

# Case Report: Symptomatic Oral Herpes Simplex Virus Type 2 and Asymptomatic Genital Shedding

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## KEY WORDS

■ ORAL HSV-2 ■ ORAL HSV-2 SHEDDING ■ ASYMPTOMATIC GENITAL SHEDDING

## SUMMARY

A 42-year-old bisexual man with a history of recurrent oral herpes and no history of genital herpes was noted to have antibody to herpes simplex virus type 2 (HSV-2) only. During a symptomatic oral recurrence, HSV-2 was found in a perioral lesion as well as in the genital area.

## Introduction

RECURRENCES OF ORAL herpes simplex virus type 2 (HSV-2) after a primary oral and genital infection are rare (mean monthly frequency of recurrence is 0.001).<sup>1</sup> Oral lesions in the absence of genital lesions occurred on only 3 of 58 days, even among people who reactivate HSV-2 orally (3.2% in one study).<sup>2</sup> This case report highlights the importance of viral identification of oral lesions and concurrent genital infection in the absence of symptomatic genital disease in HSV-2 seropositive patients.

## Case Report

A 42-year-old bisexual man presented to the University of Washington Virology Research Clinic, USA, with a 19-year history of oral lesions consistent with herpes simplex that recurred annually. He had no history of genital lesions. He reported having had a commercial type-specific HSV antibody test that was positive for HSV-2 and negative for HSV-1. He had never used episodic or suppressive antiviral medication. The patient was concerned about asymptomatic genital and oral shedding, and transmission of HSV-2 to his partners.

HSV antibody testing by Western blot, at the University of Washington, confirmed the patient's serology status as HSV-2 positive and HSV-1 negative.<sup>3</sup> An HIV antibody test was negative. The patient enrolled in a study where he collected separate swabs of the oral mucosa and genital area daily, and a separate swab of any oral or genital lesion that appeared. Oral mucosa and genital swabs were obtained by the patient rubbing a sterile swab on his buccal mucosa and tongue; and the skin surface of his penis, the area between the scrotum and anus, and perianal area, respectively.<sup>4</sup> All swabs were tested for HSV-1 and HSV-2 DNA by type-specific polymerase chain reaction (PCR).<sup>5</sup> Fifty-nine oral and 59 genital secretion swabs were collected on consecutive days. The patient did not experience any oral or genital lesions during the collection period, and all oral and genital HSV PCR assays were negative.

Six months later, the patient returned to clinic reporting the onset of a 'pimple' near his lip 3 days

earlier. Prior to the clinic visit, the patient obtained oral mucosa, perioral lesion and genital swabs for HSV DNA detection by PCR. He was instructed to obtain oral mucosa, genital and lesion swabs at the first indication of an HSV recurrence. Swabbing and clinic notification was delayed 3 days because the patient did not initially recognize the perioral lesion as an HSV recurrence. Examination revealed a 0.4 cm crusted lesion 1 cm from the right corner of the patient's mouth. HSV-2 was isolated in culture from the perioral lesion swab collected in the clinic, and  $10^{6.3}$  copies/ml of HSV-2 DNA were detected. HSV-2 DNA was also detected in the swabs, obtained by the patient, from the perioral ( $10^{6.9}$  copies/ml) and from the genital skin ( $10^{3.6}$  copies/ml). Oral mucosa swabs obtained at home by the patient and in clinic were negative for HSV PCR assay.<sup>5,6</sup>

## Discussion

We report oral and genital HSV-2 shedding in an HSV-2 seropositive man without a history of genital herpes. The difference in viral copy numbers between the two sites (oral and genital) can be attributed to the presence of the lesion in the oral area. The infrequent oral recurrences, absence of genital lesions and lack of detection of HSV DNA during daily swabbing suggests that HSV reactivates infrequently in this patient. Despite the clinical evidence of perioral herpetic disease, he has HSV-2 infection both orally and genitally, and he is at risk of transmitting HSV-2 to his partners during sexual activity.

