CMV&Pregnancy

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Introduction

- CMV is a ubiquitous DNA herpesvirus. it becomes latent after a primary infection but can reactivate with renewed viral shedding.
- CMV is the most common congenital viral infection, with birth prevalence of 0.48 to 1.3 percent in recent decades .
- Congenital infection may be asymptomatic or symptomatic; symptomatic disease can be severe and life-threatening.

Seropositive individuals for CMV

- Lower socioeconomic strata
- Contact with children under age 3 years, especially if they are in daycare
- Non-Hispanic black or Mexican-American versus non-Hispanic white race
- Age older than 25 to 30 years
- Higher parity
- Residence in a developing country

Clinical findings

- Primary CMV infection may cause a mild febrile illness and other nonspecific symptoms (rhinitis, pharyngitis, myalgia, arthralgia, headache, fatigue), but is not clinically apparent in approximately 90 percent of cases.
- CMV mononucleosis can be accompanied by dermatologic manifestations in approximately one-third of patients including macular, papular, maculopapular, rubelliform, morbilliform, and scarlatiniform eruptions.

Screening

- ACOG and Society of Maternal-Fetal Medicine recommend against routine serological screening for CMV for several reasons:

➢ No vaccine is available to prevent infection in seronegative women.

➢ In seropositive pregnant women, it is difficult to distinguish between primary and nonprimary infection or determine the timing of the infection.

➢ Seropositive women remain at risk of fetal infection from reactivation of latent virus and/or reinfection with a new viral strain.

Screening

- no evidence that antiviral drug treatment of primary infection in pregnant women prevents or mitigates sequelae of CMV infection in the neonate.
- use of hyperimmune globulin to prevent congenital infection did not establish a benefit, in contrast to observation studies.
- Although fetal infection can be detected, there is no way to accurately predict whether or not the fetus will develop significant sequelae.
- Routine screening can lead to unnecessary, and potentially harmful, intervention

Behavioral risk reduction interventions

- Practice good personal hygiene throughout pregnancy, especially hand washing with soap and water after contact with diapers or oral and nasal secretions
- Avoid kissing children under age 6 on the mouth or cheek; instead, kiss them on the head or give them a hug.
- Do not share food, drinks, or oral utensils (eg, fork, spoon, toothbrush, pacifier) with young children.
- Clean toys, countertops, and other surfaces that come into contact with children's urine or saliva

CMV in Pregnancy

DX and TX

Dr. Davarpanah

CMV DX

- Serology (IgM, IgG)
- Routine CMV serology not recommended in pregnancy
- Indications: mononucleosis like Sx in mother , fetal anomaly infavor of CMV infection .
- CMV IgM: not accurate , sensitivity 75-90% , remains positive one year , may be positive in other viral infections such as EBV.
- IgG seroconvertion
- IgG avidity (low avidity indicative of infection during the last 2-4 months)

CMV DX

- Amniocentesis and CMV PCR for fetal involvement (sens 70-100% , after GA21 wks or 6 weeks after acute infection is more sensitive)
- Repeat amniocentesis in suspicious cases with negative PCR
- Fetal sonography for evidence of anomaly including periventricular calcification , ventriculomegaly , microcephaly , IUGR , hyperechogenic bowel , ascites , pleural effusion , hepatosplenomegaly , liver calcification , oligohydramnios , polyhydramnios , hydrops , placentomegaly.
- Repeat fetal sono with interval 2-3 wks in fetal infection

CMV DX

- Termination for severe anomalous fetuses
- Fetal MRI in suspicious cases
- Normal sono is not sufficient for rule out of fetal involvement
- Normal sono beside negative CMV PCR does not rule out fetal involvement but symptomatic fetus is very unlikely in these situations

CMV TX

- Contraception for at least 3-4 months after acute CMV infection
- Seronegative blood products for seronegative pregnant mothers and neonates
- No documented therapeutic modalities for acute CMV infection in pregnant cases

CMV in Neonate

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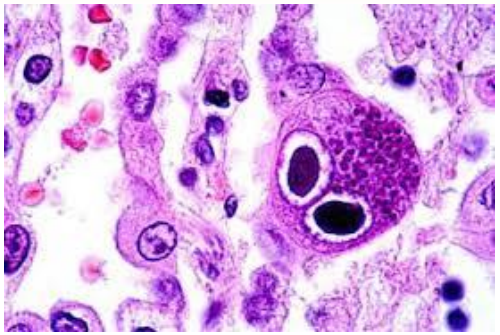
Neonatal CMV Epidemiology



fetal transmission rate:

- **Primary maternal infection**: **30% to 40%.**
- **maternal virus reactivation or reinfection : 1% to 2%**

- **50% of congenital infections are due to primary maternal** infection.

- early gestation → **severe fetal disease.**

Congenital CMV:

- **10%** → symptomatic disease at birth.
- **10% to 15%** of the asymptomatic neonates

sequelae in the first year of life, (most **hearing loss**).

