

CASE REPORT

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Atypical presentation of herpes simplex virus 2 primary infection: a case report

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Abstract

Background Cervicitis, an infectious or noninfectious inflammation of the cervix, encompasses a wide range of clinical conditions, from asymptomatic infections to severe lesions, making its diagnosis difficult. Acute cervicitis may develop into pelvic inflammatory disease. In patients with cervicitis, current guidelines recommend testing for herpes simplex virus when external genital lesions are present. Here, we present the case of a patient with an atypical primary herpes simplex virus 2 infection manifesting as cervicitis without genital lesions.

Case presentation A 29-year-old Caucasian woman was hospitalized for pelvic inflammatory disease. The patient complained of severe suprapubic pain, fever, and heavy vaginal discharge. The external genitalia were unremarkable, so empirical antibiotic treatment was initiated. Despite 48 hours of well-administered antibiotic therapy, her complaints persisted. Polymerase chain reaction for possible microbial causes was negative for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. There was no bacterial vaginosis. Repeat gynecological examinations with endovaginal ultrasound revealed an enlarged cervix, and pelvic magnetic resonance imaging supported a diagnosis of cervicitis. At this point, additional screening for other sexually transmitted infections and infectious disease-related etiologies of cervicitis was performed, and the polymerase chain reaction analysis of newly isolated samples was positive for herpes simplex virus 2. No antiviral treatment was initiated given the delay in diagnosing herpes simplex virus 2 infection and the slow but spontaneous abatement of symptoms.

Conclusion Herpes simplex virus infection should be considered as a possible cause of cervicitis, even in the absence of typical genital lesions. Early detection of herpes simplex virus allows early treatment, helping to reduce the duration and severity of symptoms and therefore potentially reducing recurrences and improving disease control. These data and data from future cases might spur changes in the guidelines on cervicitis testing and treatment.

Keywords Herpes simplex virus, Cervicitis, Genital lesions, Antiviral, Case report

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Introduction

Cervicitis is a clinical syndrome characterized by inflammation of the cervix, which can present with wide clinical variability, ranging from no symptoms to mucopurulent cervical discharge and systemic signs. The exact prevalence of cervicitis is unknown due to the lack of a standard definition and variation between populations. It may affect 30–40% of patients seen in sexually transmitted infection (STI) clinics [1]. For patients with cervicitis, the current guidelines recommend testing for herpes simplex virus (HSV) when external genital lesions are present [1, 2]. HSV, especially type 2, is one of the most common STIs worldwide, with a seropositivity rate of approximately 12% in the European population in 2023 [3]. Genital HSV infection ranges from asymptomatic to typically painful vulvar ulcers but can manifest as cervicitis, which makes it difficult to diagnose [4]. Here, we report a rare case of cervicitis due to HSV infection with no lesions to highlight the importance of considering HSV in the etiological diagnosis of any cervicitis, even in the absence of typical genital lesions, because early recognition of the infection allows for better management of the disease.

Case presentation

A 29-year-old Caucasian woman with no relevant personal history other than cephalosporin allergy was admitted with suspected pelvic inflammatory disease (PID). She presented to the emergency department with 24 hours of suprapubic pain and 48 hours of pyrexia. She described mild mictalgia and a liquid, transparent, odourless vaginal discharge requiring a change in sanitary napkins every 2 hours; 3 days before admission, the patient had been separately seen by an emergency physician at the same hospital for discharge, which was initially considered urinary incontinence, resulting in the prescription of a single 3-g dose of oral fosfomycin. This antibiotic treatment did not improve her symptoms. Her last sexual intercourse, with an occasional male partner, was 14 days prior and involved the use of a condom. The patient was nulliparous and compliant with combined oral contraceptives. Her previous gynecology consultation session was 2 years before admission, and her last cervicovaginal smear, performed 3 years earlier, was unremarkable.

