianal ulcers are mainly caused by herpes simplex virus (HSV) (1). Extensive ulcerative herpetic infection in the genital or perianal area manifests almost exclusively in immunosuppressed patients and tends to be chronic. Importantly, in patients with acquired immunodeficiency syndrome (AIDS), perianal lesions, which tend to have an atypical manifestation, are present in up to one-third of cases. Atypical ulcers are regarded as being extensive, rapidly spreading in or presenting with vegetations or even necrosis (5).

Therefore, an atypical perianal ulcer should raise the suspicion of possible immunosuppression, most likely HIV infection or AIDS. Here we describe the case of a young male with perianal ulceration lasting several months that started to progressively spread within a few weeks. A previously unrecognized stage 4 HIV infection (AIDS) was detected, and urgent life-saving antiretroviral treatment was started. Interestingly, a rapid and progressively spreading extensive ulcerative perianal lesion was the only clinical clue to the diagnosis of AIDS.

Case report

A 24-year-old male was referred from a proctologist's office to the dermatology outpatient clinic with an extensive superficial perianal ulcer lasting a few months but showing rapid spread during the previous 5 weeks. He initially presented to a proctologist in March 2018 due to anal pruritus and blood in stool. During the examination, multiple perianal and anal condylomas were discovered, which were also confirmed by histopathology. He was prescribed imiquimod 5% cream in May 2018 for perianal condylomas. He used the cream for only a few days. In December 2019 he returned due to perianal ulceration, which the proctologist believed was a complication of treatment with the imiquimod cream. After 6 months of follow-up, the ulcer had not improved, and therefore in June 2020 he was referred to a dermatologist. The patient reported rapid spreading of the ulcer with serosanguinous discharge starting a few weeks before the visit to the dermatology office. Moreover, the patient reported that he had experienced 10 kg of involuntary weight loss during the previous 6 months. He had no history of chronic illness and was receiving no medication. Aside from having perianal condylomas, there was no prior history of sexually transmitted or opportunistic infections. Physical examination was unremarkable, and no signs of peripheral lymphadenopathy were revealed. In laboratory tests, mild anemia

Table 1 | **Differential diagnosis of perianal lesions.**

Lesion cause	Differential diagnosis
Infections	HSV infection, HPV infection (condylomas), cytomegalovirus infections, tinea inguinalis, candidiasis, erythrasma, molluscum contagiosum
Inflammatory diseases	Psoriasis, chronic inflammatory bowel disease, anal eczema (due to atopic dermatitis, irritative or allergic contact dermatitis), lichen planus, lichen sclerosus, hidradenitis suppurativa
Tumors	SCC, Kaposi sarcoma, extramammary Paget disease, basal cell carcinoma, melanoma
Classic proctology diseases	Anal fistulas, fissures, abscesses, hemorrhoids
Sexually transmitted diseases	Syphilis, chancroid, genital herpes, condylomata acuminata, lymphogranuloma venereum

HSV = herpes simplex virus, HPV = human papillomavirus, SCC = squamous cell carcinoma.

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(hemoglobin 101 g/l), low eosinophils, elevated C-reactive protein (18.3 mg/l), and elevated sedimentation rate (60 mm/h) were revealed. A chest X-ray was normal. Abdominal ultrasound revealed mild hepatosplenomegaly. Fecal occult blood tests were negative three times.

Dermatological examination revealed an extensive shallow perianal ulcer of uniform depth with yellow discharge and arcuate margins (Fig. 1). Perianal condylomas were not apparent. A PCR test of the ulcer smear detected herpes simplex virus (HSV)-1/-2 but did not distinguish between them. He tested negative for hepatitis B and C, syphilis, lymphogranuloma venereum, gonorrhea, and chlamydia infection. However, he was positive for HIV infection with CD4+ cells 34/mm³ (4%) and was therefore in stage 4 of the disease (AIDS). The viral load was 305,000 copies/ml. After the diagnosis of stage 4 HIV infection was made, he was referred to an infectious disease specialist for treatment of HIV/AIDS and HSV infection. Initially, the patient denied having anal sexual intercourse, but after confirmation of HIV he stated that he had indeed participated in anal intercourse during the previous 4 years. He started treatment with antiretroviral therapy (ART) and valacyclovir 1,000 mg twice daily for 14 days, after which the dose was reduced to 500 mg once daily as a long-term prophylactic treatment.

