Diseases of the Fetus and Neonate

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PGY 2
Overview

- Toxoplasmosis
- Cytomegalovirus
- Varicella Zoster
- Parvovirus B19
Toxoplasmosis

- The Organism exists in three forms
  - Oocyst
  - Trophozoite
  - Cystozoite or bradyzoite (tissue cyst)
Oocyte

- Cats are the definitive host for *Toxoplasma gondii*
- Produced during reproduction of the parasite in the small intestine
- Secreted in the feces, up to 10 million per day.
Trophozoite

- This is the invasive form of the parasite
- Formed after the ingestion of tissue cysts or oocytes
- Used for serologic testing
- Can not live extracellularly
- Responsible for acute parasitemia
Cystozoite (tissue cyst)

- Form which the organism takes during latent or chronic infections
- Can often be seen histologically for the entirety of the host's life in most tissues.
Intermediate host: birds, mammals, humans

Bradyzoites encyst within the CNS and muscle of the infected host.

Oocysts are excreted in cat feces. Contaminated soil is ingested by birds, mammals, and humans.

Tachyzoites infect all nucleated cells in the host, replicate, and cause tissue damage.

Definitive host

Toxoplastic encephalitis


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Transmission

- In Humans infection occurs after consuming undercooked meat (most commonly pork)
- Consuming contaminated food
  - Contaminated by insects that had come in contact with contaminated cat feces
- By contact with contaminated insects or soil
Clinical Manifestations-
Maternal

- Often no or nonspecific symptoms
  - only 10-20% have symptoms
  - Cervical lymphadenopathy is most common
  - Fever, malaise, night sweats, myalgias and hepatosplenomegaly are other common symptoms
Congenital Transmission

- Vertical transmission depends on gestation age that infection occurs - the later the gestation the more likely infection is to occur
  - 10-15% in first trimester
  - 25% in the second trimester
  - 60% in the third trimester
- Severity of sequelae also depends on gestation with more severe disease occurring if acquired in the first trimester
Infection of the Infant

- Most infected infants don’t have signs at birth but 55-85% will develop sequelae.
- Systems affected include:
  - Eyes
  - CNS
  - GI
  - Heart
  - Lungs
EYES

- May have uni- or multifocal lesions.
- Granulomatous lesions and chorioretinitis can be observed in the posterior chamber after acute necrotizing retinitis
- Other ocular complications include iridocyclitis, cataracts, and glaucoma
CNS

- focal and diffuse meningoencephalitis
- Involvement can lead to seizures or hydrocephalus as well as varying degrees of mental retardation
- Spinal cord involvement may manifest as paralisis, difficulty swallowing or respiratory distress.
Heart and Lungs

- Interstitial pneumonitis
- Thickened and edematous alveolar septa
- Cysts within the alveolar membrane
- Pericarditis
- Cysts and aggregates of parasites in cardiac muscle tissue
Diagnosis

- Dx of acute infection by isolation of *T. Gondii* from the blood or body fluids
- Serologic testing for a specific antibody to *T. Gondii* is the primary method.
- Fetal dx can be made most specifically by testing fetal blood after 20 wga for specific IgM
- May also test amniotic fluid for *T. Gondii* by PCR
Treatment

- Treatment reduces but doesn’t eliminate the risks of congenital infection
- Treat with spiramycin after confirmation of maternal infection
- If fetal infection is also documented add pyrimethamine, sulfonamides and folinic acid.
- Infant treatment includes pyrimethamine and sulfadiazine alternating monthly with spiramycin for one year.
Counseling

- Talk to patients about reducing high risk behaviors including
  - Avoiding undercooked or raw meat
  - Wearing gloves when working with soil
  - Avoiding caring for cats
    - Exception can be strictly indoor cats who’s food is tightly controlled
Cytomegalovirus

- A double stranded DNA virus
  - Part of the herpes virus family

- Humans are the reservoir and it is spread by close contact including blood, saliva, urine, or sexual contact

- It is endemic with no seasonal variation and no known vectors
Clinical Manifestations

- Maternal infection often goes undiagnosed as it is either asymptomatic or a mononucleosis like syndrome including:
  - Leukocytosis
  - Lymphocytosis
  - Abnormal liver function tests
  - Fever, malaise, and chills

- After primary infection the virus remains latent in host cells
Neonatal Infections

- Is a vertical transmission that can occur with both the primary infection as well as a reactivation of a latent infection
  - Transplacental infection
    - Only form that causes long term sequelae
  - Contaminated genital tract
  - Breastfeeding
- 0.2-2.2% of all neonates have CMV
  - Most are asymptomatic at birth
Congenital CMV