On initial clinical examination, there was abdominal pain in the suprapubic area and iliac fossae without guarding or rebound tenderness. The vulva was unremarkable. Pelvic examination revealed a diffusely tender vagina with uterine pain upon mobilization. Speculum examination confirmed abundant fluid discharge and revealed a slightly edematous cervix without any other lesions. Endovaginal ultrasound did not reveal adnexal masses, and biological investigation revealed a C-reactive

protein level of 76 mg/L ($N < 5$ mg/L) without hyperleukocytosis. The urinary sediment test was negative. Accordingly, the patient was diagnosed with an early presentation of PID with no adnexal abscess. Classic PID investigation, consisting of vaginal swabs for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and bacterial vaginosis, was conducted. The patient was hospitalized in our gynecology department and was given empirical antibiotic therapy. Given her allergy to cephalosporins, treatment included 100 mg of oral doxycycline twice daily, 500 mg of intravenous metronidazole three times daily, and 500 mg of intravenous ciprofloxacin twice daily (see Fig. 1 for the case timeline).

After 48 hours of well-conducted antibiotic therapy, the patient's clinical condition remained unfavorable, with increased pain and a persistent subfebrile state. Polymerase chain reaction (PCR) run on vaginal swabs for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, as well as bacterial cultures, were negative. A substantially enlarged cervix, measuring $53.9 \times 37.1 \times 39.6$ mm on endovaginal ultrasound, was evident during a repeat gynecological examination (Fig. 2), while other abdominal pathologies were ruled out by abdominal ultrasound. Findings on pelvic magnetic resonance imaging (MRI) supported a diagnosis of cervicitis, as it revealed that the cervix was substantially swollen and edematous in appearance, and diffusion-weighted imaging (DWI) revealed a hyperintense signal caused by the high water content of cervical cells, confirming inflammation. However, no significant decreases in the apparent diffusion coefficient were observed, which made malignancy unlikely (Figs. 3 and 4). Nonspecific left external iliac adenopathy measuring 8 mm was also detected. Given these results, additional screening for other STIs and infectious disease-related etiologies of cervicitis, such as syphilis, hepatitis B, hepatitis C, human immunodeficiency virus (HIV), *Mycoplasma genitalium*, *Trichomonas vaginalis*, HSV-1, and HSV-2, was performed. On day 4, PCR and culture results for HSV-2 were positive, and subsequent HSV-2 serological evaluation showed that the samples were positive for HSV-2 immunoglobulin M (IgM) and negative for HSV-2 IgG. The final diagnosis of HSV-2 cervicitis was made, and a mild favorable clinical outcome was achieved. In light of the late diagnosis and after an informal discussion with infectiologists, no antiviral treatment was given, and antibiotic treatment was stopped when she was discharged from hospital on day 6 after admission.

A follow-up assessment 1 week after hospital discharge revealed persistent and heavy vaginal discharge but resolution of pain, and 3 months after discharge, MRI revealed regression of the swelling and edema of the uterine cervix and a lack of hyperintense DWI signals (Fig. 5).

Day -3	Discharge with a diagnosis of urinary incontinence by emergency physician (single 3-g dose of oral fosfomycin was prescribed)
Day -2	Pyrexia
Day -1	Suprapubic pain
Day 0	- Admission for suspected PID (empirical antibiotics) - Endovaginal ultrasound, blood test and urinary test done - PCR for <i>N. gonorrhoeae</i>, <i>C. trachomatis</i> and culture for bacterial vaginosis
Day 1	
Day 2	- No improvement in symptoms - Second clinical examination and vaginal US: cervix oedematous and cervicitis diagnosis suspected - PCR <i>N. gonorrhoeae</i>/<i>C. trachomatis</i>, bacterial vaginosis negative → Testing for all STIs - Abdominal US to exclude other pathologies: negative - Continued antibiotic treatment
Day 3	MRI: confirmation of cervicitis diagnosis
Day 4	- All the results obtained: HSV2-cervicitis - Patient begins to get better - Discussion with infectious disease specialists: no change in management
Day 6	Discharge from hospital. Discontinuation of antibiotic treatment
3 Months	Second MRI to confirm good resolution of cervicitis

