# Cytomegalovirus induced genital ulcer in human immunodeficiency virus positive patient

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## Abstract

Cytomegalovirus (CMV) can cause life-threatening disease in immunocompromised patients, such as those with human immunodeficiency virus. It is a rare but important cause of ulceration in the female genital tract. Although cutaneous manifestations are rare, there are growing reports of CMV infections in genital and perigenital ulcers in immunocompromised individuals. CMV disease of the female genital tract may result in significant morbidity, with fever, pain, bleeding, and superinfection, and it may be associated with the development of pelvic inflammatory disease and cervical intraepithelial neoplasia. There are several options for diagnosis and for safe treatment.

**Key words:** Cytomegalovirus, human immunodeficiency virus, valganciclovir

## Introduction

Human immunodeficiency virus (HIV) patients have a wide variety of cutaneous complaints which are typical in different stages of the disease. Even though many patients present to us with genital ulcers, we tend to neglect the possibility of CMV genital ulcer in them. Here, we report an interesting case of CMV genital ulcer.

## Case Report

A 44-year-old female patient, known case of retroviral disease on tenofovir efavirenz lamivudine (TLE) regimen for 2½ years, changed to the second-line regimen for 1 month with a CD4 count of 17/mm$^3$ admitted for chronic diarrhea under evaluation presented to us with a history of painless genital ulcer since one and half month, initially started as fluid-filled lesions which later ruptured to leave behind large nonhealing ulcers without any discharge.

On examination found to have a large dry ulcer with maximum dimensions of 15*17cm, with irregular borders, nontender, nonindurated on palpation covered with pale granulation tissue which extended laterally till inguinocrural fold, anterior extension till symphysis and posterior extension till perianal region [Figure 1]. No regional lymphadenopathy was present.

Provisional diagnosis of herpes genitalis and squamous cell carcinoma was made. Tzank smear was done but no cytopathic effect was appreciated because the lesion was dry at the time of presentation. Full-thickness punch biopsy was taken from the edge of ulcer and the report showed full-thickness atypia of epithelium with extensive ulceration, active inflammation [Figure 2] and viral cytopathic changes like owl's eye inclusion bodies suggestive of CMV infection [Figure 3]. Section was negative for malignancy. Since the biopsy showed inclusion bodies suggestive of CMV, serology and polymerase chain reaction (PCR) were done to confirm the same.

Ig M antibodies to CMV were negative. IgG antibodies to CMV were >250.0 AU/ml (highly positive). Qualitative CMV DNA PCR was highly positive. Ophthalmic examination showed no signs of CMV retinitis.

With this, the diagnosis of CMV genital ulcer was made. The patient was put on tab acyclovir 400 mg tid for 10 days and patient showed partial response [Figure 4a]. Later on, she was put on valganciclovir 900 mg BD for 4 weeks and the ulcer showed significant improvement by the end of 3rd week [Figure 4b]. The patient lost follow-up thereafter.

## Discussion

Cytomegalovirus is one of the most common opportunistic agents in immunocompromised hosts with HIV infection[1] and solid organ[2,3] and hematologic transplantation and in

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the beginning of iatrogenic suppression in the treatment of cutaneous lupus erythematosus.[4] Cytomegalovirus is

