CASE REPORT

Acute cervicitis and vulvovaginitis may be associated with Cytomegalovirus

Magali Abou, Patrick Dällenbach

Department of Gynecology and Obstetrics, Division of Gynecology, Geneva University Hospitals, Geneva, Switzerland

Correspondence to

Dr Patrick Dällenbach,
patrick.dallenbach@hcuge.ch

SUMMARY

Cytomegalovirus (CMV) infection in immunocompetent hosts is generally asymptomatic or may present as a mononucleosis syndrome. Its association with acute cervicitis and vulvovaginitis has rarely been reported.

A 24-year-old woman presented with pelvic pain, vulvodynia, abnormal vaginal discharge, burning with urination, fatigue, fever, vomiting and diarrhoea. The vulva and cervix were red with vesicular lesions on the cervix. Genital herpes simplex infection (HSV) was suspected and valacyclovir was given orally. However, serial viral cultures performed 7 weeks apart did not isolate HSV as suspected, but CMV was confirmed by immunofluorescence and early antigen research. Blood tests confirmed an acute CMV infection. Typical inclusions were found at histology. Symptoms resolved slowly with persistence of cervical lesions at 7 weeks from diagnosis.

The frequency of CMV genital infection is probably underestimated. The infection is not always asymptomatic and might be confused with genital HSV infection. The clinical course is longer.

BACKGROUND

CMV can be identified in the cervix in a considerable proportion of women (24–29%, and up to 39% among prostitutes).^{1 2} However, most cases are asymptomatic and diagnosed fortuitously in cervical cytology. We present a case of acute cervicitis and associated vulvovaginitis with negative culture for HSV infection but positive for CMV, which was initially misdiagnosed as HSV infection. To reassure the patient and provide long-term care, we believe that it is important to make the right diagnosis as the clinical course is very different from that of HSV as illustrated in this case report.

CASE PRESENTATION

A 24-year-old woman, gravida 0, with no relevant medical and gynaecological history apart from recurrent urinary infections and appendicitis during childhood, presented at our walk-in gynaecological clinic with pelvic pain lasting since 3 weeks. She described thick and yellowish vaginal discharge, vulvodynia, unusual fatigue and intermittent fever. Since the last 3 days she had also had diarrhoea and vomiting and complained of slight burning with frequent urination. She used an oral combined contraceptive pill and had menstruations 10 days previously. The last sexual intercourse was about 6 weeks ago, and she had no dyspareunia.

At clinical examination, the vulva, the vagina and the cervix were red. Vesicular lesions were observed

at the junction zone on the cervix. Pelvic examination was painful. There was no rebound tenderness or guarding, and no inguinal adenopathy. At admission, she had no fever.

Bacteriological and viral samples were performed on the cervix and sent to our institutional virology and bacteriology laboratory. Direct microscopic examination of the vaginal and cervical discharge revealed that it was rich in white blood cells, but had no myceliae or germs such as *Trichomonas vaginalis*. The pregnancy test and urine test (dipsticks) were negative. At transvaginal ultrasound, structure and echogenicity of the uterus and ovaries were normal; there was no adnexial mass and no liquid in the pelvis.

We diagnosed cervical and vaginal inflammation and suspected a primary genital HSV infection. Antiviral therapy was prescribed (valacyclovir 500 mg twice a day for 10 days). We planned a second appointment 1 week later to discuss results and for follow-up. Cervical and vaginal lesions were still present as well as abdomino-pelvic pain, diarrhoea and asthenia. The patient complained of vulvar itchiness and persisting white vaginal discharge confirmed at examination. Microscopic examination revealed myceliae and diagnosis was made of additional candidosis probably consecutive to disturbance in the vaginal flora equilibrium. Bacterial cervical smears of the initial consultation were all negative with the absence of bacteria and of candida, but the viral culture was positive for a virus from the herpes family. Valacyclovir treatment was continued with local antifungal treatment. After immunofluorescence testing and research of early antigen, the final diagnosis was not HSV as initially suspected, but CMV instead.

