Viral Infection in the Newborn Infant

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June 25, 2014

Objectives:
• Highlight and increase the awareness of the most common causes of viral infection in NICU
• Approach to diagnosis
• Treatment of viral infection
• Prevention

Clinical presentation

Skin rash
• Common in newborn
• Most are transient and benign
• Infants with rash and unusual presentations or signs of systemic illness should be evaluated for underlying cause (Candida, viral, and bacterial infections)

Common symptoms of viral infection

Nonspecific symptoms
• irregular temperature <36.5 °C, > 38.0 °C
• poor feeding and difficulty waking to feed
• excessive sleepiness
• irritability
• rapid breathing at a rate over 60/min
• change in behaviour
Additional signs/ symptoms:
• difficulty breathing
• bluish tinge around mouth
• pale or grayish mottled skin
• high/low body temperature
Shock and may lead to death.

Congenital Rubella Infection

• Single-stranded RNA virus

• Vaccine-preventable disease
  – No longer considered endemic in the U.S.

• Infection earlier in pregnancy has a higher probability of affected infant
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**Congenital Rubella Infection**
- May lead to fetal death/abortion (40%), premature delivery, or congenital defects
- The incidence of congenital defects, 80% in the 1st trimester
- Little risk of congenital defects after 18-20 wks GA
- IUGR may be the only sequela of 3rd trimester infection
- The majority of infants with CRI are asymptomatic at birth but develop manifestations over time

**Diagnosis**
- Virus can be isolated from nasopharyngeal secretions, cultured from blood, placenta, urine and cerebrospinal fluid
- Isolation of rubella virus is possible for several years from lens tissue in children with cataracts or cerebrospinal fluid in children with encephalitis
- Serologic testing, rubella-specific IgM antibody or infant’s IgG rubella antibody level that persists at a higher level and for a longer time than expected
- Detection of rubella virus RNA by PCR (throat swabs, respiratory secretions, CNS tissues and CSF, amniotic fluid)

**Treatment**
- Prevention by immunization
- Supportive care only with parents education
- Infants should be isolated while in the hospital
- Should be kept away from pregnant women when sent home if they are not immune

**Genital herpes simplex virus (HSV) infection during pregnancy poses a significant risk to the developing fetus and newborn.**

In incidence is 1 in 3000 - 20000

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[Image of CRS graph]

- 2005-2011
- Only 4 cases were reported, USA
- (CDC, unpublished data)
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HSV

- HSV type (1-2)
  70-85% of neonatal herpes is caused by HSV- 2
- HSV is transmitted shortly before or during delivery, primarily through an infected maternal genital tract

HSV

- >75% of infants who acquire HSV infection are born to mothers with no history or clinical findings of HSV
- The mother acquires primary HSV infection and the fetus acquires the infection transplacentally or via an ascending infection from the cervix.
  Miscarriage, preterm labor and IUGR
- Transmission is greater with primary infection (50%) than reactivation of previous infection (5%)

Clinical manifestations

- Most newborns appear normal at birth or may be born prematurely.
- Symptoms appear usually at 5-10 days of life
- Initial manifestations very nonspecific with skin lesions NOT necessarily present

One of three patterns:

- Skin, eyes, and mouth, 45%
- Meningitis/encephalitis, 30%
- Disseminated disease, 25%

Diagnosis

- Should be considered in any septic looking baby, liver dysfunction with negative blood culture
- Culture of maternal lesions if present at delivery
- Cultures in infant:
  - Skin lesions (vesicles), oro/nasopharynx, eyes, urine, blood, rectum/stool, CSF
- CSF PCR
- Serologies: IgM (IgG is not helpful)

Treatment

- Supportive treatment
- Parenteral acyclovir
  - X21 days for disseminated, CNS disease
  - X14 days for SEM
- Topical therapy for ocular involvement
- Mortality:
  80% in untreated disseminated HSV infection
  30% even with early and appropriate treatment
- Survivors experience considerable disability
Prevention

- Avoiding acquisition of HSV during late pregnancy (education)
- Avoiding exposure of the infant to herpetic lesions during delivery

All pregnant women should be asked whether they have a history of genital herpes

Congenital Varicella Syndrome

Rare - 90% of pregnant women are immune
Occurs in 2-3% of infants born to mothers who got the disease in the first 20 weeks of pregnancy

- Skin scarring
- Hypoplasia of limbs
- CNS (hydro-microcephaly, cortical atrophy and seizures)
- Eye defects (cataract and chorioretinitis, microphthalmos, nystagmus)

CVS carries a 30% mortality rate

Neonatal Varicella Infection

- Could be fatal for the infant of a mother who develops varicella between 5 days before to 2 days after delivery.

Manifestation:
- Severe skin rash
- Pneumonia
- Hepatitis
- Mortality - 20-30% of cases

Diagnosis

- It can be isolated from scrapings of vesicle base during the first 3-4 days of eruptions
- Significant increase in IgG
- PCR detection of varicella DNA (body fluid or tissue)
- Treatment: parenteral acyclovir

Congenital Syphilis
**Congenital Syphilis**

- Transplacental infection of Treponema pallidum (spirochete)
- Humans are the only natural host
- Transmitted via sexual contact in adults
- Placental transmission
  - Typically occurs during 2nd half of pregnancy
  - Increasing frequency as gestation advances

**Congenital Syphilis**

- Untreated women (primary/secondary) syphilis are more likely to transmit syphilis to their fetuses than women with latent disease (60–90% versus 40% in early latent and <10% in late latent syphilis)
- Large decrease in congenital syphilis since late 1990s
  - In 2002, only 11.2 cases/100,000 live births reported