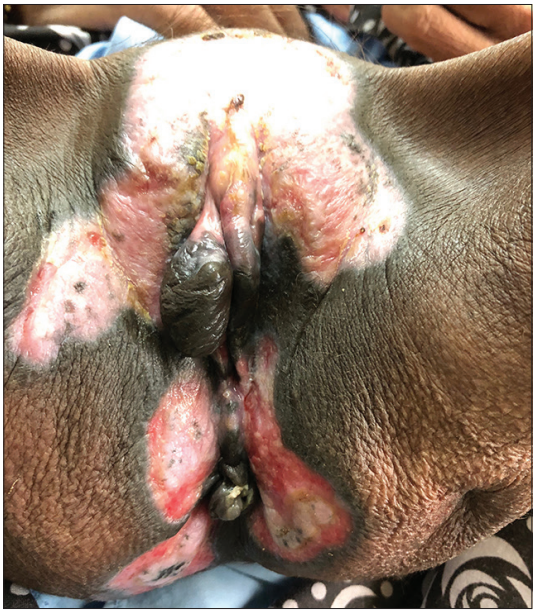

**Figure 1:** Initial presentation of the ulcer

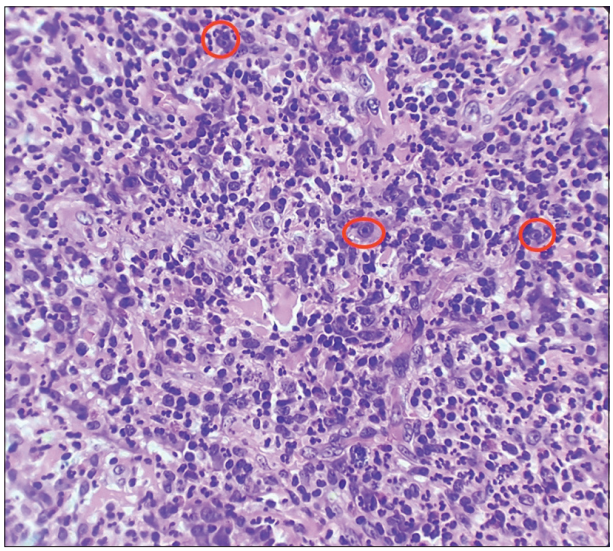

**Figure 3:** Multiple owl's eye inclusion bodies are encircled, (Hematoxylin and Eosin, ×40)

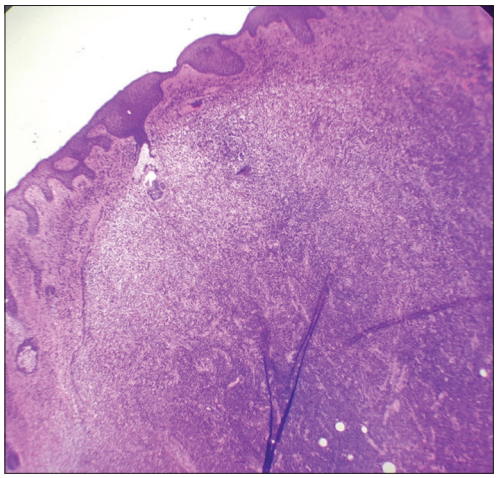

**Figure 2:** On histopathology section, there was full-thickness atypia with neutrophilic infiltration up to deep dermis (Hematoxylin and Eosin, ×4)

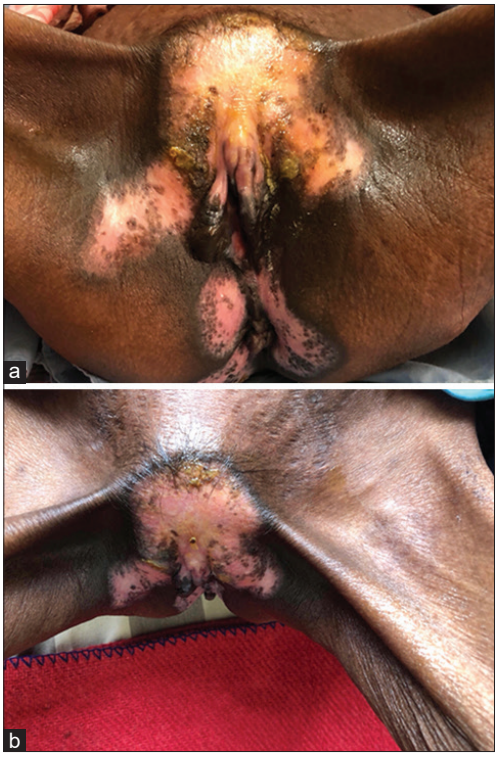


**Figure 4:** (a) Partial response after 2 weeks of acyclovir (b) Significant re-epithelialization after 3 weeks of valganciclovir