Fig. 1 Case timeline

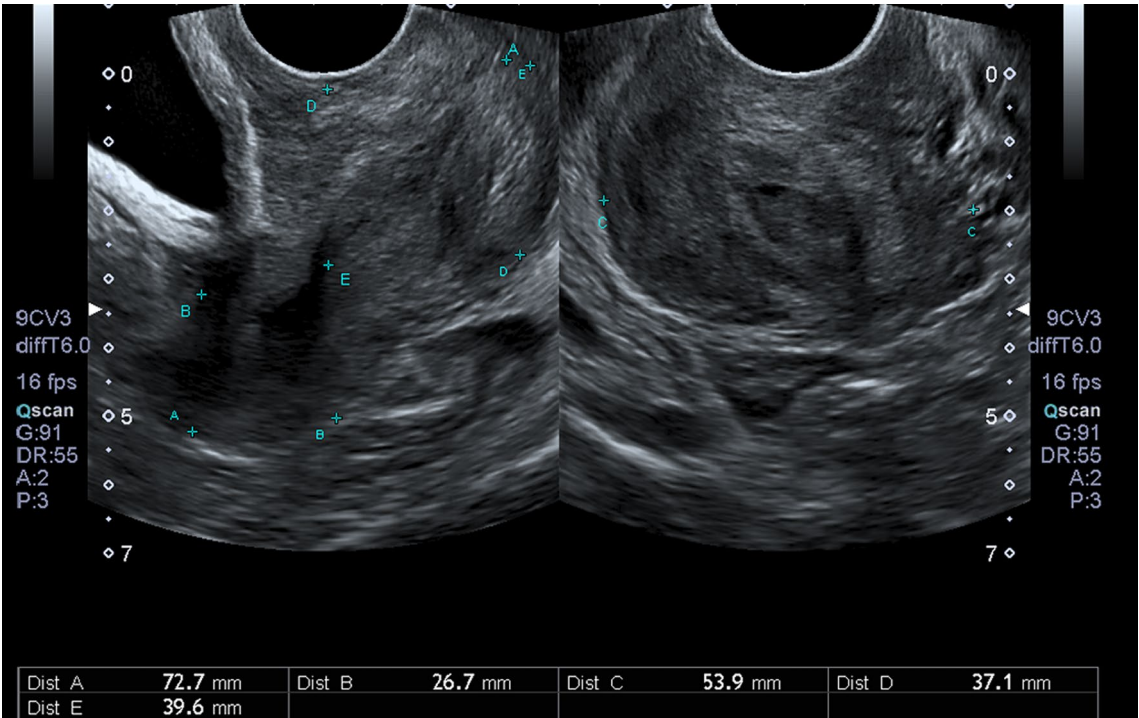


Fig. 2 On day 2 after admission, endovaginal ultrasound revealed an enlarged cervix measuring 53.9 × 37.1 × 39.6 mm

Discussion and conclusion

We report a case of cervicitis resulting from a primary genital HSV-2 infection whose diagnosis was delayed due

to the absence of external genital lesions. This case report describes a patient with a clinical presentation on admission suggestive of PID who, upon subsequent clinical,

