Detection of Human Herpesvirus 8 in Cervical Cells of Chinese Women with Abnormal Papanicolaou Smears

Human herpesvirus 8 (HHV-8), also known as Kaposi’s sarcoma (KS)–associated herpesvirus, is the first member of the genus *Rhadinovirus* known to infect humans [1]. HHV-8 has been strongly associated with KS in both immunocompromised and immunocompetent patients. HHV-8 has also been detected in high percentages of primary effusion lymphomas, cases of multicentric Castleman’s disease, and bone marrow dendritic cells of patients with myeloma. There is controversy about whether HHV-8 is ubiquitous and how the virus is transmitted in the healthy population. Reports on the frequency of virus shedding in the genital tract are being disputed, and the role of heterosexual transmission is also uncertain.

We have examined the presence of HHV-8 DNA in cervical scrapes from 404 consecutive Chinese women referred to a colposcopy clinic because of abnormal Papanicolaou smears. These patients were aged 16–88 years (mean, 40.6 years; SD, 11.7). None were commercial sex workers, 25% reported regular use of barrier contraception, 16% reported having >1 sexual partner, and 2% recalled having had sexually transmitted disease(s). None of the women were pregnant or had a history of cervical premalignant/malignant disease.

Colposcopy was performed for all the patients, and biopsies

References


Alena Jandourek, Patricia Brown, and Jose A. Vazquez

1 Department of Internal Medicine, Division of Infectious Diseases, Wayne State University School of Medicine, and 2 Henry Ford Hospital, Detroit, Michigan

Financial support: UGC direct grant 2040622 from Chinese University of Hong Kong.

Reprints or correspondence: Dr. Paul K. S. Chan, Department of Microbiology, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China (paulkschan@cuhk.edu.hk).

Clinical Infectious Diseases 1999;29:1584–5

© 1999 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/1999/2906-0049$03.00
were performed whenever abnormal lesions were observed. The quality of cervical samples was assessed by PCR with use of primers specific for the \( \beta \)-globin gene [2]. HHV-8 DNA was detected by a previously described nested PCR with use of outer primers KS1 and KS2 [1] and inner primers NS1 and NS2 [3] targeting the ORF26. Positive results were confirmed by a second nested PCR amplifying a nonoverlapping region at ORF25 [4].

Human papillomavirus (HPV) DNA was detected by a single-round PCR based on the degenerate primers MY09 and MY11 [5]. These primers are capable of amplifying a 450-bp DNA fragment from the L1 ORF of at least 40 genital HPV types. The ubiquitous human cytomegalovirus (HCMV) was also detected in parallel, by means of nested PCR [6], to serve as a reference for comparison.

Of the 404 samples, 35 (8.7%) were positive for HHV-8 DNA. No significant association was found with use of barrier contraception, having \( \geq 1 \) sexual partner, or age distribution. Seven (20%) of the 35 HHV-8 DNA–positive patients had biopsy-proven high-grade cervical lesions (3 patients had invasive squamous cell carcinoma and 4 had intraepithelial neoplasia grade 3). Two hundred and four samples (49.8%) were positive for HPV DNA.

The distribution of HPV DNA positivity with respect to the degree of cervical lesions is shown in Table 1. The overall rate of positivity for HCMV was 9.2%, with 8 patients having biopsy-proven cervical intraepithelial neoplasia grade 3. A statistically significant trend of association between HPV positivity and the degree of cervical lesions was observed, but no such association was found with regard to positivity for HHV-8 or HCMV (table 1).

Rates of HHV-8 positivity among the HPV-positive and HPV-negative groups were similar (9.4% vs. 8.0%). Of the 21 patients who were HPV-negative and had high-grade cervical lesions, 2 were infected by HHV-8. However, there were too few patients in this subgroup for further statistical analysis.

Although it is known that HCMV can be detected in the cervix of \( \sim 10\% \) of seropositive women [7], reports regarding the cervical shedding rate of HHV-8 are still limited [8]. Although we do not have data on the HHV-8 serostatus of our study population, our results nevertheless indicate that HHV-8 infection of the uterine cervix, as with HCMV infection, is not uncommon. The observation of similar rates of positivity for HCMV and HHV-8 in uterine cervixes of Chinese women has also led us to postulate that HHV-8, as with HCMV, is prevalent in the Chinese population.

Our observations, together with the detection of HHV-8 DNA in semen and prostate glands [9] and the recent report that HHV-8 seroprevalence was almost 4 times higher in female commercial sex workers than in other females [10], suggest the significant role of heterosexual transmission of this novel virus. However, the potential role of vertical transmission still requires further study.

Although a statistically significant association between HHV-8 and high-grade cervical lesions could not be demonstrated, the role of such an association in cervical malignancy deserves further evaluation.

### Table 1. Prevalence of HHV-8, HPV, and HCMV DNA in cervical cells of 404 Chinese women with abnormal Papanicolaou smears.

<table>
<thead>
<tr>
<th>Cervical lesion</th>
<th>No. tested</th>
<th>HHV-8 DNA</th>
<th>HPV DNA</th>
<th>HCMV DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/cervicitis</td>
<td>207</td>
<td>19 (9.2)</td>
<td>58 (28)</td>
<td>17 (8.2)</td>
</tr>
<tr>
<td>CIN 1</td>
<td>36</td>
<td>8 (14.3)</td>
<td>40 (71.4)</td>
<td>9 (16.1)</td>
</tr>
<tr>
<td>CIN 2</td>
<td>34</td>
<td>1 (2.9)</td>
<td>17 (50)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>CIN 3</td>
<td>77</td>
<td>4 (5.2)</td>
<td>63 (81.8)</td>
<td>8 (10.4)</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>30</td>
<td>3 (10)</td>
<td>23 (76.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>404</td>
<td>35 (8.7)</td>
<td>201 (49.8)</td>
<td>37 (9.2)</td>
</tr>
</tbody>
</table>

NOTE: CIN, cervical intraepithelial neoplasia (grade 1, 2, or 3); HCMV, human cytomegalovirus; HHV-8, human herpesvirus 8; HPV, human papillomavirus.

---

**References**