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Case Report

Cytomegalovirus Primo-Infection, a New Sexually Transmitted Disease? Two Cases Report

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Abstract
Cytomegalovirus (CMV) is a well-known and ubiquitous virus that causes damage in pregnant women, immunocompromised individuals, and babies in the nursery. It is a direct transmission through biologic liquids, asymptomatic in most cases, sometimes with a mononucleosis-like syndrome. It can be diagnosed using a serologic, or much better, a PCR test. Two cases of primary CMV infections are discussed and linked to probable sexual transmission.
Keywords: Cytomegalovirus, Primo-infection, Sexual transmission, PCR

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Introduction

Human cytomegalovirus (HCMV) is extremely prevalent in the population. In the majority of cases, it remains asymptomatic or paucisymptomatic (mononucleosis syndrome). Its consequences are serious, especially for pregnant women and immunocompromised individuals. The following two observations suggest an unusual direct transmission.

Clinical Cases

Case 1

A 35-year-old homosexual patient consulted on May 23 for general symptoms that were not very suggestive. Several days later, some cutaneous lesions suggestive of monkeypox appeared. But, a week later, as the smallpox lesions improved, the patient complained of fever, especially in the evening, headaches, and sore throats. Fifteen days after the onset, the headache subsided, but the patient complained of asthenia and a persistent fever. The blood biological check-up is as follows: ALT 101 U/L (N = 16 – 63 U/L), AST 75 U/L (N = 15 – 37 nU/L); CRP: 20; sterile blood culture ; and hepatitis C serology negative. Faced with this picture of persistent fever and hepatic cytolysis, the serologies of *Bartonella henselae* and hepatitis A and E were checked. They all turned out to be negative. The PCR tests for *Bartonella*, varicella-zoster, and hepatitis E were negative.

However, 23 days after the onset of the disorders, the RT-PCR cytomegalovirus (CMV) was positive, at 4.29 log, or 19540. After 32 days, a small increase in AST persisted to 63, with the balance being normal elsewhere. However, RT-PCR CMV was still positive at 3270, with positive serology showing anti-CMV IgG antibodies (795 U/mL) and anti-CMV IgM positive antibodies (87.3 U/mL). An anti-CMV IgG avidity assay did not find IgG. IgG had not yet appeared, and it started to appear 15 days later at 79. In the sample taken nearly 4 months after the infection, the CMV infection showed an IgG level of 209.4 U/mL and a positive IgM test (index 1.18), confirming the primary infection.

Case 2

A 45-year-old bisexual man, using poppers and smoking shit with protected anal intercourse, has had a fever of 38 °5 for 21 days, which was well tolerated. He only reported the notion of a recent trip a week before having sex with others. A clinical examination revealed splenomegaly. The laboratory check-up showed CRP at 10, 5790 lymphocytes/mm3, LDH at 622 IU/l (N = 85 – 227), AST at 253 U/l, and ALT at 103 U/l. Blood culture was negative, as were the serologies of *Coxiella, Rickettsia, Brucella*, *Leishmania*, varicella-zoster, and hepatitis A, B, C, and E. CMV PCR is positive (9675). CMV serology revealed anti-CMV IgG-positive antibodies (36.3 U/ml) and IgM-positive anti-CMV antibodies (62.4 U/mL). One month after the start of the infection, the ALT was 66 U/L and the CMV PCR was negative.

Discussion

A Ubiquitous Human Virus

HCMV (human herpes virus type 5, HHV-5) is a DNA virus of the subfamily β herpesviridae. This subfamily includes the sixth (HHV-6) and seventh (HHV-7) human viruses. HCMV has a diameter of 150 nm with linear, double-stranded DNA of approximately 240 kb (1) (Figure 1). This virus is very fragile at room