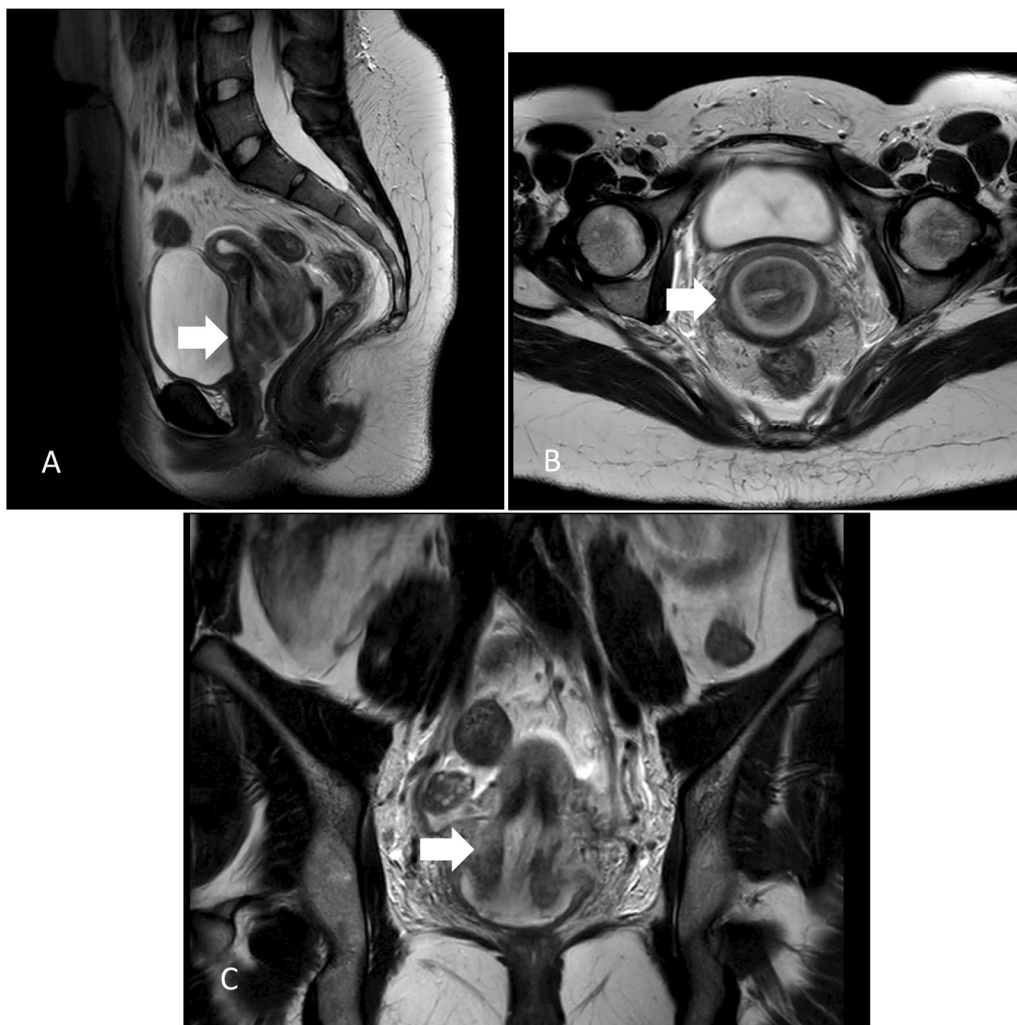


Fig. 3 T2-weighted magnetic resonance (MR) images showing significant cervical swelling and edema on (A) sagittal, (B) transverse, and (C) coronal views (white arrows)

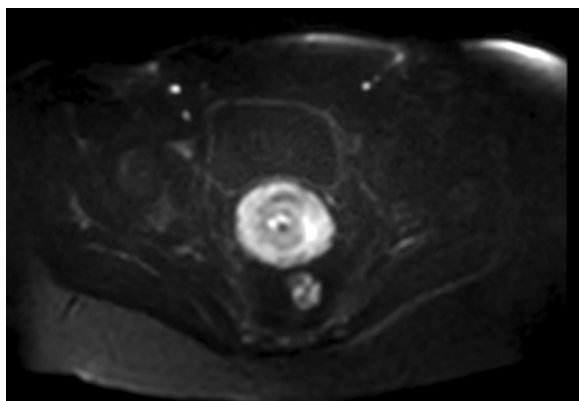


Fig. 4 Diffusion-weighted (DW) image showing a hyperintense signal from the cervix (transverse view)

imaging and laboratory examination, was diagnosed with an atypical genital HSV-2 infection manifesting as cervicitis without external lesions.

Cervicitis is characterized by mucopurulent endocervical exudates, and sometimes, cervical friability with endocervical bleeding. This condition can have either an infectious or noninfectious origin, the latter of which includes chemical or mechanical irritation [5]. In this case, despite the absence of a friable cervix or metrorrhagia, the patient was diagnosed with cervicitis on the basis of the presence of transparent leukorrhea and cervical edema observed during speculum examination, which was further confirmed by imaging (US and MRI).