- Vertical transmission may occur at any stage of pregnancy
  - Overall risk of infection is greatest if infection occurs in the third trimester
  - Most serious sequelae occur after infection during the first trimester
- During a primary infection risk of transmission is 30-40% and only 10% will show signs of infection at birth.
Clinical finding in the Infant

- Symptomatic infants may have clinical finding that are often multi-organ including:
  - CNS
  - Eye
  - Liver
  - Hematopoietic system
  - Kidney
  - Lungs
  - Placenta
CNS

- Focal encephalities and periependymitis
  - Can affect both the gray and white matter
  - Rarely found in the CSF (spinal taps are not beneficial)
- Resolution of the acute systems leads to gliosis and calcification typically found periventricular
  - May lead to microcephaly and hydrocephalus
Eye

- Sequelae may include
  - Optic neuritis
  - Cataract formation
  - Microophthalmos
  - chorioretinitis
Liver

- Hepatomegaly from hepatits
  - Elevated transaminases as well as direct hyperbilirubinemia are often seen
  - Often caused by mild cholangities of the bile ducts which leads to intralobular cholestasis and obstructive cholestasis-eventual liver calcifications
- Liver disease often subsides in time
Hematopoietic System

- Thrombocytopenia, anemia, and extramedullary hematopoiesis with or without petechiae
- Major splenomegaly
- Often resolves within the first year
The most common findings at birth are jaundice, petechiae, thrombocytopenia, hepatosplenomegaly, growth restriction, and nonimmune hydrops.

90% of symptomatic patients will have long term complications:
- Vision, hearing, mental retardation, seizures, paraparesis or diplegia
Most cases of adult CMV are asymptomatic

Cytomegalovirus may be detected by culture or PCR of infected blood, saliva, urine, cervical secretions, or breast milk.

More common is to do anti-CMV IgG 3-4 weeks apart and see seroconversion or increase in titer
Abnormal Maternal CMV Screening
CMV IgG: positive
CMV IgM: positive

CMV-specific IgG and IgM by EIA,
CMV-specific IgG avidity by EIA, and
CMV-specific IgM by immunoblot

CMV IgG: negative
CMV IgM: negative

CMV uninfected;
No further evaluation

CMV IgG: positive
IgG avidity index: high
CMV IgM: negative

Latent CMV infection
No further evaluation

CMV IgG: positive
IgG avidity index: low
CMV IgM: positive

Primary CMV infection
Invasive follow-up

Uncertain serologic results

Undefined CMV infection

CMV IgG: positive
IgG avidity index: high
CMV IgM: positive

Recurrent CMV infection
Noninvasive follow-up

Diagnosis - Fetal

- After documented Maternal infection or sonographic finding consistent with CMV
  - Abdominal and liver calcifications
  - Calcifications of later border of the later ventricles
  - Hydrops
  - Echogenic bowel
  - Ascites
  - Hepatosplenomegaly
  - Ventriculomegaly
- CMV can be detected in amniotic fluid by 21 weeks by PCR or culture
Treatment

- No current therapies available for maternal or fetal CMV infection
- Hyperimmune gamma globulin is used in the treatment of neonates with congenital CMV
  - Effectiveness has not yet been proven
Counseling

- Factors that increase the risk of acquiring CMV infection include abnormal cervical cytology, lower socioeconomic status, birth outside North America, first pregnancy younger than 15 years
- Prevention is though good hand hygiene (especially around young children) and avoiding high risk behaviors
Varicella

- *Herpesvirus varicellae*
- Is a DNA herpes virus
- One of the most communicable human diseases
  - Spread by respiratory droplets and close contact
  - Easily crosses the placenta
Clinical Manifestations

- Chicken pox
  - Generalized exanthem with vesicles in successive crops
  - The vesicles rapidly evolve to pustules, crust and scabs
- Shingles
  - Only occur in people with prior chicken pox exposure
  - Painful vesicular eruption restricted to one dermatome
Congenital transmission

- Varicella infection is uncommon in pregnancy
  - 0.4-0.7 per 1,000 patients
- Although uncommon when it does occur it is often with severe consequences
- VZV crosses the placenta but only causes congenital VZV syndrome if this occurs during the first 20 weeks of pregnancy
  - Transplacental infection occurs in 1-2% of cases of maternal VZV infection
Clinical Finding in the Infant

- Congenital VZV infection often leads multisystem complications.
- Neonatal infection is associated with a high death rate due to the immaturity of the neonatal immune system and lack of maternal antibody protection.
Congenital Infection