INVESTIGATIONS

We contacted the patient to perform complementary investigations. Valacyclovir treatment was already over. We organised a colposcopic examination which showed vesicle-like lesions, pink to yellow at the junction zone. Biopsies of the cervix and endocervical curettage were performed and showed typical CMV inclusions (owl's eye cell) at histology (figure 1). Immunostaining with specific monoclonal antibodies confirmed CMV infection. Blood tests and antibody dosage with Microparticle Enzyme Immunoassay were compatible with an acute CMV infection. IgM were 1.40 UAb/ml (>0.50) and IgG were 959 UAb/ml (>15). CMV DNA was detected in the blood test with 6.5 E+1 copy/ml. CMV was also present in the urine culture analysis. Full blood count, serum electrolytes, tests of the liver and renal function were

To cite: Abou M, Dällenbach P. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-008884

Figure 1 Voluminous nuclear inclusion (simple arrow) and fine cytoplasmic granulations (double arrow) suggest the presence of cytomegalovirus in an endocervical gland epithelial cell (H&E $\times 400$).

normal. HIV testing was negative. There were neither blood nor leukocytes in the stool.

TREATMENT

No further treatment was given.

OUTCOME AND FOLLOW-UP

The next appointment was scheduled 1 month later. Diarrhoea, fatigue and vaginal discharge remained during this period but improved progressively. The cervix was still red with small vesicular lesions and a small ulcer was present at 3 h. Repeat culture of the cervical and vaginal discharge was still positive for CMV. Laboratory exams showed persistence of the virus in the urine, with a reduction of IgMs in the blood. IgM decreased to 0.40 UAb/ml and IgG were still elevated to 972 UAb/ml. CMV DNA was still present at 5.4×10^1 copy/ml. There was no lymphopaenia and cervical cytology was normal.

Symptoms resolved slowly over many weeks with persistence of cervical lesions at 7 weeks from diagnosis.

DISCUSSION

CMV is a DNA virus belonging to the herpes virus family. It can infect many organs. After acute primo infection, the virus remains persistent in unknown reservoirs. Secondary symptomatic infection may present later in life reflecting either a reactivation of latent CMV or reinfection with another strain. CMV infection is common in immunocompromised patients. The infection in immunocompetent hosts is generally asymptomatic, or may present as a mononucleosis syndrome with fever and fatigue. Potential complications are colitis, hepatitis, encephalitis, pneumonia, pericarditis, myocarditis or retinitis.

Seroprevalence rates range between 40% and 100% of the general population. Transmission can occur via multiple routes: sexual, close contact, blood and tissue exposure, perinatal. The illness is generally self-limited, and antiviral therapy is usually not indicated. The efficacy of antiviral agents (ganciclovir, valganciclovir, foscarnet and cidofovir) has been evaluated in immunocompromised patients, but their clinical utility in immunocompetent hosts remains unproven.³

Female genital CMV infection is rarely described in the medical literature, even if it can be identified in the cervix in a considerable proportion of women with diagnostic methods using PCR.^{1 2}

We found only two cases of symptomatic CMV cervical infection, described in immunocompromised women, and one report

of recurrent ulcerative vaginal lesion in a postmenopausal woman.⁴⁻⁶ Cases of CMV endometritis have also been reported.² Our report is the first one (to our knowledge) to describe symptomatic cervicitis with vulvovaginitis caused by CMV in an immunocompetent patient.

