

CLINICAL REPORT

Recurrent Genital Herpes in a Population Attending a Clinic for Sexually Transmitted Diseases

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Patients with recurrent genital herpes attending a sexually transmitted disease clinic were studied and transmission of the infection was elucidated by evaluating serostatus in their partners. Of 84 patients attending for recurrent genital herpes, 94% had a herpes simplex virus type 2 (HSV-2) infection and only 6% (5 patients) a type 1 infection. The mean age of the patients was 36 years and the duration of their infection was up to 37 years (median 4 years). In most patients the number of recurrences had not decreased between the first year and the last year. About half had experienced a more severe first episode infection. Of the patients, 64% were not aware of asymptomatic shedding and the risk of sexual transmission without clinical symptoms. Of 67 steady partners of patients with genital HSV-2, 15% had a history of genital herpes. By HSV serology, HSV-2 antibodies (indicating subclinical genital herpes) were demonstrated in more than half of the partners. The duration of the relationship or condom use did not seem to influence the frequency of transmission to the partner, which may indicate an individual susceptibility for acquiring a genital HSV-2 infection. Eleven per cent of the patients were on suppressive antiviral therapy, while 39% had no experience of antiviral therapy. Type-specific HSV serology was found to be of value in counselling partners of patients with genital herpes. **Key words:** HSV types; serology; condom; subclinical infection; transmission.

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Since type-specific serology for herpes simplex virus (HSV) types 1 and 2 was introduced, genital infection caused by HSV type 2 (HSV-2) has been shown to be one of the most common sexually transmitted diseases (STDs) in the Western world (1, 2). An increasing number of cases of genital first-episode herpes caused by HSV type 1 (HSV-1) has been reported, especially from Europe (3–5). The tendency to recur has been shown to be much lower for an HSV-1 than for an HSV-2 genital herpes infection (6). Although a benign disease in most cases, genital herpes in many cases negatively influences the patient's psychosexual and social life (7). Much distress and concern relates to the risk of transmitting the virus to a partner. The aim of this study was to elucidate the spectrum of recurrent genital herpes in an STD population concerning the prevalence of HSV-1 and HSV-2 infections, number of recurrences and use of antiviral therapy, and to evaluate HSV-2 serology in partners without clinical disease.

PATIENTS AND METHODS

Patients

Consecutive patients with recurrent genital herpes, including new as well as long-term attendees, seen by the authors at the STD clinics of Sahlgrenska University Hospital and Borås Hospital between November 1996 and February 1999, were recruited to the study. In total, 84 patients, 49 men (age 18–60, mean 36 years) and 35 women (age 21–69, mean 36 years) were included.

Questionnaires

A structured questionnaire was filled in including questions about the duration of the disease, number of recurrences during the first and last year, antiviral therapy, sexual history, including questions about the duration of the relationship, condom use and genital herpes in partners.

Partners

Patients with an HSV-2 infection who had a steady partner were asked to invite him or her to a visit at the clinic for counselling and a blood test for HSV-2 antibodies. Steady partner was defined as a partner in an ongoing relationship. Of 67 steady partners 26 (17 men, 9 women) agreed to attend the clinic. Information about the history of genital herpes in partners who did not attend was given by the index patients.

Virological methods

When blisters or erosions were present, specimens were collected for HSV culture and the isolated virus was typed in a multiwell cell-culture system by means of an enzyme-linked immunosorbent assay (ELISA) and monoclonal antibodies specifically reacting with HSV-2 glycoprotein G (gG) and HSV-1 glycoprotein C (8). Blood was drawn for HSV serology and antibodies reacting with type common and type 2 specific (gG) HSV antigen were assayed by an ELISA-based method (9).

Statistical methods

To test differences in the duration of relationship between seropositive and seronegative partners (seroconcordant and serodiscordant couples), the 95% confidence interval (CI) for the difference between means of duration in the 2 groups was calculated.

The study was approved by the Ethics Committee of Göteborg University and verbal informed consent was obtained from the patients.

RESULTS

The diagnosis was based on a positive culture and/or specific serology, as well as the history and clinical picture. Of 84 infections, 79 (94%) were diagnosed as HSV-2 and 5 (6%) as HSV-1.

HSV-1 infections

Of the 5 HSV-1 infections, 3 were verified by culture and in 2 cases the diagnosis was based on the history, clinical picture and serology (positive for type common HSV antigen and negative for HSV-2). Of the 5 patients with HSV-1 infections, 3 were women and 2 men. Three patients had only 1–2 recurrences per year, while 1 patient reported 4 and 1 patient 12 recurrences during the last year. Although 12 recurrences per year is uncommon for an HSV-1 infection the infection was not classified as HSV-2 since the patient was seronegative for HSV-2. The HSV-1 infections are not included in the following presentation.

HSV-2 infections

Of 79 HSV-2 infections, 59 were verified by positive culture and 20 by serology and a typical clinical picture.

Duration of the disease. Seventeen patients had a history of genital herpes of less than 1 year and 13 patients of more than 10 years (data were missing for 1 patient). Thirty-one (53%) of 59 recalled that their first episode of genital herpes was much more severe than later episodes (see Table I).

Recurrences. The number of recurrences during the first and last year of infection are shown in Table I. Seventeen patients with a history of less than 1 year are not included, and when evaluating the number during the last year patients with a history of less than 2 years are not included. A further 14 patients could not give an estimate of the number of recurrences during the first year of their infection and for the last year data were missing for 5 patients. For 37 patients with genital herpes for more than 2 years information concerning the number of recurrences was available from both their first and last year with genital herpes. The number of recurrences had increased in 17 (46%) patients, decreased in 6 (16%) and was unchanged in 14 (38%).

