

CASE REPORT

AFRICAN JOURNAL OF CLINICAL AND EXPERIMENTAL MICROBIOLOGY MAY 2018 ISBN 1595-689X VOL19 No.2
AJCEM/1817 <http://www.ajol.info/journals/ajcem>
COPYRIGHT 2018 <https://dx.doi.org/10.4314/ajcem.v19i2.7>
AFR. J. CLN. EXPER. MICROBIOL. 19 (2):121 -124

ATYPICAL PRESENTATION OF GENITAL HERPES IN A RETROVIRAL DISEASE PATIENT ON HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY

Nwadike¹, V. U., Anaedobe², C. G., Azeez¹, R. A, Jinadu¹, S.S , & Chigozie¹, J. O.

¹Medical Microbiology Unit, Department of Pathology, Federal Medical Center, Abeokuta;

² Department of Medical Microbiology and Parasitology, College of Health Sciences, University of Abuja

Correspondence: Dr. Anaedobe Chinenye Gloria, Department of Medical Microbiology and Parasitology, University of Abuja, FCT, Nigeria. Phone: +234 806 784 4403 Email: chimedico@yahoo.com

ABSTRACT

Herpes Simplex Virus type 2 (HSV-2) is the leading cause of Genital Ulcer Disease (GUD) worldwide. In HIV infected persons, it typically presents with increased number of recurrent genital lesions which often have severe and prolonged presentations. There are reports that patients receiving highly active antiretroviral therapy (HAART) may be more prone to chronic genital ulcers and a higher risk of acyclovir-resistant herpes infection than is seen in immune competent patients. We present a case of recurrent genital herpes infection in a sexually active 15 year old known HIV patient.

Keywords: Recurrent genital ulcer, HSV-2, HIV, HAART

PRÉSENTATION ATYPIQUE DE L'HERPÈS GÉNITAL CHEZ UN PATIENT DE LA MALADIE RÉTROVIRALE HAUTEMENT ACTIVE SUR LA THÉRAPIE ANTIRÉTROVIRALE

Nwadike¹, V. U., Anaedobe², C. G., Azeez¹, R. A, Jinadu¹, S.S , & Chigozie¹, J. O.

¹Unité de microbiologie médicale, Département de Pathologie, centre médical fédéral, Abeokuta;

²Département de microbiologie médicale et parasitologie, Collège des Sciences de la santé, l'Université d'Abuja

Correspondance: Dr. Anaedobe Chinenye Gloria, Département de microbiologie médicale et de parasitologie, Université d'Abuja, Nigéria, FCT. Téléphone : +234 806 784 4403 Email : chimedico@yahoo.com

RÉSUMÉ

Herpès simplex type 2 (HSV-2) est la principale cause d'ulcérations génitales (UG) dans le monde entier. Les personnes infectées par le VIH, en règle générale, elle présente à l'augmentation du nombre de lésions génitales récurrentes qui ont souvent des présentations grave et prolongée. Il y a des rapports que les patients recevant un traitement antirétroviral hautement actif (HAART) peuvent être plus sujets à des ulcérations génitales chroniques et un risque plus élevé de l'infection d'herpès résistant à l'acyclovir qu'est vu dans l'abri les patients compétents. Nous présentons un cas d'herpès génital récurrent dans une infection sexuellement actif 15 ans VIH connues du patient.

Mots-clés: ulcère génital récurrent, HSV-2, le VIH, la multithérapie

INTRODUCTION

Genital herpes is typically caused by HSV-2 but can also be caused by HSV-1 (1, 2). In HIV patients with genital herpetic ulcers, particularly those receiving HAART, the presentation is often more severe and chronic with increasing episodes of recurrent genital ulcers. Several reasons have been postulated including immune reconstitution inflammatory syndrome (3, 4). It is believed that more severe clinical symptoms occurs following HAART due to

the improved immune status and more effective ability to mount an immune response against a pathogen (3).

Case Presentation

A fifteen year old boy from an urban lower class setting presented to the General Out-Patient Clinic (GOPD) of Federal Medical Center, Abeokuta, with a seven (7) month history of non-healing ulcerative lesion affecting the penile organ.

The ulcer was said to have been painful, pruritic and discharging serous fluid several months earlier. However, there was neither history of trauma to affected region, nor use of drugs besides prescribed ones. He had unprotected sexual intercourse on multiple occasions, two weeks before onset of the penile ulcer. Patient is known with vertically transmitted HIV infection and had been commenced on highly active anti-retroviral therapy (HAART) 22 months prior to presentation. He was compliant on his medications up to the time of presentation. His past medical history was otherwise notable for recurrent left neck sore of two years duration.