At histology, CMV is diagnosed by characteristic nuclear inclusions in the epithelial endocervical cells, and cytoplasmic granulations (figure 1). In cervical biopsies of asymptomatic women referred for colposcopy following cervical smears showing borderline nuclear changes or dyskaryosis performed in a single institution over an 8-month period, McGalíe *et al*² found cervical CMV inclusions in five biopsies from four immunocompetent patients. CMV inclusions were located mainly in the endocervical glandular epithelial cells, but also in the endothelial and mesenchymal cells. Inclusions were not seen in squamous cells. Inclusions were eosinophilic and intracytoplasmic rather than intranuclear. They were positive for CMV on immunohistochemistry. Immunohistochemical staining was then performed on 30 additional consecutive cervical biopsies in which CMV inclusions were not seen, to determine whether this might identify additional cases that were not diagnosed on morphological examination. They were all negative, suggesting that active CMV infection does not occur in the absence of histologically demonstrable inclusion bodies.² Other authors reported similar typical histological findings present in immunocompetent and immunocompromised patients.^{4 5 7} Two reports related intracytoplasmic inclusions in the intermediate squamous cells.^{3 8}

This diagnosis is challenging and can be easily missed if the pathologist does not have a high level of suspicion for a CMV infection. The differential diagnosis of CMV infection of the cervix is HSV infection, but histology is different. In general, herpes lends itself to exclusion because of the multinucleation and moulding of the nuclei.⁴ The inclusions of HSV appear glassy, whereas those of CMV appear more eosinophilic.⁴

As cytopathological changes can be seen on a cytological cervical smear, a liquid-based specimen could then be used for the screening, and in addition, immunohistochemistry and CMV DNA detection by PCR could be done to confirm the diagnosis.⁸

The frequency of CMV cervicitis is probably underestimated and misdiagnosed in the immunocompetent patient. The infection is not always asymptomatic and might be confused with genital herpes infection. The course of the disease is different and may be associated with other symptoms due to the systemic dissemination of the virus such as diarrhoea, vomiting and fatigue. No treatment is required but diagnosis has to be made to reassure the patient of the self-limiting course of the infection and to provide long-term care.

Learning points

- ▶ Vulvovaginitis and cervicitis may be caused by cytomegalovirus and might be confused with the genital herpes simplex infection.
- ▶ The frequency of this condition is probably underestimated.
- ▶ The clinical course is different and needs to be explained to reassure the patient.
- ▶ Treatment is symptomatic, and the benefit of antiviral therapy remains unproven in the immunocompetent host.

Contributors Both authors participated equally in the conception and drafting of this case report and approve the final version to be published.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Shen CY, Chang SF, Lin HJ, *et al*. Cervical cytomegalovirus infection in prostitutes and in women attending a sexually transmitted disease clinic. *J Med Virol* 1994;43:362–6.
- 2 McGalíe CE, McBride HA, McCluggage WG. Cytomegalovirus infection of the cervix: morphological observations in five cases of a possibly under-recognised condition. *J Clin Pathol* 2004;57:691–4.
- 3 Hunt JL, Baloch Z, Judkins A, *et al*. Unique cytomegalovirus intracytoplasmic inclusions in ectocervical cells on a cervical/endocervical smear. *Diagn Cytopathol* 1998;18:110–12.
- 4 Venkataraman G, Kouria G, Mehrotra S, *et al*. Cytomegalovirus inclusions on a cervical pap test: report of a well-known organism at an uncommon site. *Diagn Cytopathol* 2007;35:618–20.
- 5 Oei AL, Salet-van de Pol MR, Borst SM, *et al*. 'Owl's Eye' cells in a cervical smear of a transplant recipient: don't forget to inform the referring physician. *Diagn Cytopathol* 2007;35:227–9.
- 6 Abulafia O, DuBeshter B, Dawson AE, *et al*. Presence of cytomegalovirus virus inclusion bodies in a recurrent ulcerative vaginal lesion. *Am J Obstet Gynecol* 1993;169:1179–80.
- 7 Huang JC, Naylor B. Cytomegalovirus infection of the cervix detected by cytology and histology: a report of five cases. *Cytopathology* 1993;4:237–41.
- 8 Sekhon HS, Press RD, Schmidt WA, *et al*. Identification of cytomegalovirus in a liquid-based gynecologic sample using morphology, immunohistochemistry, and DNA real-time PCR detection. *Diagn Cytopathol* 2004;30:411–17.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow