

CMV INFECTION IN CHILDREN

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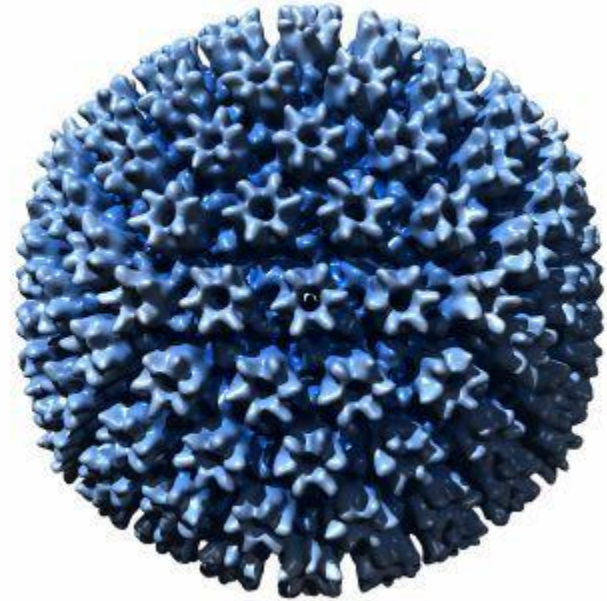
DIPS meeting, October 5, 2012

Cytomegalovirus

- Most patients/parents never heard about it before
- Ubiquitous
- Infects all persons at all ages all over the world
- The most common congenital infection in Europe
- The leading nongenetic cause of sensorineural hearing loss in the developed world

The virus

- A herpesvirus (HHV-5)
- The largest 240 kb
- Double stranded linear DNA with an envelope
- Like other herpesviruses primary infection causes lifelong latency



Epidemiology

- In developed countries 40-80% of adults are seropositive
(By 1 year of age 25% are seropositive)
- In developing countries almost all children are seropositive by 1 year

Epidemiology

- 0,7 % of newborns are congenitally infected
- 12,7 % have symptoms at birth
- Permanent sequelae in 40-58%
- Further 13,5 % will develop progressive sensorineural hearing loss
- 80 % will stay healthy

Dollard et al.

Rev. Med. Virol. 2007; 17: 355–363

Screening

- No screening of pregnant women or newborns anywhere
- But the conditions have changed with treatment possibilities
- In the future screening pregnant woman ?
- Screening newborn children on DBS or saliva tests?

Transmission

- Only from human to human
- Direct exposure to bodily fluids: Urine, saliva, tears, semen, cervical secretions & breast milk
 - Transplacentally
 - (Blood transfusions (if not leucodepleted))
 - (Transplantation)
- After primary infection a long period (years) of excretion especially in congenital CMV/perinatally acquired CMV
- The rate of transmission from mother to fetus is 40 times higher in maternal primary infection versus recurrent infection or reactivation
- Incubation time is 4-8 weeks

Transmission

Transmission after birth:

- 1/3 from mothers breast milk
- In daycare
- Adolescence
- Women of childbearing age

CMV infection

Congenital CMV infection:

- Around 90 % are asymptomatic
- 12,7 % have symptoms: trombocytopenia, peticchia, rash, IUGR, hepatosplenomegaly, microcephaly, intracerebral calcifications, chorioretinitis, sensorineural hearing loss

CMV infection

Postnatal:

- Premature children receiving CMV infected breast milk from their mothers → hepatitis, pneumonitis, GI disease, thrombocytopenia, sepsislike syndrome
- In immunocompromised (transplant/HIV)
 - retinitis, pneumonia, hepatitis, GI symptoms, encephalitis

Diagnosis

- Earlier: culture was gold standard, the result would be available in 3 weeks
- Serology: gives indirect evidence for recent infection if there is a change in antibody titers at different time points in a clinical course
 - Many different techniques are available:

Diagnosis

- Detection of IgM antibodies should be interpreted with caution
- IgM may persist for months and can be unspecific
- The observation of at least a fourfold increase in CMV specific IgG titers in paired specimens obtained at least two to four weeks apart
- Or a good confirmatory test (fx in house capture competition ELISA, SSI)

Diagnosis

- Confirmed primary infection in the first part of the pregnancy
 - Cerebral UL sound findings in the fetus
 - Amniotic fluid examined with PCR after gestational week 21 (at least 6 weeks after the maternal infection)
- indication for provoked abortion

Diagnosis

Congenital CMV:

- Up to three weeks from birth:
- urine or saliva for PCR
- After that use the DBS/PKU card to determine if it was congenital CMV
- (In DK the blood spot cards are kept "forever")