At follow-up after 2 months, complete re-epithelialization of the ulcer was observed (Fig. 2). He continued to receive prophylactic treatment with valacyclovir 500 mg once daily and ART. He complained about having pearly papules on his chin and neck, which were diagnosed as molluscum contagiosum and successfully treated with curettage. After 2 months of ART therapy, his lymphocyte count CD4+ was 191 cells/mm³ and viral load was 113 copies/ml. Recurrence of the herpetic ulcer upon prophylactic treatment with valacyclovir was not detected. After 3 months of follow-up, the infectious disease specialist observed an improved T-cell immune response, with an increase of CD4+ count to 232 cells/mm³ (16%) and HIV < 40 copies/ml, and prophylactic treatment with valacyclovir was therefore discontinued. At the follow-up after 12 months on a stable ART, the patient's viral load remained undetectable (HIV1 RNA < 40 copies/ml), and his CD4+ count rose to 413 cells/mm³ (23%). There was no recurrence of the ulcer.

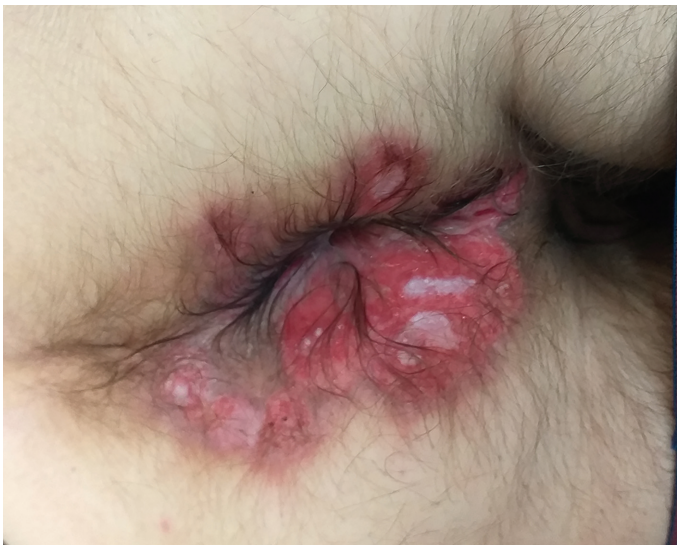

Figure 1 | Extensive shallow perianal ulcer of uniform depth with yellow discharge with arcuate margins.

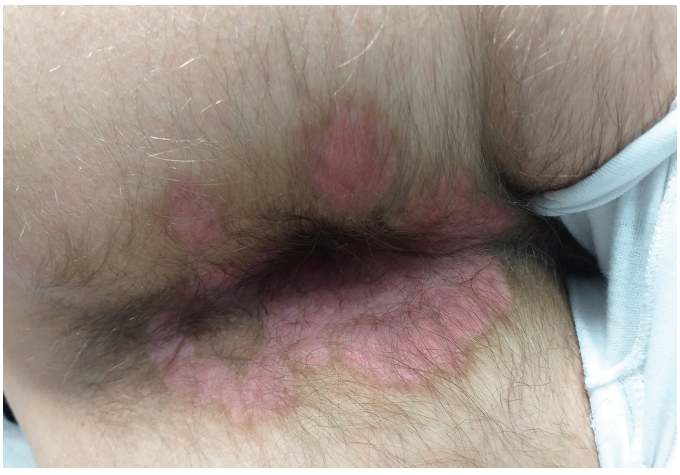

Figure 2 | Full re-epithelialization of the ulcer was observed at follow-up after 2 months.

Discussion

Timely diagnosis of HIV infection is crucial for efficacious treatment and prevention of progression to AIDS. In our case, the suspicion and later confirmation of the HIV infection with laboratory criteria for AIDS was made primarily on the basis of a rapidly spreading perianal herpetic ulcer. The patient initially denied having receptive anal intercourse, which is probably the reason why he was not tested sooner for sexually transmitted diseases.

The differential diagnosis of perianal skin lesions is presented in Table 1. The differential diagnosis of ulcerative lesions in the perianal area includes syphilis, genital herpes, lymphogranuloma venereum, candidiasis, lichen planus, and squamous cell carcinoma (SCC) (3).

Perianal herpetic infections are caused by HSV-2 in 80% of cases. The typical finding of herpetic infection characterized by grouped vesicles is usually absent in the perianal region. Moreover, in the perianal area of an immunocompetent patient it typically presents as erythema with swelling or with a small, circular, shallow ulcer that can coalesce to form an arcuate border (6). Typically, in immunosuppressed individuals, manifestation of herpetic infection is atypical, being ulcerative, vegetative, necrotic, or spreading rapidly (3). The ulcer found in our patient was extensive, which is the most common presentation of herpetic infection in the perianal area of immunosuppressed patients (1). Another characteristic of our patient's ulcer was its rapid spreading in the last weeks after being relatively stable for a few months previously. Again, this could be attributed to worsening immunosuppression. In addition to being extensive, the ulcer was shallow, with a uniform depth and arcuate borders, as also reported in other case series of HIV patients with herpetic perianal ulcers (6).

