

Genital Herpes

JMAJ 45(12): 511–515, 2002

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Abstract: Among STDs, genital herpes ranks third in terms of the prevalence in Japan, after genital chlamydia infection and gonococcal infection. The most significant problem with this disease is its propensity for recurrence, which may cause both physical and mental distress to patients. Indeed, some people believe that a person, once infected with genital herpes, has to give up the idea of marrying, or that a woman with the disease cannot bear children. Such false propaganda should be checked. While antiviral agents such as acyclovir are extremely effective for the treatment of genital herpes, it must be remembered that these drugs are not cures in themselves. Continuous oral acyclovir suppression may be required for preventing frequent recurrences.

Key words: Genital herpes; Herpes simplex virus; Sexually transmitted disease

Introduction

Genital herpes may be caused by herpes simplex virus type 1 (HSV-1) or herpes simplex virus type 2 (HSV-2). Both HSV-1 and HSV-2 infections may be associated with small vesicles, erosions, and shallow ulcers in the genital area. After the clinical course of the illness, the virus remains latent in certain nerve cells in the sacral ganglion, and causes repeated recurrence.¹⁾ HSV, which invades the skin and mucous membranes, may also cause keratitis, retinitis, encephalitis, encephalomyelitis, and even systemic infection in newborn babies or immunocompromised patients.

Several newly-developed drugs, including acyclovir, are effective in the treatment of

herpes. These drugs usually relieve the acute symptoms associated with genital herpes. However, reactivation of HSV cannot be prevented even by these potent drugs. Once infected with HSV, a person usually continues to experience recurrences throughout his/her lifetime.

Genital herpes is a sexually transmitted disease. The re-emergence of this disease in Japan may be associated with the change in people's views on sex. The percentage of teenagers engaging in sexual encounters has been on the increase, and the prevalence of genital herpes has been increasing, especially in the youth. Unfortunately, most people with genital herpes do not have symptoms, and these people may transmit the infection to their sexual partners even without their own knowledge. Further-

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 126, No. 9, 2001, pages 1149–1152).

more, when a person is diagnosed with genital herpes, and his/or her partner becomes aware of the risk of transmission of the infection, their personal relationship may be jeopardized. The patient himself/herself often feels guilty and wary.

Epidemic of Genital Herpes

A sharp increase in the number of patients with genital herpes was observed in the United States between 1970 and 1980. The weekly "Time" magazine featured genital herpes on their cover, depicting the shadow of a man and woman standing face to face, with 'The Scarlet Letter' written in relief. "The Scarlet Letter" is a story illustrating the prevalence of adultery among Puritans in Boston in the 17th century. In Japan also, the print media have discussed the subject with sensational headlines. The result was that some people came to believe falsely that a person contracting genital herpes infection has to give up the idea of marrying, or that women, once infected with herpes, cannot bear children. In fact, a significant segment of the population with or without genital herpes panicked to the point of becoming neurotic.

Epidemiological data on the prevalence of genital herpes in our country are contained in the annual survey of sexually transmitted diseases in Japan initiated by the Ministry of Health and Welfare (MHW, now reorganized as the Ministry of Health, Labor and Welfare) in 1987. The survey covers patients with STDs who visited 606 pre-selected medical institutions across the country.²⁾ According to the survey, approximately 6,000 new cases of genital herpes infection have been diagnosed annually since 1987. As to its prevalence in comparison with other STDs, genital herpes takes the third place, after genital chlamydia infection and gonococcal infection. Genital herpes infection is estimated to develop in 40 people per 100,000 every year. The incidence now appears constant, and has shown no tendency towards increase.

Another survey conducted in 1998 by the Infectious Diseases Sentinel Surveillance Workgroup, organized by the MHW, revealed that the annual morbidity rate of genital herpes infection in 7 model prefectures was 59.36 per 100,000 overall, being 36.20 in men and 81.63 in women. The ratio of women to men with the infection was 2.25.³⁾ Based on these data, it is estimated that 22,000 men and 49,000 women suffer from genital herpes infection in Japan. In reality, however, a much larger number of people must suffer from HSV, considering that HSV infection is often asymptomatic.

Clinical Problems Associated with Genital Herpes Infection

HSV infection is frequently asymptomatic. Adult genital herpes is usually transmitted by sexual intercourse. Symptoms of genital herpes may appear within 2 to 10 days after the infection, and consist of vesicles and erosions in the genital area. Primary infection in adult associated with acute symptoms such as fever, swollen regional lymph nodes, multiple vesicles, and erosions is often caused by HSV-1, which is transmitted from the mouth of a partner. In this type of infection, recurrence may be rare. In contrast, symptoms of HSV 2 infection are usually relatively mild, but recurrences are frequent.

The virus multiplies at the site of entry, and travels upward along the nerve endings at the site of infection to the sacral ganglia to enter a latent phase. Sexual intercourse, overwork, and stress may trigger recurrences. Recurrent genital herpes often manifests as 5 or 6 vesicles in isolation, which may resolve in 7 to 10 days' time, even without treatment. However, 6 or more recurrences per year are not rare. Multiple recurrences may cause deep depression in some people, with the need for professional counseling. The frequency of recurrence, however, may decrease gradually on its own after several years, with recurrent episodes eventually becoming rare. This infection is curable.

In the majority of patients, recurrences begin with warning signs or prodromal symptoms, including mild neuralgia, pain radiating to the thigh, dysphoria, or bladder irritation, before the vesicles eventually develop.

1. Decrease in the percentage of people carrying anti-HSV antibody

Previously, most Japanese people became infected with HSV-1 during their childhood. Thus, when genital herpes infection occurred at sexual maturity, they had a much milder first clinical episode, because of the homology between HSV-1 and HSV-2, and immunological memory. With the society becoming increasingly cleanliness-oriented, however, the incidence of HSV-1 infection in early life has decreased. Currently, the percentage of people at the age of 20 who test positive for anti-HSV antibody is less than 50 percent.