## Table 1: Case reports of CMV ulcers

| Case Report | Details of the case | Clinical findings | Outcome |
|---|---|---|---|
| Pariser (1983) | 39-year-old renal transplant with specific skin lesions of CMV | Generalized maculopapular rash with two genital ulcer | Patient did not survive to initiate treatment |
| Toome *et al.* (1991) | Case report of 36 year old AIDS patient with CMV ulcer | 2 cm ulcer on with thin crust on left knee | Patient refused treatent |
| Katherine *et al.* (1995) | Retrospective cohort of 307 patients of HIV with genital ulcer. One patient showed CMV | 8 months history of periurethral painful ulcer. Biopsy and culture confirmed CMV | Ganciclovir regimen for 5 weeks and gradual improvement |
| Moodley *et al.* (2003) | CMV and HSV in vulval lesions of HIV patient | Solitary ulcer of 8×5 cm on left labia, nonhealing since years | IV ganciclovir for 14 days. Lesion regressed markedly after 1 month |
| Rasniksingh *et al.* (2017) | Case series of cutaneous CMV | One case of B-cell lymphoma had rash with oral and genital erosions another case, 45-year-old HIV-positive male with nodules and erosions on legs | Treatment not mentioned |

CMV=Cytomegalovirus; HIV=Human immunodeficiency virus; HSV=Herpes simplex virus; IV=Intravenous

a member of the herpes family of DNA viruses. They have a latent period followed by acute disease followed by an asymptomatic, quiescent state. Infection with CMV in most immunocompetent hosts is asymptomatic but can present as a mononucleosis like syndrome. Host immunosuppression can lead to reactivation of latent viruses and viral proliferation.

Ninety percent of patients with AIDS are infected with CMV. In an AIDS-infected host, CMV can cause pneumonia, encephalitis, gastrointestinal ulcers, hepatitis, retinitis, and disseminated disease. Retinitis is the most common manifestation of CMV in an HIV-positive patient.[5]

There are infrequent reports in the literature of cutaneous CMV infections [Table 1]. This may be because cutaneous CMV infections are uncommon and show subtle histopathological findings. Skin lesions of CMV can present as maculopapular rashes, urticarial eruptions, scarlatiniform eruptions, cutaneous ulcers, oral ulcers, papules, nodules, morbilliform eruptions, verrucous lesions, perifollicular papulopustules, and vesiculobullous eruptions.[6] Cutaneous CMV lesions often herald disseminated infection and are usually associated with a mortality of 85% within 6 months.[7]

There is some controversy surrounding the pathogenic role of CMV in cutaneous lesions. It has been argued that CMV found in ulcerative lesions could be due to disseminated hematogenous infection, reactivation within the endothelial cells, or auto-inoculation through urine, feces, or saliva shedding because the majority of CMV ulcers are found in the genital and perianal regions.[8]

Ganciclovir, valganciclovir, and foscarnet have been efficacious in the treatment of cutaneous CMV. Valganciclovir was approved by the Food and Drug Administration in 2001 for the treatment of CMV retinitis in immunocompromised hosts. 60% of oral valganciclovir is absorbed versus 6% to 9% of oral ganciclovir. Plasma levels of oral valganciclovir are comparable with those of intravenous ganciclovir,[9] with almost same efficacy and adverse effects. This therapeutic option is extremely valuable because valganciclovir does not require an IV line and thus reduces all of the complications associated with these devices, which is especially important in an immunocompromised patients.

Valganciclovir 900 mg BD per oral for a minimum of 2 weeks to be given for cutaneous infection or until viral eradication is achieved on quantitative viral assay on two separate occasion at least a week apart.[10] Foscarnet and cidofovir can be added in resistant cases.

## Conclusion

Even though there are very less case reports of CMV genital ulcer, any suspected case of genital herpes with partial response to acyclovir should be thoroughly investigated to rule out the possibility of CMV genital ulcer. Adequate treatment with valganciclovir may help in significant healing of the ulcer.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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