To identify the etiology of suspected cervicitis, current guidelines recommend testing for *C. trachomatis* and *N. gonorrhoeae*, as these pathogens account for up to 25% of infectious cervicitis cases, and testing should



Fig. 5 T2-weighted MR images showing regression of the swelling and edema of the uterine cervix on (A) sagittal and (B) transverse imaging (white arrows)

also include *M. genitalium* and *T. vaginalis* [2, 6]. Testing for HSV in the context of cervicitis is not recommended unless there is high clinical suspicion (diffuse erosive and hemorrhagic lesions accompanied by frank ulceration) [1, 2, 5], although genital HSV infections are frequently unrecognized due to their subclinical or atypical presentations [6]. Cervicitis is thought to occur in 15% of women with clinically evident primary HSV-2 genital infection [5]. Our patient had no characteristic genital lesions suggesting that HSV was the pathogenic agent. Corey L. *et al.* reported that up to 8% of women who presented to their clinic with mucopurulent cervicitis without evidence of external genital lesions tested positive for HSV-2, but they noted that no such cases had been published [7]. Only a few cases of primary herpes infections mimicking cervical neoplasia without ulcerated skin lesions in immunocompetent individuals have been documented [8–11]. Our case differs from those published, given the acute nature of the complaints and the appearance of the cervix on clinical examination, which did not suggest a malignant cause. Our initial diagnosis of PID was called into question given the unfavorable clinical evolution of the patient after well-conducted antibiotic therapy. Upon diagnosing cervicitis, we promptly conducted all necessary infection tests to determine its etiology. Despite no strong clinical suspicion of herpes, we tested for it. The positive result highlights the importance of including HSV in the panel of tests in cervicitis patients even in the absence of clinical external lesions.

After primary infection, HSV-2 spreads in a retrograde manner to the sensory ganglia and establishes a latent infection. The virus may reactivate and induce asymptomatic viral shedding or recurrent infections [7].

Recurrence can be increased by several factors, such as immunodeficiency and the severity and length of the primary episode [12, 13]. Given the chronic nature of the disease, HSV infection can be detrimental to the physical, psychological, and social functions of infected individuals and may significantly impact a patient's quality of life [14]. According to moderate-quality evidence [4], early oral antiviral therapy seems to decrease the duration and severity of symptoms by days to weeks, with minimal adverse drug effects, as well as reduce the risk of complications of infections (for example, urinary retention). Even persons with first-episode herpes who have mild clinical manifestations initially can experience severe or prolonged symptoms during recurrent infections. Therefore, all patients with first episodes of genital herpes should receive antiviral therapy [6]. Treatment should last 7–10 days. All three available antiviral drugs (valacyclovir 1 g orally twice a day, acyclovir 400 mg orally 3 times per day, and famciclovir 250 mg orally 3 times per day) have equivalent benefits and adverse effects [4, 6]. European guidelines recommend treatment initiation within 5 days of clinical onset or when new lesions are identified [15]. In our patient, no antiviral treatment was initiated, as the diagnosis of HSV-2 infection was confirmed 7 days after the onset of symptoms, and no new lesions were observed at the time of diagnosis. Earlier suspicion of HSV-2 could have allowed earlier treatment and might have reduced the duration and severity of the patient's symptoms. The proposed management strategies for cervicitis are presented in Table 1.

This case highlights the importance of considering HSV infection in the etiological diagnosis of cervicitis, even in the absence of typical genital lesions. Awareness of the

Table 1 Suggested management of cervicitis

Cervicitis		
Symptoms	Laboratory evaluation	Treatment
- Mucopurulent endocervical exudate - Endocervical bleeding (friability) Additional symptoms: dysuria, cervical edema, dyspareunia, postcoital bleeding	- <i>C. trachomatis</i> and <i>N. gonorrhoeae</i> - <i>Trichomonas vaginalis</i> (bacterial vaginosis) - <i>Mycoplasma genitalium</i> - Herpes simplex virus (even without any typical external lesions) - Consider noninfectious etiologies	Treat according to the etiology: If positive for HSV, consider antiviral treatment for all patients, ideally within 5 days of the start of the episode [15] * Treatment [4, 6]: - Acyclovir 400 mg three times daily for 7–10 days - Valacyclovir 1000 mg twice daily for 7–10 days - Famciclovir 250 mg three times daily for 7–10 days

possibility of HSV-2 in cervicitis patients may prevent the underdiagnosis of genital herpes. Early detection of the first episode of genital HSV infection is essential because it enables early initiation of antiviral treatment, efficiently reducing the severity and duration of symptoms. In addition to antiviral therapy, patient education, recurrence management, and transmission prevention are crucial for reducing the individual and socioeconomic impacts of this chronic infection. Additional evidence could help influence the current guidelines on testing for the presence of HSV infection in patients with cervicitis.

