Atypical Genital Herpes: Report of Five Cases

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Abstract

Manifestations of human genital herpes virus (HSV) infection are not limited to the typical cluster of genital lesions. Here we present 5 case histories suggestive to clinically atypical genital herpes (HSV detected with the polymerase chain reaction) collected in 2001 from a private outpatient clinic specializing in dermatological and venereal diseases. The clinical presentations included mucopurulent cervicitis, haemorrhagic cystitis, recurrent urethritis, and lower back pain.

INTRODUCTION

Herpes simplex viruses (HSV) are ubiquitous human pathogens. Genital herpes is among the most common sexually transmitted diseases (STD) worldwide. Epidemiological studies have revealed that the majority of HSV-2 infections remain undiagnosed and unrecognized. Furthermore, the escalating incidence of primary genital HSV-1 infection suggests that seroprevalence studies based on HSV-2 type-specific assays underestimate the overall prevalence of genital herpes (1).

Genital HSV infection encompasses a broad spectrum of clinical conditions, from classical painful vesicular eruption to truly asymptomatic infections, which can be detected by serological (antibody) testing. Symptomatic infection is generally described as ‘genital herpes’ and occurs as primary, first-episode and recurrent infections; these episodes are classically characterized by genital and perigenital vesiculation and ulceration accompanied by pain and dysuria. About 20% of patients with HSV-2 antibodies have no disease symptoms (2).

In Estonia, genital herpes has been a reportable disease since 1991, showing increasing incidence over the last 10 y (0.9/100,000 inhabitants in 1991, 23.9/100,000 in 2000) (3). The incidence of neonatal herpes infection is estimated to be approximately 1 per 4,000 deliveries (3). The diagnosis is frequently made on clinical grounds; culturing of HSV is not available; antigen detection and polymerase chain reaction (PCR) is possible in few centres only. In the current context, the growing number of diagnoses may indicate better recognition of the disease by physicians and patients, and better diagnostics, yet it does not give a very good description of the actual epidemiological situation.
The following are case histories of 5 patients with a clinically atypical genital herpes; the material was collected during 2001 from a private outpatient clinic specializing in dermatological and venereal diseases.

**MATERIALS AND METHODS**

**Patients**

During a period of 10 months 24 patients were tested for genital HSV infection using PCR. Of these, 12 (50%) tested positive for HSV (10 for HSV-2 and 2 for HSV-1). Asymptomatic shedding was detected in 2 patients, and 5 patients (3 females and 2 males, age between 25 and 35 y) were affected by atypical genital herpes (with extragenital or unusual morphological presentations). Patients with atypical genital herpes were tested on the basis of clinical/medical history indications (recurrent character and/or unidentified cause of chronic disease). Clinical history, examination and laboratory findings were recorded. Testing sites were decided clinically. However, cervical and urethral swabs were taken from all female patients and urethral swabs from all male patients. To exclude concurrent infections caused by other agents, samples were tested for several sexually transmitted pathogens (Herpes simplex, Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma genitalium, Urea-plasma urealyticum, Trichomonas vaginalis). Patients with positive PCR results on HSV only, with no concomitant infections, were included in the present review. All patients were immunocompetent.

**Methods**

Read et al. have described a set of primers used for PCR to detect HSV (4); Kahn et al. for Chlamydia trachomatis (5); Farrell et al. for Neisseria gonorrhoeae (6), and Martinelli et al. and Nelson et al. for Mycoplasma genitalium and Ureaplasma urealyticum (7,8). Trichomonas vaginalis infection was identified by culture (Trichomonas Medium No. 2, Oxoid Ltd., UK).

**RESULTS**

We identified 5 patients (3 females and 2 males) with clinical presentations suggestive to atypical genital HSV infection, i.e. typical clustered vesicular/ulcerative genital herpes lesions were absent. All patients had HSV-2 infection.

Observed clinical representations included: mucopurulent cervicitis \((n = 2)\), haemorrhagic cystitis with urethritis \((n = 1)\), recurrent urethritis \((n = 1)\), and lower back pain \((n = 1)\).

Four patients (cases 1, 2, 3, and 4) had chronic recurrent course of disease; and either history of sexually transmitted disease (genital Chlamydia trachomatis infection) or formerly diagnosed syndrome possibly indicative of sexually transmitted disease such as urethritis or prostatitis (cases 2, 3, 4, and 5) (Table I).

Follow-up information on therapeutic response to specific antiviral therapy is available for 2 out of 5 cases (case 2, case 5). Both had favourable effect of patient initiated episodic treatment with valacyclovir.

**DISCUSSION**

This report describes 5 cases of clinically overt genital disease that could be attributable to atypical genital HSV infection. Without typical clinical symptoms, the patient is generally not screened for HSV infection. These cases were identified due to recurrent character or unidentified cause of chronic disease and availability of PCR testing.