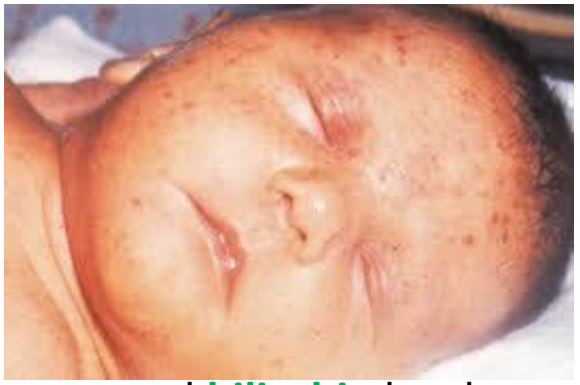
- Congenital CMV infection is **more common among HIV-exposed** infants, and coinfected infants may have more rapid progression of HIV-1 disease. Therefore, screening for congenital CMV infection in HIV-exposed infants is advised.

Clinical disease:

1. Congenital symptomatic CMV disease
2. Asymptomatic congenital infection at birth
3. Peripartum and postnatally acquired CMV infection
4. CMV pneumonitis
5. Transfusion-acquired CMV infection

1. Congenital symptomatic CMV disease:

A) Acute fulminant infection **B) Symptomatic without lifethreatening complications**



A) Acute fulminant infection: multiple organ systems

- **petechiae or purpura** (79%),
- **hepatosplenomegaly** (HSM) (74%),
- **jaundice** (63%),
- **pneumonitis**,
- **blueberry muffin spots**
- **preterm** (30%),
- **IUGR** (30%) and **microcephaly**.
- **Mortality** (30%)

Laboratory abnormalities include **elevated hepatic transaminases** and **bilirubin** levels (as much as half conjugated), **anemia**, and **thrombocytopenia**. Hyperbilirubinemia may be present at birth or develop over time and can persists beyond the period of physiologic jaundice.

1. Congenital symptomatic CMV disease:

B) Symptomatic without lifethreatening complications:

- **SNHL** (most commonly)
- **IUGR**
- **disproportionate microcephaly** (48%)
- **intracranial calcifications**: These calcifications may occur anywhere in the brain but are classically found in the periventricular area.

- Other findings of CNS disease: can **include ventricular dilatation, cortical atrophy, and migrational disorders such as lissencephaly, pachygyria**, and **demyelination** as well as **chorioretinitis** in approximately 10% to 15% of infants.

Babies with CNS manifestations almost always have **developmental abnormalities** and **neurologic dysfunction**

These range from **mild learning** and **language disability** or **mild hearing loss** to **IQ scores below 50**, **motor abnormalities**, **deafness**, **visual problems.**

- failing the newborn hearing screen → screened for CMV infection.
- documented congenital CMV infection → assessed for hearing loss as **neonates** and throughout the **first 2 years** of life.

2. Asymptomatic congenital infection at birth:

- in **5% to 15%** of neonates can manifest as late disease in infancy, throughout the first 2 years of life.

