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Unrecognized Primary Genital Herpes Infection (Case Report)

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Abstract: The authors present a case report of unrecognized herpes genitalis, which was caused by primary HSV-1 infection. The 28-year old female was examined by three board certified gynaecologist and initially treated as mycotic vulvitis. The authors point out the atypical course in the patient without anti-HSV-1 and HSV-2 antibodies. This infection is rather very painful, extensive and with complications. Thus, it is necessary to consider the diagnosis and to begin antiviral therapy as soon as possible.

Introduction

Herpes genitalis is the most common local genital ulcerative disease. It is caused by herpes virus type 2 or type 1 (HSV-2, HSV-1, respectively).

Both, HSV-1 and HSV-2 belong to herpesviridae, large double-stranded DNA viruses. HSV-1 and HSV-2 share 83% sequence homology of their protein-coding regions. The structure of their genomes is almost similar; they can be differentiated by molecular methods [1].

HSV infection is acquired by a close contact with an infected person that is shedding virus from the skin or mucosa. The virus is shedded by 3% of asymptomatic patients and there is no difference between patients that have had symptomatic infection and persons, who have contracted the infection asymptomatically [2]. Initially, HSV enters the body through skin or mucosa and begin cytolytic replication in epithelial cells at the site of entry. HSV penetrates through the dermis and enters the ends of peripheral sensory nerves, then is transported in a retrograde manner to the neural soma in the sensory nerve root ganglia [3, 4]. Neuronal HSV infection does not lead to cell death. HSV persists in a latent state in the sensory ganglion of the infected person [3, 5].

Recurrent episodes take place when HSV reactivates in neurons with latent infection and is transported in the peripheral nerves back to the mucosa or skin. Viral shedding might occur in the absence of clinically recognized symptoms. Probably all persons, who are seropositive for HSV antibodies, shed HSV intermittently, and sexual transmission of HSV usually occurs during periods of subclinical shedding [6, 7].

Previous infection with HSV-1 could offer partial protection against HSV-2 infection; conversely HSV-2 infection seems to protect against HSV-1. Women, who experienced oral herpetic gingivostomatitid in childhood, have primary HSV-2 genital infection unapparent or with a mild course [8, 9]. On the contrary, the course of infection in women without protective cross-reacting antibodies can be very severe and extensive [10].

HSV-1 primoinfection mostly causes extensive oral infection in childhood. The sero-prevalence is approximately 70% in adults in developed countries. In the past decade, the USA, Canada, and some European countries reported an increased a number of genital HSV-1 infections [11, 12, 13]. It probably results from a delay in acquisition of oral HSV-1 infection in childhood in these countries, and therefore,

young people at the beginning of their sexual life are more sensible to genital HSV infection [14]. The increase in genital HSV-1 infection can be partially caused by increasing preference of oral sex, which is considered to be safer than intercourse and with no potential risk of pregnancy [15].

The HSV primoinfection in women with no HSV-1 or HSV-2 antibodies can proceed dramatically to necrotic vulvitis. We must take this infection into consideration and initiate the antiviral therapy as soon as possible.

We report a case of genital herpes in a woman that was examined at least by three board certified gynaecologists. None of them raised a suspicion of HSV infection, and the woman got adequate therapy with a delay – on the 5th day from her first visit of a gynaecologist.

Case report

The 28-year old female was admitted to the Department of Gynaecology and Obstetrics with acute inflammation of external genitalia. She was examined by her gynaecologist four days before the admission because of vaginal discharge, burning and swollen genitals. The gynaecologist had a suspicion for mycotic infection, and he prescribed metronidazol (Entizol™) for vaginal application as well as lactobacillus (Gynoflor™). The patient was re-examined because of unsuccessful treatment at the gynaecologic outpatient department of our facility three days from the beginning of the therapy. Her symptoms were getting worse with aggravation of discharge, oedema of the labia and increasing tenderness of external genitalia. Clinical findings demonstrated swollen genitals with surface painful erosions between the labias and thin whitish vaginal discharge. Initially, she was treated with local antiseptics (Betadine™ and Menalind™) and with oral cephalosporin cefprozil (Cefzil™). Blood count, urinary and vaginal cultures were performed. The next day the symptoms were still getting worse. The patient suffered from heavy pains and retention of urine. She was admitted with a diagnosis of acute vulvovaginitis. Clinical findings were as follows: severe oedema

