Cytomegalovirus (CMV) in Pregnancy

Background
1. General info
   o Human cytomegalovirus found worldwide
   o Congenital CMV: caused by primary infection or viral reactivation during pregnancy
     ▪ Most common congenital viral infection
     ▪ 5-20% affected infants have overt symptoms
     ▪ Primary CMV infection:
       • Virus initially acquired by mother during pregnancy
     ▪ Recurrent CMV infection:
       • Maternal antibody to CMV present prior to conception
       • Associated with less severe fetal disease

Pathophysiology
1. CMV - member of the herpes virus family
   o May cause a lytic infection
   o Also capable of latency and reactivation
2. CMV replicates in
   o Salivary gland, lung, liver, kidney, intestine, adrenal gland, and the central nervous system
3. Maternal CMV infection:
   o Prevalence:
     ▪ 50-80% of adults seropositive by age 40
   o Transmission:
     ▪ Sexual contact
     ▪ Contact with infected body fluids (eg saliva and urine)
     ▪ Blood transfusion
     ▪ Little risk with casual contact
   o Usually no symptoms
   o May present with flu-like illness or mono-like illness
   o Heterophile antibody tests negative
   o May have lymphocytosis and/or elevated transaminases
   o Risk factors:
     ▪ Caring for pre-school children in the year before delivery
     ▪ Onset of sexual activity <2 years before delivery
     ▪ STDs during pregnancy
     ▪ Household size >3
     ▪ Maternal age <25
   o Maternal deaths very rare
4. Congenital CMV infection:
   o Primary maternal infection during pregnancy leads to fetal infection in 40% of cases
   o Congenital infection risk from seropositive mothers <1%
   o Transmission risk increases with gestational age
   o Severity of disease increases the earlier it occurs in pregnancy
   o Incidence:
     ▪ Approx 1% of newborns are born congenitally infected with CMV
Morbidity:
- Up to 90% of congenitally infected infants without symptoms initially; up to 15% may develop progressive hearing loss, usually unilateral
  - Congenital CMV infection may account for up to 30% of cases of deafness\(^2\)
  - Of the 10% born with overt symptoms, 2/3 will have neurological involvement, e.g., microcephaly, seizures, an abnormal neurological exam, feeding difficulties

Mortality:
- Approaches 10% in children with symptomatic congenital CMV infection\(^3\)

**Diagnostics**

1. History:
   - Usually no symptoms
   - May have prolonged mono-like illness including fever, sore throat, malaise\(^4\)

2. Physical:
   - Maternal:
     - Fever, swollen glands
     - No specific findings
   - Fetal:
     - Fever, microcephaly, jaundice, hepato-splenomegaly

3. Diagnostic testing
   - Mother:
     - Diagnosis made by serology
     - Rule out mono with heterophile antibody test
   - Newborn:
     - Isolation of CMV in urine or saliva samples within the first 3 weeks of life
   - Prenatal period:
     - Ultrasound showing microcephaly, hepato-splenomegaly and/or intracranial calcifications should raise the possibility of the diagnosis
     - Isolation of virus by culture or DNA detection in amniotic fluid is diagnostic

4. Routine screening:
   - Insufficient evidence to recommend for or against routine screening for CMV\(^5\)

**Differential Diagnosis**

1. Maternal:
   - Mononucleosis
   - Influenza
   - Streptococcal pharyngitis

2. Congenital CMV infection:
   - Rubella
   - Toxoplasmosis
   - Syphilis
   - Herpes simplex virus infection
   - Enterovirus infection
Therapeutics
1. Maternal:
   o No specific Tx is required in immunocompetent host
2. Symptomatic congenital infection:
   o Ganciclovir
     ▪ Available but is not used routinely as may cause granulocytopenia, anemia, thrombocytopenia and abnormal liver function tests
     ▪ Little evidence of clinical benefit
     ▪ Infants with severe disease, including pneumonia, or with life or sight threatening illness may be candidates for treatment
3. Congenital infection without Sx:
   o No treatment is indicated

Follow-up
1. Women diagnosed with primary CMV infection during pregnancy might benefit from consultation with a perinatologist

Prognosis
1. Congenital CMV without symptoms:
   o 10-15% of these infants may have progressive hearing or vision loss
   o It may not be clinically apparent for months or even years
2. Congenital CMV with symptoms:
   o 80% develop late symptoms
     ▪ Hearing or vision loss, mental retardation, and delay in psychomotor development
   o 9% mortality in all children with symptomatic congenital acquired CMV infection
   o 30% mortality in infants with severe disease
     ▪ Jaundice, petechial rash, hepatosplenomegaly, and multiorgan involvement

Prevention
1. Wash hands thoroughly with soap and water, especially after changing diapers
2. Do not kiss children under the age of 6 directly on the mouth; they may shed virus in their saliva for months after acquiring the virus
3. Do not share food, drinks, utensils with young children
4. Mother who has yet to conceive may wish to learn whether or not she is immune to CMV
   o If positive
     ▪ She can know there is little chance her baby will be infected with CMV
   o If negative
     ▪ She can be advised to diligently follow the above guidelines to protect herself from becoming infected
5. No vaccine is currently available
References


7. Centers for Disease Control referenced at www.cdc.gov/cmv/faqs.htm

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