Interestingly, the ulcer did not respond to treatment with imiquimod prescribed by the proctologist. It has been reported in the literature that progressed herpetic infections in the perianal area that do not respond to antiviral treatment can be successfully treated with imiquimod (1, 7). Thus, we can presume that, if our patient had used imiquimod cream as advised and not only for a short period, the ulcer might have improved. The patient's ulcer was responsive to treatment with antiviral therapy (valacyclovir) along with ART treatment, and rapid re-epithelization was observed 2 months after his first visit. After 3 months of follow-up, the infectious disease specialist observed an improvement of T-cell immune response with an increase in CD4+ count to 232 cells/mm³ (16%) and HIV < 40 copies/ml, and prophylactic treatment with valacyclovir 500 mg once daily was therefore discontinued. After 12 months of follow-up there was no recurrence of the ulcer.

Our patient had concomitant HSV, HPV, and HIV infection.

The possible interplay between these viruses is intriguing. The assumption that HSV and HIV infections could act synergistically has been reported. HSV infection increases the risk of acquiring HIV by two- to threefold (8). In addition, it might accelerate progression of the disease (9). The median duration of progression of untreated HIV infection from infection up to stage 4 (AIDS) usually lasts 10 years (10). Applying this to our case, progressive untreated HIV infection might facilitate the development and rapid worsening of herpetic perianal ulceration and, vice-versa, chronic HSV infection likely accelerated the progression of HIV infection to AIDS. Namely, the patient reported having receptive anal intercourse only during the previous 4 years. In addition, he reported having symptoms and signs 3 years previously that were consistent with acute HIV infection. Of course, these interesting assumptions underlying our case and suggested in the literature would need confirmation by a larger study.

From a clinical point of view, the association between rapid spreading of a perianal ulcer and progression of HIV to AIDS is especially interesting. Our case supports previous reports of the appearance of perianal lesions as a marker of progression to AIDS (4, 11, 12). It is also known that perianal lesions affect up to 34% of patients with AIDS (4). Therefore, all patients with perianal lesions should be screened for HIV or, when on therapy, monitored for the stage of the disease or possible non-adherence to therapy. This appears to be a valuable clinical recommendation. In our case, the patient would have certainly developed severe life-threatening AIDS-related complications if he had not been diagnosed with HIV and treated accordingly.

HPV infection in our patient should also be considered in the light of HIV infection. The data suggest that ART has a limited effect on reducing the incidence of high-grade squamous intraepithelial lesions (HSIL) or inducing HSIL regression (13, 14). On the other hand, a recent cross-sectional study of HIV-infected MSM showed that prolonged ART (2 years or longer) was associated with a lower prevalence of anal HSIL (15). A similar protective effect of ART was also seen for cervical HSIL and cancer in HIV-infected women (16). Further studies will reveal the exact effect of ART on HPV-related cancers. Until then, an HIV-infected patient with a chronic ulcer of any cause, especially with concomitant HPV infection as in our patient's case, should be routinely screened for SCC of the perianal area or anus because HPV-related cancers are still among the most common cancers in this population (14).

Overall, the following issues should be considered on the basis of our case and the literature when treating a patient with perianal lesions: 1) the presentation of herpetic infection in the perianal area of an immunocompromised patient is usually atypical, being ulcerative, necrotic, or vegetative, rather than typical as with immunocompetent patients, in whom the ulcer is small, circular, and shallow; 2) although patients may deny having had receptive anal intercourse when they present with any perianal lesion, they should be screened for sexually transmitted diseases, especially HIV; 3) when the perianal lesion is atypical, immunosuppression must be suspected and a search is necessary for the cause of immunosuppression; 4) when the herpetic infection manifests as a new ulcer, or a previously stable ulcer starts to progressively spread, there is a possibility that the patient has AIDS (or that the conversion from HIV infection to AIDS has recently occurred) and should therefore also be screened for HIV in order to begin immediate treatment; and 5) the effect of ART on concomitant HPV infection is not known, and therefore patients with perianal lesions should be routinely screened for possible SCC during the following years.

Conclusions

Patients with perianal lesions represent a significant proportion of patients that visit a dermatologist. Perianal lesions have a wide range of differential diagnoses; however, they are mainly caused by infections, most commonly by HSV-1 or HSV-2. All patients with infectious perianal lesions should be screened for sexually transmitted diseases. Clinical findings of HSV infection are usually atypical, especially in the case of immunosuppression, where lesions can be ulcerative, necrotic, or even vegetative. Perianal lesions, especially extensive and rapidly spreading perianal ulcers, should raise suspicion of an underlying immunosuppressive disorder, such as HIV or AIDS, which requires timely treatment.

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