Patient presented afebrile and vital signs were within normal limits. Examination of the genitals revealed a non-tender, non-pruritic shallow ulcer extending from the lower border of his glans penis anteriorly to the anterolateral border of the shaft of his penis. This can be seen in Figure 1. All other systemic examinations were non-contributory.

VDRL done at presentation was non-reactive and wound swab culture yielded no growth after 48 hours of incubation, however, serology for HSV-2 done via ELISA was positive in the patient and absolute CD4+ count was 480 cells/mm³. He was commenced on a 10 day course of oral Acyclovir 200mg four times daily; he was also prescribed acyclovir cream, erythromycin and his routine anti-retroviral medications. He was booked for regular weekly STI clinic visits. Follow up clinic visits showed marked improvement of ulcer and resolution of the wound.



FIGURE 1: PENILE ULCER AT FIRST PRESENTATION

Six months later, the patient presented to the STI clinic with a recurrent penile ulcer that first appeared as a discharging blister with associated itching and pain on contact three weeks earlier. The lesion was large, measuring about 4cm by 3cm, had no clearly defined edges, and was tender to touch. There was no inguinal lymphadenopathy.

A diagnosis of reactivation of latent herpes simplex genital ulcer was subsequently made and he was placed on oral and topical acyclovir. He was also advised on good wound care and scheduled for follow up clinic visits. Subsequent clinic visits revealed increasing size of penile ulcer despite antiviral therapy. Patient however gave a history of poor drug compliance due to severe financial constraint. Efforts were made to ensure availability of drugs and proper drug compliance while patient was placed on acyclovir 400 mg PO daily as suppressive therapy. Subsequent follow up clinic visits several weeks later confirmed complete resolution of lesion.

DISCUSSION

Genital herpes, a well-recognized and globally endemic sexually transmitted infection (1, 2) is mostly as a result of HSV-2 infection (1). However, both HSV-1 and HSV-2 are capable of establishing latent infection in the sensory root ganglion of the lumbosacral region with capability for subsequent reactivation of the disease in later time. The statistics for the current prevalence and incidence of HSV-2 in Nigeria is not well documented. However, as at 2012, global estimated figures revealed that 417 million people aged 15–49 years were living with HSV-2 infection, of which 267 million were women (5). Also, 19.2 million individuals aged 15–49 years were newly-infected (5). The highest burden was in Africa (5).

Genital Herpes typically presents as a cluster of painful vesicular or ulcerative muco-cutaneous lesions on an erythematous base. These lesions often crust, re-epithelialize and heal without scarring. Transmission typically occurs when the virus enters into the body through broken skin or mucous membranes by direct sexual contact with the secretions or mucosal surfaces of an infected person (1). The virus subsequently multiplies at the point of entry before ascending along the sensory nerve roots to the dorsal root ganglion where it establishes latency. Reactivation triggers the transfer of the virus from the dorsal root ganglion back down to the nerve root on the muco-cutaneous surface where it usually causes symptoms to occur. However, subclinical viral shedding has been documented in more than 80 percent of HSV-2 seropositive persons with no reported lesions (6).

Index case is a case of a 15 year old boy known with vertically transmitted HIV infection who presented to our facility on account of a seven months history of recurrent penile ulcer which he noticed two weeks after series of unprotected sexual intercourse. He was subsequently diagnosed serologically positive for HSV-2 IgG. With onset of sexual activity at age of 15 years, this patient typifies those infected with their

first genital herpes infection which coincides with the onset of sexual activities. The history of immunosuppression further increases the risk of contracting the disease. There is a well-known relationship between human immunodeficiency virus and genital herpes infection as it has been observed and documented that the interaction between HSV-2 and HIV may result in more efficient transmission of HIV and an increased rate of HIV replication during HSV-2 reactivation (6-8).

Genital herpes in HIV infected persons typically presents with increased number and size of lesions both in primary and recurrent infections, atypical disease presentations and increased risk of genital shedding, more than is seen in immune competent patients (3, 4, 8). Also, the lesions are usually chronic, more severe and may or may not be associated with pain (3, 4). Studies have shown that as immunosuppression worsens with a drop in CD4 cell count, recurrent genital herpes increase in frequency, chronicity and severity unless interventions are made (3-6). Although HAART has been shown to reduce the duration of genital ulcers; there are reported cases of Immune Reconstitution Inflammatory Syndrome (IRIS) in HIV patients with genital herpes (3, 4, 7, 8). This is a paradoxical clinical worsening of an existing condition or the appearance of a new condition after initiating antiretroviral therapy in HIV-infected patients.