developmental abnormalities,

hearing loss,

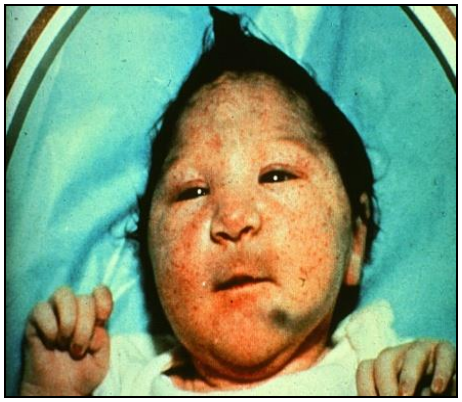
seizures,

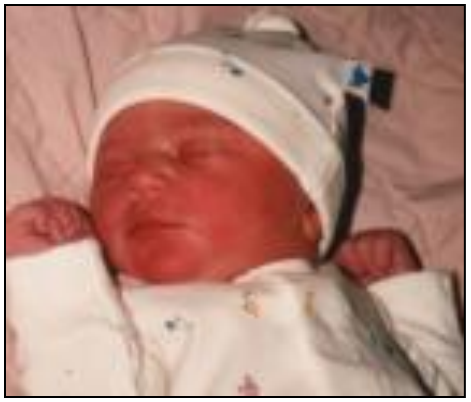
mental retardation,

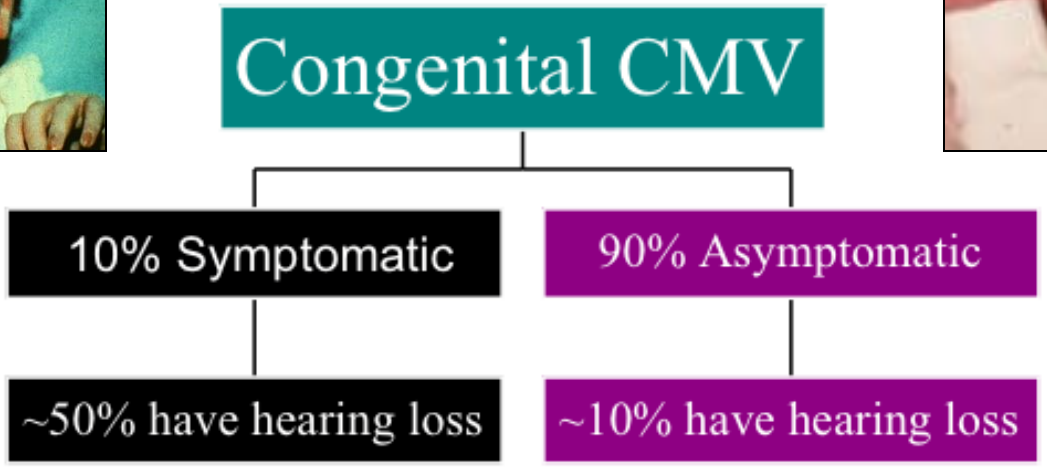
motor spasticity,

acquired microcephaly.

SNHL: the most common sequela of CMV infection







2/3 of children with CMV-related SNHL are 'asymptomatic' at birth the leading infectious cause of (SNHL),

3. Peripartum and postnatally acquired CMV infection:

(i) from intrapartum exposure to the virus within the **maternal genital tract**,
(ii) from postnatal exposure to infected **breast milk**,
(iii) from exposure to infected **blood or blood products**,
(iv) nosocomially through **urine or saliva**.

The time from infection to disease **presentation varies from 4 to 12 weeks**.

- **Term** infants: Almost all asymptomatic,(exception of severely immunocompromised).

- **preterm** infants: **longterm abnormalities:**(developmental and neurologic) (rarely)
  acute infection syndrome:neutropenia, anemia, thrombocytopenia, HSM

Data suggest that all infants regardless of gestational age should have hearing testing over the first 2 years of life if documented to have acquired CMV.

Congenital CMV infection Diagnosis

Dr Gholamreza Pouladfar

Approach to testing

- Laboratory diagnosis :
  1. isolation or
  2. molecular detection of CMV
  - PCR is more sensitive compared with rapid culture
  - PCR: more accurate
    - especially if the sample must be transported to a reference lab over a long distance
  - PCR: quantitative results : Low load…repeat PCR or perform culture

- Samples: urine or saliva
  - Saliva is easier to collect
  - more susceptible to sampling errors (ie, inadequate amount)
  - false-positives: rarely in infants with CMV-infected mothers

- Time: within the first three weeks of life.

- Testing blood samples for CMV is not recommended as a first-line test because not all infected infants are viremic.

- Serologic testing for CMV IgM antibody is not recommended as the sole diagnostic test, because it is less sensitive and specific than the other methods.

- Positive CMV PCR on **a dried blood spot** confirms the diagnosis of congenital CMV infection.

- However, a negative result does not exclude CMV infection; false-negative results may occur, particularly in newborns with few or mild symptoms.

Alternative methods of testing

Three weeks to one year

- If testing of the dried blood sample is negative or cannot be performed, They include:

1. Testing the urine or saliva for CMV (via viral culture, shell vial assay, or PCR)
2. Measurement of CMV IgG antibody in the blood

- Detection of CMV (by any of these methods) in a symptomatic infant at age three weeks to one year **suggests, but does not confirm**, congenital CMV infection because of the possibility of postnatal infection.

CMV in neonate

Management

A. Sanaei

Professor of Pediatric Infectious Diseases

CMV Management

Antiviral regimen : initial antiviral agent (IV ganciclovir versus oral valganciclovir) depends upon the severity of disease

1- Life-threatening disease :

IV ganciclovir initially for infants with any of the following :

- Viral sepsis-like syndrome
- Pneumonitis
- Myocarditis
- Severe hepatitis
- Enterocolitis
- Severe and refractory thrombocytopenia
- Sight-threatening retinitis
- Severe neurologic disease
- Underlying primary immune disorder (eg, severe combined immunodeficiency [SCID]) regardless of degree of symptoms

- For infants with severe sight-threatening CMV-associated retinitis, systemic antiviral therapy may not be sufficient and intraocular antiviral therapy may be required.
- The dose of ganciclovir is 6 mg/kg per dose administered intravenously every 12 hours .
- Ganciclovir should be administered through a central venous catheter when possible.
- Infants may be transitioned to oral valganciclovir if clinically stable and able to take oral medications, usually after two to six weeks.
- it not routinely recommend more than six weeks of IV ganciclovir due to risks of toxicity with prolonged treatment.
- After transition to oral valganciclovir, therapy should continue for a total of six months in most cases

2- CMV. Non-life-threatening disease

Non-life-threatening disease is defined more by the infant's general medical condition than by CMV-specific symptoms .

Infants with non-life-threatening disease are those that meet ALL of the following criteria:

- microcephaly or intracranial calcifications without seizures or encephalopathy;
- jaundice or hepatosplenomegaly without severe hepatitis or refractory thrombocytopenia
- isolated hearing loss

- non-life-threatening disease IS treated with valganciclovir oral solution and monitored closely for clinical response
- The recommended dose of valganciclovir is 16 mg/kg per dose administered orally every 12 hours for six months of in most cases of non-life-threatening infection.