- Skin scaring
- Eye abnormalities
  - Chorioretinitis, horner’s syndrome, nystagmus
- Abnormal limbs
  - Hypoplasia, abnormal or absent
- Prematurity/Low birth weight
- Cortical atrophy/mental retardation
- Early death
Maternal Complications

- Often a severe infection with complications that include
  - Secondary infections with step or staph
  - CNS- encephalitis, cerebellar ataxia, aseptic meningitis and myelitis
  - Glomerulonephritis
  - Myocarditis
  - Arthritis
  - Pneumonia (responsible for the majority of fatalities)
Diagnosis

- Maternal Dx is based on clinical findings
  - If lab tests are needed VZV antigen can be demonstrated in skin lesions using immunofluorescence.

- Fetal Dx is often based on known exposure and ultrasound findings
  - Hydrops, hyperechogenic foci in the liver and bowel, cardiac malformations, limb deformities, microcephaly and IUGR
Treatment

- Oral acyclovir can be given to children and adults to decrease the length and severity of the disease.
- If varicella pneumonia is diagnosed, IV acyclovir should be used.
- However, the use of acyclovir in pregnant women has not been proven to reduce the incidence of congenital VZV syndrome.
Counseling

- Patients should be asked about their personal history of chicken pox or if they received the vaccine.
- In non-pregnant patients that report no hx of chicken pox they may receive the vaccine.
- Patients with a negative chicken pox history should be advised to avoid contact with anyone infected with chicken pox.
- If contact occurs they may receive VZIG which may prevent or attenuate the disease however it may not prevent fetal infection.
Parvovirus B19

- Nonenveloped single stranded DNA virus
- When humans are infected with Parvovirus B19, it causes a rash illness known as erythema infectiosum or fifth disease.
- More common in winter and spring
- Another manifestation is aplastic crisis
  - More common in those with underlying hemoglobinopathy
- Most infections are mild and only require supportive care
Transmission

- Most commonly spread though respiratory secretions and hand-to-mouth contact.
- Infected person is contagious 5-10 days after exposure prior to the onset of rash or other symptoms
  - Once the rash occurs the person is no longer infectious
- There is about a 33% transmission rate across the placenta
Clinical Manifestations

- **Maternal-** febrile prodrome followed by a facial rash. May also get arthralgia’s and aplastic crisis
  - rarely cause hepatitis, vasculitis, myocarditis, glomerulosclerosis, or meningitis
- **Fetal-** most serious if acquired before 20 WGA
  - Nonimmune hydrops resulting from aplastic anemia, myocarditis or chronic fetal hepatitis
  - Spontaneous abortions
  - stillbirth
Diagnosis

- Detection of B19V IgM antibodies in maternal serum
- Fetal diagnosis can be made through isolation of viral particles in abortueses or placental specimens
- In the live fetus PCR can be used to detect B19 in amniotic fluid
- After exposure serial sono’s should be done to look for signs of hydrops for 10 weeks
  - If no signs in 10 weeks after maternal infection additional testing is not needed.
Exposure to parvovirus B19

Clinical disease: rash, pruritis, headache, fever, pharyngitis, arthralgias, myalgias, joint swelling, nausea, anorexia, transient aplastic crisis

Nonimmune hydrops fetalis

Maternal serological testing: parvovirus B19 IgM and IgG

IgG (+) IgM (-)
Prior infection
Immune no further evaluation

IgG (-) IgM (-)
Repeat test in 2–4 weeks
Not infected; no further evaluation
Sonographic evidence of fetal infection: hydrops fetalis, hepatomegaly, splenomegaly, placental enlargement, elevated MCA peak systolic velocity

IgG (-) IgM (+)
Recent parvovirus B19 infection
Targeted ultrasound +/- MCA velocimetry every 2 weeks for 10 weeks after exposure or infection

IgG (+) IgM (+)

Yes
Cordocentesis for CBC, reticulocyte count, parvovirus B19 RNA (PCR); consider intrauterine transfusion

No
No further evaluation; notify pediatric service at delivery

IgG (-) IgM (+)

IgG (+) IgM (-)
Treatment

- If fetal hydrops develops percutaneous umbilical blood sampling can determine fetal hematocrit, leukocyte and platelet count and viral DNA
- If needed transfusion can be used for supportive care
- Only treatment for maternal, fetal or neonatal is supportive.
Counseling

- It is unrealistic to remove susceptible women from the work force due to B19 outbreaks.
- Difficult to avoid as people are infectious before the onset of symptoms and are no longer infectious once symptoms have set in.
Questions?
References