Cytomegalovirus in Pregnancy

New Zealand Maternal Fetal Medicine Network

This guideline was updated in June 2016 by Dr Margaret Harpham with input from members of the New Zealand Maternal Fetal Medicine Network.

Background

Cytomegalovirus (CMV) is a DNA herpesvirus. Humans are the only known host.

It is the most common congenital viral infection affecting 0.5 -2.5% of live births. CMV can infect the placenta and be transmitted to the fetus with potentially devastating effects. Congenital CMV infection is the leading infectious cause of neurodevelopmental disability and sensory neural deafness. There is no effective treatment or vaccine.

CMV is usually spread by person to person contact with infected nasopharyngeal secretions, urine, saliva, semen, cervical/vaginal secretions, breast milk or blood.

Risk factors for infection:

- Women with contact with young children, especially child care workers and parents of children in day care are the highest risk group
- Immunocompromised women (organ transplants recipients, HIV)
- Blood transfusions
- Sexual contact

After primary infection, the virus lies dormant and exists in latent state. Reactivation can result in recurrent or secondary infection.

Objective

To guide accurate diagnosis, investigation and management of possible maternal CMV infection.

Definition

Primary infection: CMV infection in previous seronegative person

Non Primary infection: reactivation of latent virus or reinfection with new strain

Congenital infection: transplacental transmission of CMV and fetal/neonatal infection

Maternal Infection

Clinical manifestation and symptoms:

Primary CMV infection in pregnancy

- Most infections are asymptomatic
- Can have mild febrile illness and non-specific symptoms
- Fever, flu-like symptoms, mild hepatitis

If immunocompromised: Myocarditis, hepatitis, pneumonitis, meningoencphalitis

Differential Diagnosis

Other viral infections: Toxoplasmosis, Parvovirus, Rubella, Viral upper respiratory tract infections.

Risk of Transmission

Primary maternal infection

- Risk of transmission to fetus varies by gestational age.
  - 1st trimester ~36%

- 2nd trimester ~40%
- 3rd trimester ~65%

- The severity and sequelae of congenital infection decreases with gestational age

Non primary infection:

- Risk of transmission is ~1%

Pre-existing maternal antibody to CMV is the most important protective factor against congenital CMV infection, but does not prevent reactivation or reinfection with new viral strains. Seroprevalence increases with age, and varies internationally. More than half of women entering pregnancy are likely to be seropositive. 1-7% of women will seroconvert during pregnancy.

Clinical Manifestations of Infection

Clinical manifestations of severe congenital CMV infection include:

- Hepatosplenomegaly, hepatitis, jaundice, thrombocytopenia
- Hearing loss
- Microcephaly
- Seizures
- Chorioretinitis
- Developmental delay and neurodevelopental disability

Primary infection:

- Asymptomatic infection:
- 85-90% of babies will be asymptomatic at birth
- 10-15% will develop neurologic sequelae
- Sensory neural hearing loss and chorioretinitis most common

Symptomatic infection:

- 10-15% of babies are symptomatic at birth
- 5-10% mortality
- >50% risk of sequelae
- Microcephaly (35-50%)
- Seizures (10%)
- Chorioretinitis and other ocular complications (10-20%)
- Developmental delay (up to 70%)
- Sensory neural hearing loss (25-50%)

Non-primary infection:

- Almost all infants are asymptomatic at birth
- Low risk of long term neurodevelopmental morbidity
- Overall risk of sequelae following non-primary CMV infection is <10%
- Late sequela of infection include: visual and auditory deficits and developmental delay

Investigation and Diagnosis

Routine screening for CMV in pregnancy is not recommended

Indications for antenatal testing include:

- Clinical suspicion of CMV infection
- Exposure to person known to be infected with CMV
- Findings on ultrasound that could be attributable to CMV infection

Diagnose maternal infection:

- Send maternal blood for CMV IgM and IgG testing (add IgG avidity testing if IgG and IgM both positive and clinical suspicion of infection)
- IgM response can remain positive for > one year after acute infection and can become positive again with reactivation or re-infection
- IgG seroconversion is diagnostic of new acute infection
- IgG avidity is helpful in differentiating acute, chronic and past infection
- Avidity index: % of IgG bound to antigen
  - High avidity index >60% = past or secondary infection
  - Low avidity index <30% = recent primary infection (<3 months)
- Minimum 2 blood samples at least 2 weeks apart showing seroconversion

Primary CMV infection is

- Seroconversion: new CMV IgG in previous seronegative woman
- Low IgG avidity

Diagnosis of congenital infection

Amniocentesis:

- Offer amniocentesis to assess fetal infection
- Send amniotic fluid for PCR as well as viral culture and viral load. Sensitivity of amniocentesis if higher if performed after 21 weeks gestation and > 6 weeks from CMV infection

Fetal blood sampling is not helpful

- Risk associated with cordocentesis
- Fetal CMV IgM does not develop till late in pregnancy

Ultrasound

- Perform detailed anatomy scan to assess fetal growth and look for stigmata of CMV infection, for example:
- IUGR
- Cerebral ventriculomegaly/periventricular echogenicity
- Microcephaly

- Intracranial calcifications
- Echogenic fetal bowel
- Hepatosplenomegaly +/- liver calcifications
- Ascites/pleural effusion/hydrops
- Oligohydramnios/polyhydramnios
- Placental enlargement

Ultrasound has <30-50% sensitivity and low specificity for CMV infection.

Normal USS does not exclude possibility of symptomatic neonate or development of long term neurological morbidity.

MRI may be useful in addition to ultrasound to assess neurological abnormalities.

On-going Management

There is no effective treatment for prevention of fetal disease or reduction in risk of sequelae

1. The maternal infection is likely to be mild and self-limiting. No specific treatment is needed in immunocompetent women
2. Arrange serial ultrasound to aid in prognosis although normal ultrasound does not guarantee normal outcome
3. Consider fetal MRI
4. Offer amniocentesis
5. Termination of pregnancy may be considered

The use of intravenous hyperimmune globulin (IVIG) to reduce transmission and sequalae of CMV infection in pregnancy cannot be supported by evidence at this stage, but this may change in the future

Post delivery

- Cord blood: CMV IgM, full blood count, liver function tests
- Urine and saliva: CMV PCR and culture
- Arrange hearing screen and ophthalmology assessment
- There may be a role for valganciclovir given to the neonate to improve hearing outcomes
- Neonates confirmed to be infected with CMV continue to shed the virus in secretions and urine for at least the first year of life
- Ensure paediatric follow-up arranged

Prevention

All women should be given advice regarding primary prevention of CMV and particularly to women known to be seronegative.

- Good personal hygiene: handwashing after contact with nappies or oral secretions
- Do not kiss children on mouth or cheek
- Do not share food, drinks, utensils with young children
- Use of CMV negative blood products when transfusing

Future pregnancy

Wait at least 6 months after primary infection before conceiving again

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