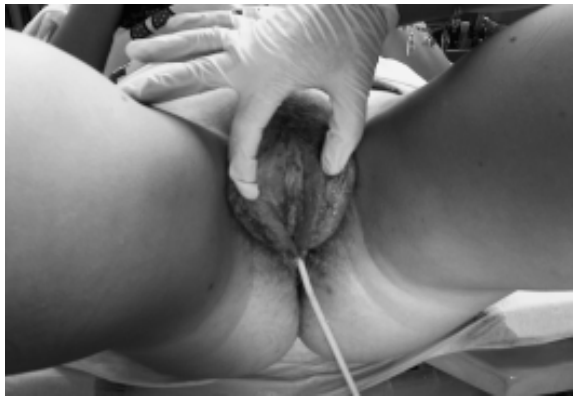

Figure 1 – Acute herpes genitalis.

of external genitals and abundant erosions of skin and mucosa. The vaginal examination could not be performed because of strong soreness. The patient was afebrile, orientated, with no general manifestation of infection.

All laboratory investigations including vaginal culture were negative. The blood test for BWR, HIV was also negative. The attending physicians recommended starting treatment with oral fluconazol (Mycomax™) and analgesics. The physician on duty was called to insert urinary catheter. When he found such a wide infliction of genitalia he raised suspicion for herpes genitalis, and he recommended dermatological consultation – see Figure 1 (local findings at admission). The dermatologist made diagnosis of acute herpes genitalis and he recommended Herpesin 400 mg five times a day as well as local treatment with antiseptic solution. The dermatologist didn't recommend direct virologic diagnostics due to obvious clinical finding of herpetic infection. The improvement had occurred on the second day of antivirotic therapy and that time she did not need any analgesics. On day 4 the patient was able to urinate spontaneously. The erosions healed up gradually and new lesion did not appear. On day 8 of hospitalization the HSV serology was tested: HSV-1 and HSV-2 IgM and IgG antibodies measured by KFR and ELISA were evaluated as negative. On the basis of serological tests, the attending physician ruled out herpetic infection. The patient was discharged from hospital without additional treatment.

Table 1 – The possibilities of laboratory tests of genital HSV infection

Name of methods	Principle	Material	Sensitivity	Note
Culture	Viral culture on tissue media	Swab from lesions	80% sensitivity in primary infection	Need of transporting medium
PCR	Evidence of DNA virus using amplificating methods	Swab from lesions	99% sensitivity	
Antigen detection	Immunofluorescent amplification of virions ELISA evidence of antigen	Swab from lesions rubbed on glass Direct print of lesion on glass	80–95%	
Serology	Determination of specific HSV-1 or HSV-2 IgG and IgM antibodies		97–100%	IgG positivity 21–42 days after primoinfection; IgM positivity 5–10 days after the eruption of the lesion. At the time of primary eruption the serology can be negative.

We invited the patient for follow-up examination after six months. The blood test for HSV antibodies and print on glass were performed. The patient was not shedding the virus and she had positive HSV-1 IgG antibodies (KFR 1:32, ELISA diluting 1:100 positive), HSV-2 antibodies remained negative. Based on serology findings, showing HSV-1 seroconversion during the follow-up period, the case was concluded as a genital infection caused by HSV-1.

Discussion

We would like to point out the possible difficulties with clinical identifications of primary herpetic vulvitis. Typical clinical presentation of primary herpetic vulvitis in women without protective antibodies is characterized by painful erythematous papules and vesicles bilaterally on the vulva, which can reach to perineal region or upper thighs. They appear 4–7 days after sexual exposure. The ulcerations are very painful, burning, 80% women report dysuria, 70% of the patients have fever, headache, malaise and myalgias. Our patient did not report any general symptoms, however, dysuria and retention of urine were present.

Clinical suspicion for the infection should be confirmed by laboratory tests. The possibilities of laboratory tests are summarized in Table 1. It is important to start the therapy as soon as possible even before laboratory confirmation of the diagnosis. Only effective, sufficient and in time applied antivirotic treatment leads to fast regression of symptoms, rapid healing, reduction period of shedding of the virus and prevention of eruption of new lesions. The therapy also prevents serious complications such as meningitis and retention of urine [16].