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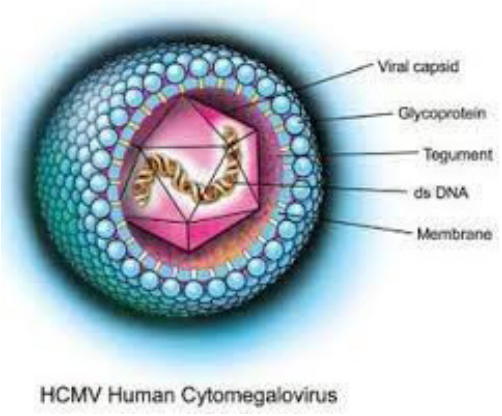

Figure 1. Human cytomegalovirus (Permission copyright from WHO)

temperature, with a survival rate of a few hours to 7 days (8 hours on average). Humans are the only known reservoirs, although other species can be infected with species-specific CMV, which sometimes serves as a model for human infection. HCMV is a ubiquitous virus. Its seroprevalence worldwide varies from 35% to 100%, depending on the population. In fact, it infects 50% of populations in industrialized countries and 100% of people from low-income countries (2).

In most countries, 50% of pregnant women are CMV-negative. There are two peaks in HCMV infections: the first in early childhood, when children discover objects by putting them in their mouths, and the second in adolescence and young adults during their first sexual contact. During primary infection, the virus is excreted in saliva, respiratory secretions, urine, tears, breastmilk, cervicovaginal secretions, and semen (3). It infects a large number of human cells, especially epithelial cells. Latency occurs mainly in hematopoietic cells in the bone marrow, such as monocytes and macrophages (4), but also in endothelial cells (5).

Long-term Contagiousness

HCMV can be responsible for either primary infection or secondary infection by reactivation of an endogenous strain or by reinfection by an exogenous strain, which is much rarer (6). Contagiousness can last for several years and can be continuous or episodic. About 20% of adults are intermittent shedders. Reinfections with a new strain are rare but still possible because antibodies do not provide absolute protection; they last 20 to 40 days on average, but vary from 3 to 8 weeks after blood transfusion and from 3 to 12 weeks after delivery.

Exclusive community-to-human transmission occurs not only through direct mucosal contact with infectious excretions and secretions, particularly infected saliva, urine, blood, tissues, or organs, but also possibly through indirect contact with soiled objects (Figure 2). Other modes of infection are sexual and organ transplants. The virus is naturally transmissible, vertically from mother to

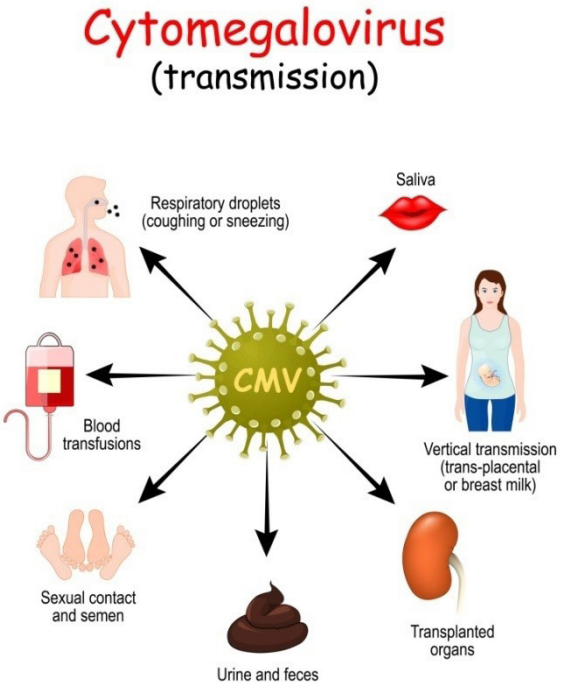

Figure 2. Mode of transmission of human cytomegalovirus (Permission copyright from WHO)

child (Figure 3), transplacentally, with a high frequency (7) during childbirth or postpartum (especially during breastfeeding), or horizontally through direct contact with contaminated body fluids (oral, oropharyngeal, or sexual) (8).