Abbreviations

HSV	Herpes simplex virus
PCR	Polymerase chain reaction
US	Ultrasound
STIs	Sexually transmitted infections
PID	Pelvic inflammatory disease
MRI	Magnetic resonance imaging

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None.

Author contributions

All authors have made substantial contributions to the design of the work and to the acquisition, analysis, and interpretation of clinical, biological, and/or imaging data. CH, PJ, EH, AG, ML, JS, and CM significantly contributed to the writing and review of the original manuscript. All the authors have read and approved the manuscript.

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Availability of data and materials

The data that support the case report are available within the manuscript. Further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the appropriate ethics committee: Comité d'Éthique Hospitalo-Facultaire- UCLouvain, Université Catholique de Louvain, BELGIUM. Reference: 2023/06AVR/173.

Consent for publications

The patient provided written informed consent for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

None.

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References

1. Iqbal U, Wills C. Cervicitis. Treasure Island (FL); 2024 Apr. StatPearls: <https://www.ncbi.nlm.nih.gov/books/NBK562193/>
2. Guides sur les Syndromes associés aux ITS : Cervicite. Agence de la santé publique du Canada; 2021 [cited 2024 Apr 24]. <https://www.canada.ca/fr/sante-publique/services/maladies-infectieuses/sante-sexuelle-infections-transmissibles-sexuellement/lignes-directrices-canadiennes/syndromes-associes-its/cervicite.html>
3. Alareeki A, Osman A, Khandakji M, Looker K, Harfouche M, Abu-Raddad L. Epidemiology of herpes simplex virus type 2 in Europe: systematic review, meta-analyses, and meta-regressions. *Lancet Reg Health Eur*. 2023;25:100558.
4. WHO Guidelines for the treatment of Genital Herpes Simplex Virus. 2016 [cited 2024 Apr 6]. https://www.ncbi.nlm.nih.gov/books/NBK396232/pdf/Bookshelf_NBK396232.pdf
5. Marrazzo J, Martin D. Management of women with cervicitis. *Clin Infect Dis*. 2007;1(44):S102–10.
6. Workowski K, Bachmann L, Chan P, Johnston C, Muzny C, Park I, et al. Sexually transmitted infections treatment guidelines, 2021. *MMWR*. 2021;70(4):1.
7. Corey L, Adams H, Brown Z, Holmes K. Genital herpes simplex virus infections: clinical manifestations, course, and complications. *Ann Intern Med*. 1983;98(6):958–72.
8. Clure C, Rivard C. Primary herpes simplex virus infection mimicking a cervical malignancy in an immunocompetent individual. *Cureus*. 2018. <https://doi.org/10.7759/cureus.2753>.
9. Tomkins A, White C, Higgins SP. Primary herpes simplex virus infection mimicking cervical cancer. *BMJ Case Rep*. 2015. <https://doi.org/10.1136/bcr-2015-210194>.
10. Boldrini P, Vallejos G, Ballesteros P, Valenzuela G, Roncone E. Tumor-like presentation of herpetic cervicitis: a case report. *Case Rep Womens Health*. 2023;5:38.
11. Funakoshi M, Nakai G, Yamada T, Ohmichi M, Yamamoto K, Osuga K. Acute cervicitis resembling gastric-type mucinous adenocarcinoma that was definitively diagnosed by cervical conization: a case report. *Radiol Case Rep*. 2023;18(5):1767–71.
12. Benedetti J, Corey L, Ashley R. Recurrence rates in genital herpes after symptomatic first-episode infection. *Ann Intern Med*. 1994;121(11):847–54.
13. Benedetti J, Zeh J, Corey L. Clinical reactivation of genital herpes simplex virus infection decreases in frequency over time. *Ann Intern Med*. 1999;131(1):14–20.
14. World Health Organization . 2020. Massive proportion of world's population are living with herpes infection. <https://www.who.int/news/item/>

[01-05-2020-massive-proportion-world-population-living-with-herpes-infection](#)

15. Patel R, Kennedy OJ, Clarke E, Geretti A, Nilsen A, Lautenschlager S, *et al.* 2017 European guidelines for the management of genital herpes. *Int J STD AIDS*. 2017;28(14):1366–79.

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