Few studies have systematically evaluated oral HSV-2 shedding in the mouth. Among 109 men followed for a median of 64 days with daily PCR examination of oral secretions, the mean HSV-2 detection rate was 2.3%. No days of oral HSV-2 shedding were associated with corresponding lesions. In that study, men who had sex with men and those with HIV infection had a higher risk of oral HSV-2 shedding. In addition, oral HSV-2 was frequently detected during episodes of genital herpes. However, in that series, no patient reported only symptomatic oral disease and no history of genital herpes.<sup>7</sup>

Oral HSV-2 is considered rare, especially in the absence of symptomatic genital disease. Is it rare because it occurs infrequently, or because, in a clinical practice setting, recurrent oral lesions are assumed to be HSV-1? In clinical practice, the availability of type-specific HSV serologic testing and PCR DNA allows for accurate diagnosis and appropriate counselling. Of particular note, this case supports the concept that antibody to HSV-2 should be interpreted as genital herpes. Even in a person with clinically overt oral herpes, HSV-2 antibody indicated virologically active genital infection.

## Conclusion

This case illustrates the importance of serological and virological testing when patients present with oral lesions and are at risk of having acquired oral HSV-2. Patients with oral HSV-2 recurrences should be counselled about the potential for asymptomatic HSV-2 genital shedding.

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## Conflicts of Interest

No conflicts of interest were declared in relation to this article.

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## Key Papers

### Long-term acyclovir for prevention of varicella zoster virus disease after allogeneic hematopoietic cell transplantation—a randomized double-blind placebo-controlled study.

Boeckh M, Kim HW, Flowers ME, Meyers JD, Bowden RA. *Blood* 2006;**107**:1800–1805.

### VZV

Varicella zoster virus (VZV) disease occurs in 30% of allogeneic haematopoietic cell transplant recipients who have a history of VZV infection. A safe and effective prevention strategy has not been established. In a double-blind controlled trial, 77 haematopoietic cell transplant recipients at risk for VZV reactivation were randomized to aciclovir 800 mg twice daily or placebo given from 1 to 2 months until 1 year after transplantation. VZV disease at 1 year was the primary end point; VZV disease after discontinuation of prophylaxis, VZV-specific T-cell immunity, herpes simplex virus (HSV) infection, cytomegalovirus (CMV) disease, survival, and safety were secondary end points. Aciclovir significantly reduced VZV infections at 1 year after transplantation (hazard ratio [HR], 0.16; 95% confidence intervals [CI], 0.035–0.74;  $P=0.006$ ). In

the post-intervention observation period, this difference was not statistically significant (2 years: HR, 0.52; 95% CI, 0.21–1.3; 5 years: HR, 0.76; 95% CI, 0.36–1.6). There was no statistically significant difference in reconstitution of VZV-specific T-helper cell responses, HSV infections, CMV disease, chronic graft-versus-host disease, and overall survival between the groups. Aciclovir was well tolerated. Post-study VZV disease predominantly occurred in patients with continued need for systemic immunosuppression. In conclusion, aciclovir effectively and safely prevents VZV disease during the first year after haematopoietic cell transplantation. Periods of prophylaxis longer than 12 months may be beneficial for those haematopoietic cell transplant recipients on continued immune suppression.

### Transmission of integrated human herpesvirus 6 through stem cell transplantation: implications for laboratory diagnosis.

Clark DA, Nacheva EP, Leong HN, Brazma D, Li YT, Tsao EH *et al*. *J Infect Dis* 2006;**193**:912–916.

### HHV

We identified a stem cell donor with chromosomally integrated human herpesvirus (HHV)-6 and monitored the recipient for HHV-6 after transplantation. The appearance and subsequent increase in HHV-6 load paralleled engraftment and an increase in white blood cell count. Fluorescent *in situ* hybridization analysis showed integrated HHV-6 on chromosome band 17p13.3 in the donor and in the recipient after

transplantation but not in the recipient before transplantation. The increase in viral load due to the genetic transmission of integrated HHV-6 could have been misinterpreted as substantial active infection and, thus, led to the administration of toxic antiviral therapy. We suggest that the confounding influence of integration be considered in laboratory investigations associating HHV-6 with disease.