Cytomegalovirus Infection

Manitoba Health
Public Health
Communicable Disease Control Unit

Case Definition

- Newborn: Isolation of cytomegalovirus (CMV), usually from urine.
- Adult: Virus isolation, CMV antigen detection, CMV DNA detection (by PCR or in-situ hybridization), presence of CMV-specific IgM antibody, or a four-fold rise in CMV-specific IgG antibody.

Reporting Requirements

Cytomegalovirus infection is not reportable in Manitoba.

Clinical Presentation/Natural History

Congenital CMV infection:
The most severe form of this viral disease occurs in 5-10% of infants who are infected in the perinatal period, following intrauterine infection or after CMV-contaminated blood transfusion to seronegative infants. These infants may have signs and symptoms of severe generalized infection, especially involving the central nervous system and liver. Lethargy, convulsions, jaundice, petechiae, purpura, hepatosplenomegaly, chorioretinitis, intracerebral calcifications and pulmonary infiltrates can occur. Survivors may exhibit mental retardation, microcephaly, motor disabilities, hearing loss and evidence of chronic liver disease. Death may occur *in utero*; the neonatal case-fatality rate is high for severely affected infants. Although neonatal CMV infection occurs in 0.3-1% of births, 90-95% of these infections are inapparent; however, about 10% of asymptomatic congenital infections eventually manifest some degree of neurosensory disability. Deafness is one of the major problems associated with congenital CMV infection. Less specific findings in newborns are failure to thrive and recurrent respiratory infections. Fetal infection may occur during either primary or re-activated maternal infections. Primary infections carry a higher risk for severe symptomatic disease in infants, but are much less common than reactivated infections.

Acquired CMV infection:
Infection acquired later in life is generally inapparent, but may cause a syndrome clinically and hematologically similar to Epstein-Barr virus (EBV) mononucleosis, but distinguishable by virologic or serologic tests and the absence of heterophile antibodies. CMV causes up to 10% of all cases of "mononucleosis" seen among university students and hospitalized adults aged 25 to 34 years. Other features may include pneumonia, hemolytic anemia, splenomegaly and petechial rash. CMV is the most common cause of post-transfusion mononucleosis, although many post-transfusion infections are clinically inapparent. Disseminated infection, with pneumonitis, retinitis, gastro-intestinal tract disorders (gastritis, enteritis, colitis) and hepatitis, occurs in immunodeficient and immunosuppressed persons; this is a serious manifestation of AIDS.

Etiology

Cytomegalovirus is a member of the herpes virus family (herpesvirus 5).

Epidemiology

Reservoir: Humans are the only known reservoir of human CMV; strains found in many animal species are not infectious for humans.

Transmission:

Adults and Children: Intimate exposure by mucosal contact with infectious tissues, secretions and excretions. CMV is excreted in urine, saliva, breast milk, cervical secretions and semen during primary and re-activated infections. Viremia may be present in asymptomatic persons, so the virus may be transmitted by blood transfusion, probably associated with leukocytes. CMV is excreted by a large number of children in day-care centres, which may represent a community reservoir.

Perinatal: The fetus may be infected *in utero* from either a primary or re-activated maternal

infection. Serious fetal infection with manifest disease at birth occurs most commonly during a mother's primary infection, but infection (usually without significant disease) may develop even when maternal antibodies existed prior to conception. Post-natal infection occurs more commonly in infants born to mothers shedding CMV in cervical secretions at delivery; thus, transmission of the virus from the infected cervix at delivery is a common means of neonatal infection. Virus may also be transmitted to infants through infected breast milk, an important source of infection but not disease.

Occurrence:

General: Infection is generally acquired very early in life in developing countries. The prevalence of serum antibodies in adults varies from 40% in developed countries to almost 100% in developing countries. In various population groups, 8-60% of infants begin shedding virus in the urine during their first year of life as a result of infection acquired from the mother's cervix or breast milk.

Incubation Period: Illness following a transplant or transfusion with infected blood begins within three to eight weeks. Infection acquired during birth is demonstrable three to 12 weeks after delivery.

Susceptibility and Resistance: Universal. Fetuses, patients with debilitating diseases, those on immunosuppressive drugs (especially organ allograft recipients) and patients with AIDS are more susceptible to overt and severe disease.

Period of Communicability: Virus is excreted in urine and saliva for many months and may persist or be episodic for several years following primary infection. After neonatal infection, virus may be excreted for five to six years. Adults appear to excrete virus for shorter periods, but the virus persists as a latent infection. Excretion recurs with immunodeficiency and immunosuppression.

Diagnosis

Diagnosis in the newborn is made by virus isolation, usually from urine. Diagnosis of CMV disease in the adult is made difficult by the high frequency of asymptomatic and relapsing infections. Multiple modalities for diagnosis should always be used if possible. Virus isolation, CMV antigen detection and CMV DNA detection by PCR or in-situ hybridization can be used to demonstrate virus in organs, blood, respiratory secretions or urine. Serologic studies should be done to demonstrate the presence of CMV-specific IgM antibody or a significant rise in IgG antibody. Interpretation of the results requires knowledge of the clinical and epidemiologic background of the patient.

Key Investigations

No public health investigation is required.

Control

Management of Cases:

- Among immunocompetent persons, treatment in general is supportive, nonspecific and symptomatic. Disease is generally self-limited.
- Sexual abstinence or the use of condoms is indicated when clinical symptoms are present.
- Ganciclovir (IV and PO), and IV foscarnet have been approved for the treatment of CMV retinitis in immunocompromised persons. They may also be helpful, especially when combined with anti-CMV immune globulin, for pneumonitis and possibly gastro-intestinal disease in immunocompromised persons.

Management of Contacts:

- No specific action recommended.

Preventive Measures:

- Handle diapers of all infants carefully; hands should be washed after diaper changes and toilet care of all newborns and infants.
- Women of childbearing age who work in hospitals (especially delivery and pediatric wards) should use routine precautions; in day-care centres and preschools, strict standards of hygiene, such as handwashing, should be observed.
- Avoid transfusing neonates of seronegative mothers, seronegative allogenic transplant recipients, or haematopoietic stem cell transplant recipients, with blood from CMV-seropositive donors. Avoid transplanting organ tissues from CMV-seropositive donors to seronegative recipients.