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Genital herpes is usually described as painful vesicles that ulcerate and eventually heal but recur. The spectrum of clinically atypical genital herpes ranges from large chronic hyperkeratotic ulcers in immunocompromised patients to asymptomatic shedding in immunocompetent and immuno-compromised hosts. Clinically atypical presentations include either unusual sites (extragenital regions: buttocks, thighs) or atypical morphological forms of genital disease (vulvar, penile or perianal fissures, localized recurrent erythema, recurrent radicular or lower back pain, cystitis, urethritis, vaginal discharge without overt genital lesions) (9,10). These patients are at risk of transmitting the virus (11). Genital herpes has been incriminated in causing the development of labial adhesions (12), as well as masking neoplasia (13).

In about 20–30% of the cases of nongonococcal urethritis (NGU), the pathogen is unidentified; and for recurrent and chronic urethritis recognised pathogens are rarely identified (14). Here genital HSV can be one of the possible aetiological agents. The traditional approach of recurrent/persistent urethritis is that patients with microscopic urethritis lacking symptoms or signs after 2 courses of treatment are not considered persistently infected (15). Recurrent HSV urethritis, due to the character of the herpetic infection, is an important exception in this approach.

The main recognized causes of infectious cervicitis are the sexually transmitted pathogens Neisseria gonorrhoeae and Chlamydia trachomatis. The typical clinical picture of HSV consists of blistering and ulceration of the cervix. We observed 2 cases of clinically atypical HSV-cervicitis with characteristic erythema and mucopurulent discharge from the endocervical canal, while ulcers/erosions were absent. Genital HSV infection has been associated with persistent inflammatory cervical smears (16); in the same study, the increased cervical cancer risk was associated with a history of chronic cervicitis (16). In a longitudinal study focusing on gynaecological infections other than HPV as risk determinants of subsequent cervical neoplasia, association with cervical HSV infection gave the highest and statistically most significant increase in risk (17).

Herpes simplex virus infection has also been associated with a variety of urological conditions. Urinary retention due to genital HSV infection accompanied by the typical genital eruption (18) or without any evident herpetic genital or anal lesions (19) has been described; neurogenic dysfunction due to a sacral meningomyelitis has been implicated as a cause of the urinary retention (18). Haemorrhagic cystitis in conjunction with HSV-2 infection has been described in elderly females with concurrent illnesses (rheumatoid arthritis, diabetes mellitus) with no evidence of HSV infection outside the bladder (20). Our case of a sexually active female suffering from recurrent cystitis and urethritis with negative urine cultures underlines the importance of additional testing for HSV in certain 'urological' cases. Misdiagnosed infection results in unnecessary morbidity for patients and their partners, and also inhibits efforts to reduce the spread of the disease.

In this paper we present suggestive evidence that symptoms and signs described (mucopurulent cervicitis, haemorrhagic cystitis, recurrent urethritis and lower back pain) were due to HSV. Bearing in mind the possibility of asymptomatic shedding of HSV in genital sites, there is still an opportunity that some of those symptoms may have been caused by other, unidentified agents. Nevertheless, we would point out that our patients were tested for relevant pathogens known to date.

One method to establish the relationship more firmly would be to administer antiviral drugs and receive positive results. All our patients were instructed to use episodic antiviral treatment with valacyclovir (21). Two of them (case 2, case 5) were repeatedly seen on
follow-up visits and claimed having relief of symptoms with patient initiated antiviral therapy.

In conclusion, up to 70% of genital HSV infections are clinically unrecognized (22). The majority of patients with genital herpes have symptoms and signs unrecognized either by themselves or their clinicians. A recent retrospective study on clinical presentation of the disease reported 51% of cases to be atypical (11). Currently, many doctors rely on the typical clinical presentation of the disease. Underdiagnosis of genital herpes because of misinterpretation of either anatomical or morphological presentations of the disease can accelerate the spread of the epidemic.

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REFERENCES


### Table I

Summary of case histories and clinical findings

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Testing site</th>
<th>Genital symptoms</th>
<th>History</th>
<th>Genital examination findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>Female</td>
<td>Cervix</td>
<td>Vaginal discharge, unpleasant smell</td>
<td>6 months earlier: preterm delivery, chorioamnionitis, post mortem diagnosis of pneumonia of the newborn</td>
<td>Cervicitis (erythema, mucopurulent discharge) No signs of bacterial vaginosis</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>Female</td>
<td>Cervix</td>
<td>Pain in the lower abdomen and perineal area</td>
<td>Diagnosis and treatment of chlamydiosis in 1994. Recurrent pains in lower abdomen during past 1.5 y.</td>
<td>Cervicitis (erythema, mucopurulent discharge)</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>Female</td>
<td>Urethra</td>
<td>Dysuria</td>
<td>Recurrent cystitis and urethritis (3 times since beginning of the disease 6 months earlier)</td>
<td>Hemorrhagic cystitis and urethritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cervix</td>
<td></td>
<td></td>
<td>Single small, painless erythematous macula on the left labia minora Urine culture negative</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>Male</td>
<td>Urethra</td>
<td>Dysuria</td>
<td>After treatment of chlamydial urethritis 6 months earlier recurrent urethritis</td>
<td>Urethritis: meatitis</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>Male</td>
<td>Urethra</td>
<td>Lower back pains</td>
<td>Patient has been diagnosed having chronic abacterial prostatitis due to recurrent lower back and perineal pains.</td>
<td>Urethritis: meatitis and scant mucous discharge from urethra</td>
</tr>
</tbody>
</table>