Case Report

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Disseminated Cytomegalovirus Infection of the Female Genital Tract (With 1 color plate)

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Key Words

Cytomegalovirus
Immunosuppression
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Cervicitis

Abstract

A woman with severe immunosuppression provoked by the acquired immunodeficiency syndrome developed a disseminated cytomegalovirus infection of the genital tract. Using in situ hybridization and the APAAP technique, cytomegalovirus was detected in epithelial and endothelial cells as well as in macrophages in the vulva, the vagina and the cervix uteri.

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Introduction

Cytomegaly is a widespread, usually harmless and asymptomatic viral infection. About 50% of young women have already developed antibodies against cytomegalovirus (CMV) [1]. In case of immunosuppression by lymphoma, generalized malignancies, in patients with transplantations, in HIV-positive patients as well as in pregnancy, a primary CMV infection, a reactivation of a latent virus or a reinfection by an exogenous virus is frequently reported. Especially in patients with acquired immunodeficiency syndrome (AIDS) cytomegaly-related pneumonia, encephalitis, bleeding esophagus ulceration, ulceration of stomach and intestines, hepatitis, cholecystitis and retinitis are known [2].

Up to now, the involvement of the female genital tract represents an absolute rarity and has been described only in the uterine cervix [3].

Case Report

In 1989, a 26-year-old woman who had been using intravenous drugs between 1979 and 1982 delivered a HIV-positive child. Therefore, she had undergone a HIV test which also turned out to be positive. Two months before she died she attended our outpatient service because of an unusually marked ulcerated vulvitis, vaginitis and cervicitis (fig. 1). Laboratory findings: leukocytes 3,200; lymphocytes 1,856; T4 lymphocytes 245; Ts lymphocytes 861; thrombo-cytes 209,000; CMV-KBR 1/20.

We treated an oral and genital candidiasis and a trichomoniasis and used antibiotics because of the cultural growth of *Staphylococcus aureus* and *Chlamydia trachomatis*. In spite of this therapy there was no improvement so that we tried to treat her with acyclovir. The patient did not agree to hospital admission before she had been suffering from violent headache for 3 days. At that time a severe immunosuppression was recognized: leukocytes 3,500; lymphocytes 525; T4 lymphocytes 58; T8 lymphocytes 283. Furthermore, we found a thrombocytopenia of 51,000 and an immunoglobulin elevation of IgG 2,222 mg/dl; IgA 1,261 mg/dl, and IgM 301 mg/dl. A few hours later she died from a cerebral toxoplasmosis despite intensive medical care.

Autopsy revealed a generalized lymphadenopathy with destruction of follicular structure, extreme depletion of lymphocytes, marked increase of plasma cells and sinus histiocytosis. The following infections with opportunistic organisms were found: pseudo-membranous esophagitis candidosa, a diffuse necrotizing toxo-plasma encephalitis with a 2 × 1 cm parieto-occipital necrosis in the left hemisphere and a CMV infection of the adrenal gland, the vulva, the vagina and the cervix uteri.

Material and Methods

In formalin-fixed and paraffin-embedded autopsy tissue CMV was detected by in situ hybridization. 4-µm slides were heated up to 92.5 °C to separate the double helix of DNA. Biotinylated cyto-me-galy-specific DNA (Enzo-patho-gene) was diluted 1:80. Using a bio-tin-avidin-enzyme complex, CMV genome could be localized as a red color reaction. Tissue was pretreated with 0.01 % protease. As an endothelial marker we incubated factor VIII (Dako) and chose the APAAP technique. Positive and negative control sections had also been incubated.

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Results

In HE-stained paraffin sections, the vulva, vagina and cervix showed epithelial lesions with granulation tissue, infiltration of lymphocytes, plasma cells and histiocytes as well as bizarre giant cells with basophilous nuclear inclusions and perifocal clearing (so-called 'owl's eye' cells, fig. 2). By in situ hybridization these cells located in the cervix (fig. 3) and adrenal gland were positive for CMV. Also a few morphologically normal cervical cells turned out to be positive. Some macrophages and endo-thelial cells in cervix, vagina (fig. 4) and vulva showed a positive reaction for CMV.

Discussion

Only a few descriptions of cytomegaly-related cervici-tis in the female genital tract [3] have been presented in the literature. This is due to the fact that only a minority of women showed full-blown AIDS (in Germany since October 1988 6.5% of AIDS patients have been female) [5]. On the other hand, the clinical appearance of ulcerated vulvitis is often confounded with herpes genitalis and cultural proof is lacking. For cultural detection biopsy specimens with a temperature of 4°C should reach the laboratory (not deep-frozen!) within 1–2 days. Serological diagnosis of primary or reactivated CMV infection might be difficult in immunocompromised patients. Neither a positive virus excretion nor a high antibody titer is definite proof for acute CMV infection. In this case we found a normal titer of CMV (KBR 1/20). These diagnostic problems have been reflected in the article of Ismaei et al. [6], who found a visceral involvement in 40 % of autopsied patients having suffered from AIDS, opposed to only 6% of previously diagnosed cases.

CMV should be considered as an ubiquitous pathogenic agent in patients suffering from AIDS. Gerna et al. [4] found CMV antigenemia in 38% and viremia in cell culture in 25%. It is reported that HIV-positive women developed a high incidence of cervical dysplasia and neoplasia, which might be the result of an elevated prevalence of human papilloma virus [7]. Considering the fact that CMV has oncogenic potential in vitro [8] and has been shown to induce cervical tumors in mice [9], it should be discussed whether CMV contributes to the high incidence of cervical cancer in HIV-positive women.

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