Transmission can also take place during reactivations. Indeed, the virus, despite its fragility, remains present for a long time in the media. In addition, contamination can occur directly through contact with a child or a viremic patient. Some individuals shed large amounts of the virus: primary infectants, immunocompromised individuals, children infected in utero who shed the virus in urine and saliva during the first few years of life (9), and children under 3 years of age in the community.

Regarding contact with infected children, it is important to follow the standard precautions mentioned below:

Do not suck on the child's pacifier, do not take a bath with him or her, do not kiss the child on the mouth, and wash his or her hands, especially after each diaper change.

A Mononucleosis Syndrome

In the 60% to 90% of cases, the infection remains asymptomatic. In other cases, the clinical picture is inseparable from a mononucleosis syndrome caused by the Epstein-Barr virus: moderate hyperthermia, often prolonged (2-3 weeks on average), isolated with accompanying signs, such as asthenia, arthralgia, headache, weight loss, and pharyngitis. Sometimes, these are isolated and localized conditions: hepatitis, colonic lesions of acute ulcerative colitis (10), certain respiratory infections of early childhood, such as bronchitis,

whooping cough syndrome or various pneumopathies, myocarditis, pericarditis, glomerulonephritis, Guillain-Barré polyradiculoneuritis, catarrhal-like conjunctivitis contemporaneous with the onset of mononucleosis syndrome, necrotizing retinitis in immunocompromised patients (11), and chorioretinitis in the fetus (Figure 4) (12). Visceral lesions are severe in immunocompromised patients (13,14). The course is spontaneously favorable within 15 days to 3 weeks, but lymphocytosis and splenomegaly may persist for several months. A number of diseases have been associated with CMV (Table 1) (15), which also appear to have a role in the neoplastic transformation of primary cells (16).

Serologic Diagnosis

Elisa

Serology is performed by the ELISA method with the detection of anti-CMV antibodies of the IgM and IgG types. Testing for IgA, IgE, and IgD is not a standard practice. An IgG avidity test makes dating possible (Figure 5). Thus, the mere presence of IgM does not allow a formal conclusion to be drawn to a recent infection because IgM can persist for a long time, up to 6-12 months after infection, or reappear during a recurrence or a non-specific stimulation (17). In addition, they may be lacking in immunocompromised people. Thus, when the diagnosis of primary infection is essential (e.g., in pregnant women), the measurement of the avidity index of IgG antibodies should be carried out. This technique makes it possible to distinguish between low-avidity IgG, synthesized during a primary infection, and high-avidity IgG, synthesized during secondary or old infections.

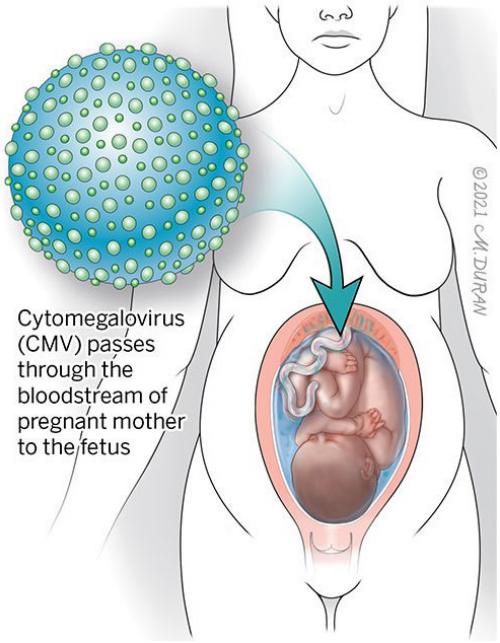

Figure 3. Human cytomegalovirus and pregnant woman (Permission copyright from WHO)

