

Extensive Atypical Genital Herpes Simplex Type 2 Infection as an Initial Manifestation of Acquired Immune Deficiency Syndrome

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Received: January 10, 2008

Accepted: June 20, 2008,

SUMMARY We present a case of an ulcerative lesion of the genitalia starting one year before in a 33-year-old man. Histopathologic examination revealed herpes virus infection, which suggested the existence of cell-mediated immunodeficiency. Human immunodeficiency virus (HIV) infection was confirmed by ELISA and Western blot test. The patient was treated with intravenous acyclovir, which led to complete remission. We underline the importance of early detecting and diagnosing patients with similar clinical manifestation as a sign of significant underlying immunodeficiency.

KEY WORDS: herpes simplex virus type 2 (HSV-2), human immunodeficiency virus (HIV), acquired immune deficiency syndrome (AIDS), oral candidiasis

INTRODUCTION

Genital herpes is a sexually transmitted viral infection, characterized by primary infection with grouped vesicles at the site of inoculation and a course of recurring outbreaks of vesicles at the same site. It is caused by herpes simplex virus type 2 (HSV-2) and less commonly by herpes simplex virus type 1 (HSV-1). In an immunocompromised host, HSV-2 may cause extensive local infection with chronic herpetic ulcers or even

widespread systemic infection. Herpetic lesions can sometimes be misleading and an accurate diagnosis may not be reached at the patient's first encounter with the physician. HSV-2 infections may often be unrecognized as lesions of viral origin, but may be ignored or mistakenly diagnosed as urinary tract infection, candidal yeast infection, allergy, factitial dermatitis, or other genital conditions (1). Improved diagnosis of HSV-2 infection



Figure 1. White plaques covering the soft palate and uvula of the patient.

could reduce inappropriate use of antibiotics and antifungal medications, as well as enable patients to receive effective treatment and take appropriate precautions to prevent the spread of the disease.

CASE REPORT

A 33-year-old male was admitted for painful ulcerative lesions of the genitalia which had developed within the past twelve months and had persisted ever since. His medical history included β -thalassemia trait and schizophrenia (satisfactorily controlled with drug therapy). He also complained of recurrent symptomatic HSV-2 genital

infections over the past eight years. The patient reported a weight loss of approximately 10 kg and several recurrent episodes of high fever during the past year. In this period, he visited several physicians and was initially given systemic antibiotic treatment for a diagnosis of perianal fistula, while on the next visits he was administered local antibiotics and corticosteroids plus systemic antibiotics for suspected recurrent febrile bacterial infections. During the last ten days, the patient reported antipyretic-resistant hyperpyrexia. On referral he was febrile with a temperature of 39.8 °C, blood pressure of 125/80 mm Hg and heart rate of 116 beats/min. Physical examination only revealed cachexia and paleness. White plaques were observed in the soft palate and uvula (Fig. 1). Cutaneous findings consisted of extended bilateral painful ulcerative lesions of the scrotum, penis, crural folds and thighs, which extended to the gluteal cleft area and buttock (Figs. 2 and 3).

The lesions were covered with pus and hemorrhagic exudate. Satellite papules and vesicles coexisted on healthy skin surrounding the main lesions. No other systemic involvement was recognized. Results of laboratory studies were as follows: hemoglobin 7.4 g/dL, hematocrit 24.2%, white blood cell count 6000/ μ L (82% neutrophil leukocytes, 11% lymphocytes), erythrocyte sedimentation rate 122 mm/1 h, albumins 23 g/L, and



Figures 2 and 3. Bilateral painful ulcerative lesions extending to the gluteal cleft area and buttock.

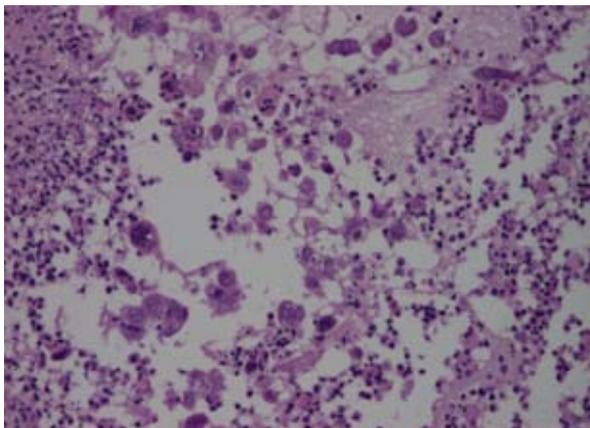


Figure 4. Histopathologic examination characteristic of HSV-2 infection.

globulins 42g/L. The remaining serum biochemistry and urinalysis results were all within the reference range. Culture of the ulcerated areas isolated a strain of β -hemolytic *Streptococcus* group F, while *Candida albicans* was isolated from the soft palate exudate. Histopathologic examination revealed disseminated intraepidermal vesicles which contained inflammatory cells. Several epithelial cells were multinucleated and contained intranuclear inclusions characteristic of HSV-2 infection (Fig. 4).