HSV-1 and HSV-2 have much in common in terms of their antigenic profile. A person with anti-HSV-1 antibody may be less susceptible to HSV-2 infection. The upsurge in the number of young people with primary genital herpes infection presenting with acute severe symptoms may be due to the lower frequency of exposure to HSV-1 in childhood. The same may explain the increase in the number of cases with genital herpes caused by HSV-2. The decrease in the percentage of pregnant women carrying anti-HSV antibody may be associated with a higher risk of HSV infection in newborns, as they are less often protected by the antibody from the mother.

2. Asymptomatic viral shedding

Asymptomatic viral shedding into vaginal secretions and semen is observed in most patients over time, resulting in asymptomatic transmission.⁴⁾ Seventy percent of people with primary genital herpes infection are often those in whom the infection has been transmitted from a sexual partner without any overt symptoms.

3. Mother-to-child infection

Transmission to newborns may occur at the time of delivery, if the mother has active genital herpes infection. The incidence of neonatal herpes in Japan is one in 10,000 to 20,000 births, but the prognosis is unfavorable, with early death occurring in approximately 30 percent of babies with neonatal herpes.⁵⁾ The risk of a mother with primary genital herpes transmitting the infection during labor and delivery is rather high and is estimated to be 50 percent; on the other hand, the risk of a mother with recurrent herpes transmitting the infection is estimated to be 0 to 5 percent.

Since neonatal herpes simplex infection may not be associated with vesicles on the skin and mucous membranes in some cases, diagnosis is rather difficult to make, and a confirmatory virus culture and the polymerase chain reaction (PCR) must be carried out, if infection is suspected. When the results are positive for HSV infection, treatment with acyclovir should be initiated.

For infection occurring within one month of the expected date of delivery, a Cesarean section may be indicated. Acyclovir suppression during late pregnancy may also be effective.

4. Diagnosis of genital herpes

Ulcerative lesions and vesicles on the external genitalia may be suggestive of genital herpes. The diagnosis is best established by viral culture and PCR. These techniques, however, are expensive and time-consuming. The more practical tests that can be performed are direct fluorescent antibody staining and the Tzanck test for detecting ballooned and multinucleated cells in smears of the fluid from the vesicles.⁶⁾

Serologic screening may not be useful for the diagnosis of herpes, since infected persons remain seronegative during the acute phase of the disease and turn positive only during convalescence. In addition, the serum antibody titers are variable, depending on whether or not the patient has recurrent herpes. Antibody

testing with glycoprotein G from the viral envelope can distinguish among the types of HSV, although the typing requiring expertise. The current prevalence of HSV-2 infection is 2.9 to 4.0 percent among men and 6.9 to 10.7 percent among women. These figures are lower than those from Western Europe and the United States.

Current Treatment

Currently available antiviral drugs for treating herpes infection are effective for inhibiting the viral growth; however, these drugs cannot eliminate viruses in the latent phase, nor completely prevent recurrent episodes. For the treatment of primary genital herpes infection associated with severe local symptoms, acyclovir is administered orally at the dose of 200 mg 5 times daily for 5 days. In more severe cases, acyclovir is administered intravenously at the dose of 5 mg/kg, three times a day. Treatment with acyclovir administered either orally or intravenously can be continued for up to 7 to 10 days depending on the clinical condition of the patient.

For the treatment of recurrent episodes of HSV, oral administration of acyclovir at the dose of 200 mg five times daily for 5 days is effective. Since earlier use during the clinical course may suppress recurrent episodes more effectively, the medication should be started at the time of occurrence of prodromal symptoms such as dysphoria and neuralgia. In milder cases, topical acyclovir ointment or vidarabine may be used several times daily.

Future Treatment

For patients with 6 or more recurrent episodes of genital herpes per year, continuous oral antiviral suppression is recommended by the Centers for Disease Control (CDC) in the United States, in order to relieve the mental distress of the patient and prevent transmission to others.⁷⁾ Continuous use of acyclovir tablets,

400 mg twice daily, suppresses recurrent episodes. Such use of acyclovir, however, is not reimbursed by the national health insurance in our country. Until now, oral acyclovir has not been reported to cause any significant adverse effects, even after several years of use. The emergence of resistant strains to acyclovir has not posed a significant problem in immunocompetent patients; however, foscarnet, rather than acyclovir, should be administered in patients with the acquired immunodeficiency syndrome (AIDS), or to patients who have undergone organ transplantation, in order to avoid the emergence of acyclovir-resistant strains due to long-term administration.

HSV vaccines under development are still far from satisfactory. Some immunomodulating agents for topical external use have been reported to be effective in the prevention of recurrent genital herpes.

Preventive Measures against the Spread of Genital Herpes

Earlier sex education with provision of accurate information about sexually transmitted diseases is useful. The necessity of using a condom during sexual intercourse in order to avoid transmission to the partner, should be stressed in patients with vesicles or ulcerative lesions in the genital area. Considering that asymptomatic shedding is common, however, it is desirable to advocate the use of condoms even to those with the inactive phases of the infection, except when the couple wants to have a baby. CDC recommends the use of condoms even when the patient is on continuous oral antiviral suppression. The use of condoms alone is not completely safe though, since lesions may also occur in the anal region, buttocks, or thigh.

Correct information about STDs and the importance of the proper use of condoms should be conveyed through sex education in order to prevent the spread of STDs, including genital herpes. Complete eradication, however,

of HSV, which has survived in humans for several million years, may not be possible.

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