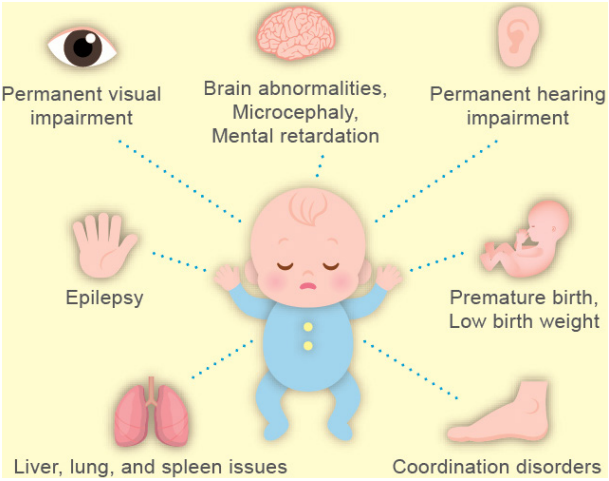

Figure 4. Complications of human cytomegalovirus in children (Permission copyright from WHO)

PCR, in Common Practice

The goal of PCR is to evaluate viral replication. The quantification of the viral load makes it possible to assess the kinetics of viral expression in a subject and thus best adapt the therapeutic strategy, especially in the transplanted subject. This PCR can be performed from a peripheral whole blood sample on EDTA but is also applicable to plasma or serum as well as any body fluid (saliva, urine, or bronchoalveolar lavage).

PP65 Antigen

PP65 antigenemia testing allows the detection of active HCMV infection, which is of interest in

Table 1. Different Diseases Associated With CMV

System	Diseases
Circulatory	Inflammatory abdominal aortic aneurysm and arteriosclerosis
Digestive	Colitis, Oesopharyngitis, colorectal cancer, and gastric cancer
Ophtalmic	Retinitis
Endocrine	Neuroglioma and breast cancer
Neurological	Glioblastoma multiforme and medulloblastoma
Urinary	Prostate cancer
Rheumatic	Systemic lupus erythematosus and an auto-immune connective tissue disease
Hematological	Idiopathic thrombocytopenic purpura

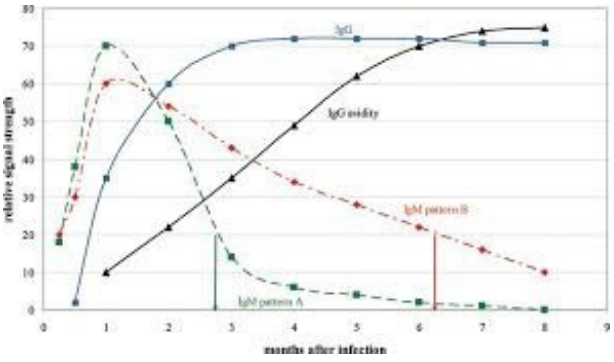

Figure 5. Serologic diagnosis of human cytomegalovirus (Permission copyright from WHO)

immunocompromised patients, transplant recipients, and AIDS patients (18-20).

Other laboratory results are non-specific: a normal blood count or the appearance of moderate leukocytosis (10 to 15 000/mm^3) after a few days of fever. Constant lympho-mononucleosis results in a reversal of lymphocyte formula (40-80% lymphocytes), a negative reaction from Paul and Bunel, normal or slightly accelerated ESR, frequent hypergammaglobulinemia, IgM-like, polyclonal, and hypertransaminasemia, mainly on ALT.

Conclusion

Primary infection also occurs in adult men. It can be considered a sexually transmitted disease. It has a transmissibility character, in particular salivary and sexual, hence the proposed abstinence of 20 days in both observations. In immunocompetent subjects, it appears benign. In any case, knowing that this virus, like the other viruses in the herpes group, remains permanently in the body, much progress remains to be made in diagnosis and treatment, especially in pregnant women.

Authors' Contribution

Conceptualization: Patrice Bouree, Vincent Jeantis.
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Supervision: Patrice Bouree.
Validation: Patrice Bouree.
Visualization: Patrice Bouree.
Writing–original draft: Patrice Bouree, Vincent Jeantils.
Writing–review & editing: Patrice Bouree.

Competing Interests

The authors have no conflict of interest to disclose.

Ethical Approval

Written consent was obtained from the two patients for the publication of these clinical cases.

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