Antiviral therapy. Twenty-seven of 70 patients had never taken antiviral therapy for their genital herpes, while 34 had experience of intermittent medication and 10 of suppressive therapy. Eight patients were on suppressive therapy at the time of the study.

Knowledge about transmission. Of 44 patients asked, 15 (34%) knew that the virus could be transmitted asymptotically.

Partners. At the time of the study, 67 (85%) of 79 patients had an ongoing steady relationship (see Table II). Only 26

Table I. Duration of disease and number of recurrences in patients with genital herpes attending an STD clinic

	Mean	Median	Range
Duration of disease (years) ($n=78$)	6	4	1–37
No. of recurrences in first year ($n=48$)	6.8	6.0	1–20
No. of recurrences in last year ($n=42$)	7.9	8.0	1–20

of 67 partners attended for counselling and a blood test for HSV-2 antibodies. Of these, 23 had no history of genital herpes. Twelve of 23 partners without a history of genital herpes and 3 with a positive history were HSV-2 seropositive. Of 11 HSV-2 seronegative partners, all but 3 had antibodies against the type common HSV antigen. Two index patients were on suppressive antiviral therapy and in both cases their partners were seronegative. The duration of the relationship was for the seropositive partners (seroconcordants) median 3 years (2 months–20 years) and for the seronegative partners (serodiscordants) median 12 years (4 months–40 years). The difference between the means for duration of the relationship in the 2 groups was 85 months (95% CI –27 months to 197 months). A condom was used seldom or never by 8 of 11 (73%) and 11 of 15 (73%) subjects in the seronegative and seropositive group, respectively.

DISCUSSION

In 94% (79 of 84) of the patients attending the STD clinics for recurrent genital herpes, the infection was caused by HSV-2 and only in 6% (5 cases) by HSV-1. In a recurrent episode of genital herpes, virus replication is of short duration (1–2 days) and the diagnosis was not verified by culture in all cases. In 1983 Corey et al. (10) reported 5 cases (1%) caused by HSV-1 in a cohort of 362 patients with recurrent genital herpes. The proportion of HSV-1 infections in first episodes of genital herpes during the study period was as high as 50% (5). Although patients with genital herpes attending an STD clinic do not reflect the spectrum of the disease in the population, the low prevalence of HSV-1 infections indirectly supports the much better prognosis concerning recurrences compared with HSV-2. About half of the patients stated that they had a more severe first episode of genital herpes. For some patients the first episode of genital herpes does not reflect a recently acquired infection but the first reactivation of a latent infection acquired asymptotically, perhaps years previously (5, 11).

The median duration of genital herpes for 78 patients was 4 years, with a wide range from less than 1 year to 37 years. In 37 patients for whom information was available about the number of recurrences during the first and last year, the number of recurrences had increased in 46%, decreased in 16% and was unchanged in 38%. This illustrates the variability among HSV-infected persons. The increasing number of recurrences from median 6 during the first year to 8 during the last year when combining data from all patients probably reflects the fact that patients with increasing recurrences are more likely to attend. The number of recurrences was estimated by asking retrospectively and

Table II. Frequency of HSV-2 infection in steady partners of 67 patients with recurrent genital HSV-2 infection; HSV-2 serostatus is presented for 26 partners

Partner with known genital herpes	<i>n</i>	%
In ongoing relationship	10/67	15
In relationship at the time of first clinical herpes	12/65 ^a	19
HSV-2-seropositive partners	15/26	58
HSV-2-seronegative partners	11/26	42

^aData missing for 2 patients.

recall bias should be taken into consideration. In an observational cohort study by Benedetti et al. (12), a significant reduction in clinical disease occurred in the majority of patients.

In most cases an HSV infection is acquired asymptotically (13, 14). Only 20–30% of HSV-2-infected individuals have clinically recognized genital herpes (15–17). Asymptomatic shedding has been shown to occur with the same frequency among those with and without clinical disease (18). In the present study, only 15% (10/67) of steady partners of patients with recurrent HSV-2 infection were aware of having genital herpes. By serology, HSV-2 antibodies could be demonstrated in 50% of partners without clinical genital herpes. The fact that partners had HSV-2 antibodies does not prove that their infections were acquired from their current partners. There was no positive correlation between the duration of the relationship and detectable HSV-2 infection in the partner. Neither was there any difference between discordant and concordant couples concerning condom use. This may indicate an individual susceptibility to contracting genital herpes. Bryson et al. (19) reported the results of 57 asymptomatic partners of index patients with recurrent HSV-2 genital herpes, 19% of whom were HSV-2 seropositive. The higher figure seen in the present study may reflect a higher background prevalence of HSV-2 infection and also the fact that duration of the relationships in these couples was longer: median 3 years for concordant couples and 12 years for discordant compared with 12.7 months and 23.6 months, respectively, in the couples studied by Bryson et al. In accordance with the present results, they did not find any correlation between transmission and condom use, frequency of intercourse or the duration of relationship.

A challenge in counselling patients with genital herpes is to provide information about the risk of transmitting the virus between clinical recurrences. Of 44 patients asked, only 34% were aware of asymptomatic shedding. Continuous antiviral therapy decreases the asymptomatic shedding of the virus (20) but the impact of this therapy on transmission has not yet been proven. Although a group of patients with frequent recurrences was studied here, only 11% were on suppressive therapy and 39% had no experience of antiviral therapy. When judging the indication for antiviral therapy, the psychosexual and social effects of this disease on the patient must be taken into account. The type-specific serology could be of value in counselling couples.

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