HSV-2 is one of the most common causes of IRIS and HSV-2 IRIS is associated with increased severity of ulcerative disease and increased frequency of recurrences (8). Some patients present with worsening genital ulcers despite receiving therapy, this is perhaps due to excessive immune reaction to the infectious agent. The IRIS can occur within few months following the initiation of HAART. There should be a high index of suspicion for it in the presence of atypical disease presentation, treatment failure with standard regimen amidst improving CD4

cell count and decreasing viral load. In this case, the patient's medical history of recurrent genital ulcers, the background of retroviral disease on HAART, atypical presentation of the ulcer and failure to respond to standard treatment regimen helped to confirm the diagnosis.

Recurrent genital herpes in HIV patients often poses a significant problem as patient often do not respond to standard treatment regimen. Acyclovir-resistant HSV infections are often seen and successful treatment with parenteral Valacyclovir, Famcyclovir and in some case topical corticosteroids, Imiquimod cream, have been reported (3, 4, 7). Suppressive Acyclovir therapy at the initiation of HAART in HIV/HSV-2 co-infected patients has been shown to blunt the anticipated increase in GUD incidence (8). It is worthy of note that an extended period of treatment with oral acyclovir was employed in the index case following failure of significant relief of symptoms after the standard 10 days of oral acyclovir therapy as per protocol. This suggests that in HIV/HSV-2 co-infected patients and particularly those on HAART, acyclovir-resistance should be looked out for and alternative treatment initiated early.

Conclusion: Genital herpes is frequent in HIV positive populations particularly those receiving HAART and may present with more severe, chronic and widespread lesions. They are more likely to be recurrent and be resistant to standard treatment regimen with oral acyclovir. Clinicians managing patients with HIV/HSV-2 co-infection should anticipate these atypical presentations and consider the use of suppressive acyclovir therapy or effective alternatives in order to reduce the severity of genital herpes in these patients.

Competing interests: The authors declare no competing interest.

Funding: The case report received no financial support.

REFERENCES

1. Looker KJ, Garnett GP, Schmid GP. An Estimate of the Global Prevalence and Incidence of Herpes Simplex virus type 2 infection. *Bull World Health Organ* 2008; 86(10): 805-12
2. Catriona Ooi and Vijay Zavar, "Hyperaesthesia following Genital Herpes: A Case Report," *Dermatology Research and Practice*, vol.2011, Article ID 903595, 3 pages, 2011.

3. Shelburne SA 3rd, Hamill RJ, Rodriguez-Barradas MC, Greenberg SB, Atmar RL, et al. Immune reconstitution inflammatory syndrome: Emergence of a unique syndrome during highly active antiretroviral therapy. *Medicine (Baltimore)* 2002; 81: 213-227
4. Couppié P, Sarazin F, Clyti E, El Guedj M, Vaz T, et al. Increased Incidence of Genital Herpes after HAART Initiation: A Frequent Presentation of Immune Reconstitution Inflammatory Syndrome (IRIS) in HIV-

- Infected Patients. *AIDS patient care STDS* 2006; **20**: (3) 143-145
5. Katharine J. Looker, Amalia S. Magaret, Katherine M. E. Turner, Peter Vickerman, Sami L. Gottlieb *et al.* Global Estimates of Prevalent and Incident Herpes Simplex Virus Type 2 Infections in 2012. *PLoS one* 2015; **10**(5): e0114989. <https://doi.org/10.1371/journal.pone.0114989>
 6. Wald A, Zeh J, Selke S, Warren T, Ryncarz AJ, Ashley R, et al. Reactivation of genital herpes simplex virus 2 infection in asymptomatic seropositive persons. *N Engl J Med.* 2000; **342**:844-50
 7. McKendry A, Narayana S, Browne R. Atypical presentations of genital herpes simplex virus in HIV-1 and HIV-2 effectively treated by imiquimod. *Int J STD AIDS* 2014; **9**: 98-99.
 8. Kenneth H. Fife, Kenneth Mugwanya, Katherine K Thomas, Jared M Baeten, Connie Celum, *et al.* Transient Increase in Herpes Simplex Virus Type 2 (HSV-2)-Associated Genital Ulcers Following Initiation of Antiretroviral Therapy in HIV/HSV-2-Co-infected Individuals. *The Journal of Infectious Diseases* 2016; **213** (10): 1573-1578,