HSV-2 antigen was detected on the epithelial cells of the lesion using direct immunofluorescence techniques (BIORAD Laboratories). The Herpe-Select Elisa IgG test (Focus Diagnostics) revealed type specific antibodies to HSV-2, whereas IgM antibodies were negative. An in-house developed PCR was also positive for HSV-2. The patient's history and clinical presentation in conjunction with the diagnosis of HSV-2 infection and atypical nature of the lesions (widespread, ulcerated and chronic) were highly suggestive of a possible underlying acquired immunodeficiency. Our patient reported that he had never been tested for human immunodeficiency virus (HIV) infection before. The HIV-1 infection was confirmed by both ELISA and Western blot methods, while the CD4 lymphocyte count revealed 114 cells/mm³ (16%) and CD8 436 cells/mm³ (61%). HBsAg and anti-HCV tests were negative. The patient was treated with intravenous acyclovir, 500 mg every 8 hours for three weeks. Immediate fever remission and progressive regression of the cutaneous lesions with marked pain reduction were observed shortly after therapy initiation. For oral candidiasis he was treated with *per os* fluconazole, 100 mg twice a day for two weeks, which resulted in reduction of the white exudate.

DISCUSSION

MEDLINE was searched using the key words HSV-2 and HIV. Articles on HSV-2, its epidemiology and interaction with HIV were reviewed. The seroprevalence of HSV-2 antibodies varies considerably among various populations and ethnic groups, and it has increased over the past few years (2). Most of the infected persons are either asymptomatic or, more commonly, have genital symptoms that remain unrecognized (3,4). HSV infections manifesting with persistent anogenital lesions were among the first opportunistic infections to be described in persons with acquired immune deficiency syndrome (AIDS) (5). Moreover, several studies have shown that HIV-induced immune impairment results in severe, persistent and recurrent genital herpes, as well as in frequent subclinical reactivations (6,7). HSV-2 shedding is significantly associated with HIV serostatus and CD4 cell count <200/mm³ (8). In recent years, a strong epidemiologic association has emerged between HSV-2 and HIV infection. Numerous studies have proved that HSV-2 seroprevalence rates are higher in HIV-positive than in HIV-negative persons (9-14). Similarly to HIV, serologic diagnosis of HSV-2 infection has been suggested as a marker of lifestyle and sexual behavior (3). In addition, there is evidence that serologically documented HSV-2 infection is a significant risk factor for HIV acquisition (15). Several epidemiologic studies have demonstrated that prevalent HSV-2 is associated with a 2- to 4- fold risk of HIV-1 acquisition (7,15). Considering the particular and extensive clinical presentation of the herpetic infection in our patient, we were surprised to find the lesion history to have extended to a period of approximately 12 months back. It seems that in our case, the majority of physicians involved actually misdiagnosed the herpetic infection as being of bacterial origin, without considering the possibility of an atypical manifestation of a viral infection in an immunocompromised host. This probably occurred because of the great extension and severity of the lesions and of their atypical form, combined with systemic manifestations (fever, anemia, cachexia). Despite the fact that eventually the patient responded favorably to the treatment, such a delay in attaining an accurate diagnosis had affected the patient since he had undergone unnecessary administration of several antibiotics, suffered for a longer period while having a low quality of life, and finally much valuable time was wasted before diagnosing the HIV co-infection, while the patient could have also contaminated other individuals during the period of undiagnosed high viral load.

In conclusion, we report a case of chronic, extensive and atypical HSV-2 infection in an HIV-1 infected patient, emphasizing the fact that in HIV-positive patients, herpetic infection can differ from the classic form and highlighting the importance of similar cases as an alerting clinical sign of profound cellular immune depression. We would also suggest that physicians should on some occasions lower the generally used and widely accepted threshold for offering HIV testing (always in accordance with the clinical picture of every individual patient), with any particular clinical presentation and according to the most recent guidelines, even as part of routine care.

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