Conclusion

Approximately 30% of women have no protective HSV-1 antibodies and they are endangered by extensive infection of genitalia [17]. We can considerably alleviate from their difficulties by early diagnosis and subsequent administration of adequate therapy. Thus, we should consider this diagnosis not only in case of eruption of typical vesicles but also in presence surface erythematous ulcerations on vulva. The interdisciplinary cooperation, which includes gynaecologist, dermatologist and infectious disease consultant, is important not only for clinical examination but also for adequate interpretation of laboratory results.

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References

1. ARDUINO P. G., PORTER S. R.: Herpes Simplex Virus Type 1 infection: overview on relevant clinico-pathological features. *J. Oral Pathol. Med.* 37: 107–121, 2008.
2. BROCK B. V., SELKE S., BENEDETTI J., DOUGLAS J. M., JR., COREY L.: Frequency of asymptomatic shedding of herpes simplex virus in women with genital herpes. *JAMA* 263: 418–420, 1990.

3. CEPICKY P.: Genital herpes. *Cesk. Gynekol*. 49: 669–673, 1984.
4. CERNIK C., GALLINA K., BRODELL R. T.: The treatment of herpes simplex infections: an evidence-based review. *Arch. Intern. Med*. 168: 1137–1144, 2008.
5. COREY L., HOLMES K. K.: Genital herpes simplex virus infections: current concepts in diagnosis, therapy, and prevention. *Ann. Intern. Med.* 98: 973–983, 1983.
6. COREY L., ADAMS H. G., BROWN Z. A., HOLMES K. K.: Genital herpes simplex virus infections: clinical manifestations, course, and complications. *Ann. Intern. Med*. 98: 958–972, 1983.
7. DOLAN A., JAMIESON F. E., CUNNINGHAM C., BARNETT B. C., MCGEOCH D. J.: The genome sequence of herpes simplex virus type 2. *J. Virol*. 72: 2010–2021, 1998.
8. GUPTA R., WARREN T., WALD A.: Genital herpes. *Lancet* 370: 2127–2137, 2007.
9. HALPERN-FELSHER B. L. , CORNELL J. L., KROPP R. Y., TSCHANN J. M.: Oral versus vaginal sex among adolescents: perceptions, attitudes, and behavior. *Pediatrics* 115: 845–851, 2005.
10. HOLUB M., LABSKA K., ROUBALOVA K.: Recidivující genitální herpes. (in Czech) *Klin. Mikrobiol. Inf. Lék.* 14: 52–58, 2007.
11. LOOKER K. J., GARNETT G. P.: A systematic review of the epidemiology and interaction of herpes simplex virus types 1 and 2. *Sex Transm. Infect*. 81: 103–107, 2005.
12. MANAVI K., MCMILLAN A., OGILVIE M.: Herpes simplex virus type 1 remains the principal cause of initial anogenital herpes in Edinburgh, Scotland. *Sex Transm. Dis*. 31: 322–324, 2004.
13. NAHMIAS A. J., LEE F. K., BECKMAN-NAHMIAS S.: Sero-epidemiological and -sociological patterns of herpes simplex virus infection in the world. *Scand. J. Infect. Dis. Suppl.* 69: 19–36, 1990.
14. PAGE J., TAYLOR J., TIDEMAN R. L., SEIFERT C., MARKS C., CUNNINGHAM A., MINDEL A.: Is HSV serology useful for the management of first episode genital herpes? *Sex Transm. Infect*. 79: 276–279, 2003.
15. ROBERTS C. M., PFISTER J. R., SPEAR S. J.: Increasing proportion of herpes simplex virus type 1 as a cause of genital herpes infection in college students. *Sex Transm. Dis*. 30: 797–800, 2003.
16. ROEST R. W., CARMAN W. F., MAERTZDORF J., SCOULAR A., HARVEY J., KANT M., VAN DER MEIJDEN W. I., VERJANS G. M., OSTERHAUS A. D.: Genotypic analysis of sequential genital herpes simplex virus type 1 (HSV-1) isolates of patients with recurrent HSV-1 associated genital herpes. *J. Med. Virol*. 73: 601–604, 2004.
17. SCOULAR A., NORRIE J., GILLESPIE G., MIR N., CARMAN W. F.: Longitudinal study of genital infection by herpes simplex virus type 1 in Western Scotland over 15 years. *BMJ* 324: 1366–1367, 2002.