**Early congenital syphilis**

Onset before two years of age

- Approximately 40-60% of symptomatic infants have at least one of the following:
  - HSM
  - Nasal discharge (snuffles)
  - Jaundice
  - Anemia
  - Pneumonia
  - Cutaneous lesions (palms/soles, mouth)
  - Perichondritis and metaphyseal dystrophy
  - Funisitis (umbilical cord vasculitis)
  - CSF (pleocytosis and high protein)

**Late congenital infection**

- Clinical manifestations with onset after two years
  - Frontal bossing
  - Short maxilla
  - High palatal arch
  - Hutchinson teeth
  - 8th nerve deafness
  - Saddle nose
  - Perioral fissures
- Can be prevented with appropriate treatment

**Available serologic testing**

- RPR/VDRL: non-treponemal test
  - Sensitive but not specific
- MHA-TP/FTA-ABS: specific treponemal test
  - Used for confirmatory testing
- RPR/VDRL screen in all pregnant women early in pregnancy and at time of birth
### Treatment

- Treat newborn if:
  - They meet CDC diagnostic criteria
  - Mom was treated <4wks before delivery
  - Mom treated with non-PCN medication
  - Maternal titers do not show adequate response (less than 4-fold decline)
- Penicillin G is the drug of choice (10-14 days)
- Maternal treatment during pregnancy very effective (overall 98% success)

### Precautions

- Standard precautions are recommended.
  (Open lesions, secretion and possibly blood are contagious)
- Gloves should be worn until 24 hours of treatment is completed

### Congenital CMV Infection

- Most common congenital viral infection
  0.5%-1.5% of births
- Transmission can occur with primary infection or reactivation of virus
  - 35% risk of transmission in primary infection
- Increased risk of transmission later in pregnancy
  - However, more severe sequelae associated with earlier acquisition

### Congenital CMV Infection

- 90% are asymptomatic at birth!
- Symptomatic infants:
  - SGA, HSM, petechiae, thrombocytopenia, jaundice, blueberry muffin appearance, chorioretinitis, hepatitis, microcephaly, periventricular calcifications, neurological deficits and hearing abnormalities
- Up to 10-15% develop symptoms later - sensorineural hearing loss and developmental delay
- >80% develop long term complications
  - Hearing loss, vision impairment, developmental delay

### Ventriculomegaly and calcifications of congenital CMV
**Diagnosis**

- Maternal IgG reflects past infection
- Viral isolation from urine or saliva in 1st 3 weeks of life confirms congenital infection
  - Afterwards may represent post-natal infection
- PCR can detect small amounts of CMV DNA in the urine
- Treatment is currently not recommended in asymptomatic infants due to side effects
- Ganciclovir for symptomatic infants
  - Valganciclovir oral form of Ganciclovir, NO RCT.
- Vaccination has not been successful yet!

**Parvovirus B19**

- Parvo B19 causes erythema infectiosum (5th disease)
- Most adults are asymptomatic
- The effects on the fetus are much greater (miscarriage, fetal anemia, hydrops fetalis, myocarditis, and/or intrauterine fetal death)
- 30 - 40% of pregnant women are susceptible to infection (seronegative for Parvo B19)

**Parvovirus B19**

- Second-trimester infections carry a 1-3% risk of hydrops; however, infection in any trimester may result in intrauterine fetal loss
- It selectively infects erythropoetic cursors and causes severe fetal anemia.
- Mild neutropenia and thrombocytopenia have been observed

**Diagnosis:**

- Parvovirus B19 specific IgM antibody

**Management:**

- Serial U/S for fetal monitoring
- Fetal intrauterine blood transfusion
- After birth: supportive treatment
  - Treat Hydrops
Enterovirus

- 2 distinct classes:
  - Polioviruses (types 1, 2, and 3)
  - Non-polioviruses (coxsackie virus, enterovirus, echoviruses)
- Unclassified enteroviruses

Enterovirus infections are not believed to cross the placenta and cause fetal disease
- However, some studies have linked coxsackie virus and echovirus to miscarriage, neurodevelopmental delay, myocarditis, and cortical necrosis
- One study linked the presence of coxsackie virus in the third trimester with respiratory failure and global cognitive defects.

Neonatal enterovirus infection

- Neonates with non-polio enterovirus infections are at a high risk of developing a sepsis-like condition
- Meningoencephalitis
- Myocarditis
- Hepatitis
- Presenting symptoms include poor feeding, lethargy, fever, irritability, seizures, hypo-perfusion, and jaundice

- Infants younger than 10 days are unable to mount a significant immune response and are at higher risk of a serious infection from echoviruses and coxsackie group B viruses.
- A history of a mother who had a febrile illness with GI symptoms around the time of birth should raise the suspicion of infection

Management

- Diagnosis:
  - PCR on CSF, nasopharyngeal secretions, blood, urine and stool for enterovirus.
- Treatment is supportive

Take home message

- Viral infection, although rare in the neonatal population, may carry high morbidity and mortality
- Symptoms and signs are initially non-specific, many viruses share the same common presenting symptoms
- Attention should be paid to the maternal history, it could aid the diagnosis
- Absence of skin rash in women does not exclude the possibility of viral infection in the newborn
- Early recognition could alter the outcome significantly
References:
• Avery’s Diseases of the Neonatology, ninth edition.
• Nelson Essential of Pediatrics, 6 edition.
• UpToDate.
• Centers for Disease Control and prevention.