Treatment

- **GANCICLOVIR** nucleoside analogue,
- **IV administration**
- **VALGANCLOVIR** prodrug for Ganciclovir, **perorally administration**

Major sideeffects reversible neutropenia

For immunosuppressed also:

- **FOSCARNET**
- **CIDOFOVIR**

Treatment

- Congenital CMV
 - CNS involvement

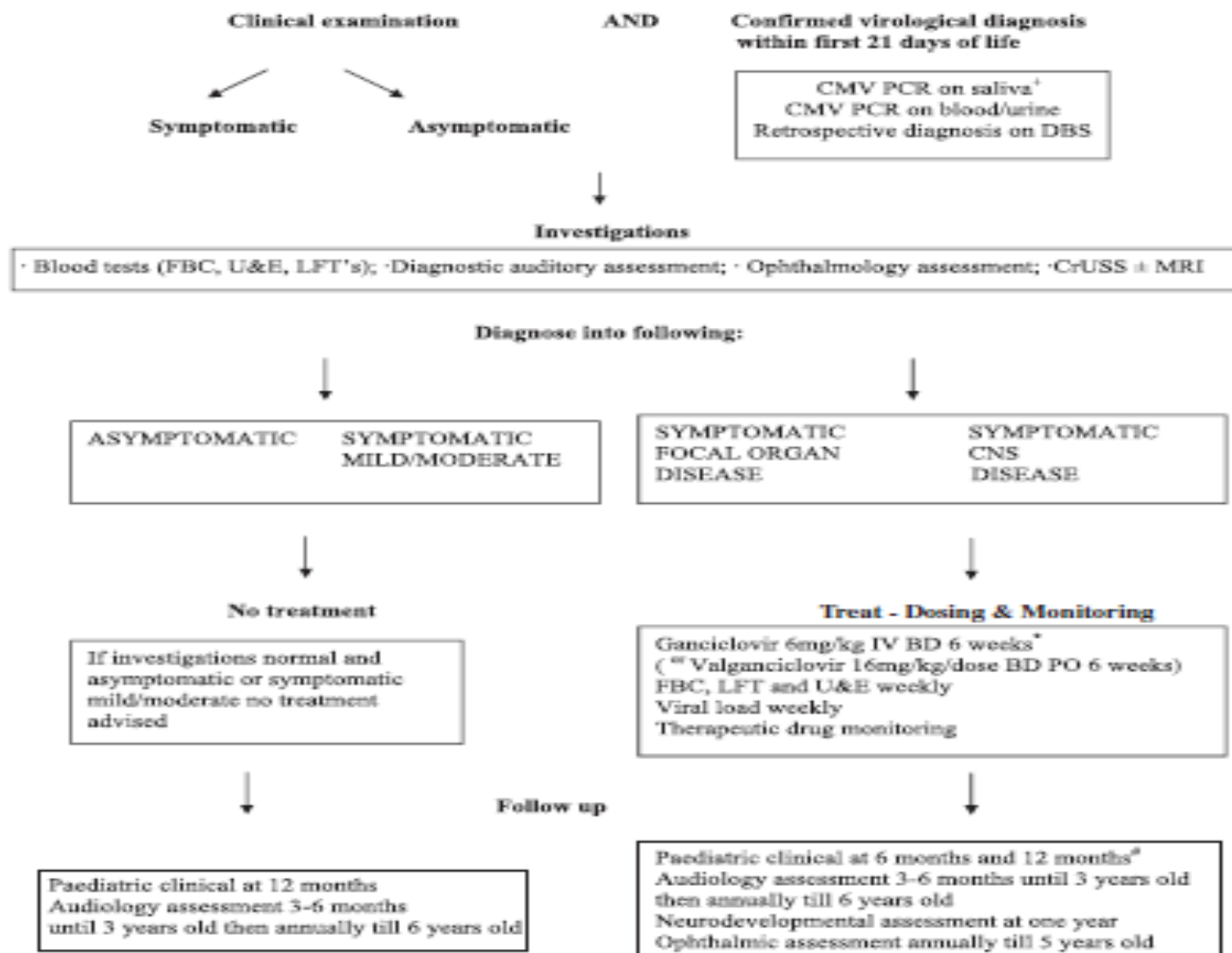
(prevents hearing deterioration, Kimberlin 2003)

6 weeks of treatment Ganciclovir the first weeks followed by Valganciclovir.

Trials are comparing 6 weeks vs 6 months Valganciclovir

- Immunocompromised children (transplant/HIV)

5. Management algorithm for the treatment of congenital CMV



Key:

- + Where possible to perform in first instance.
- * Where tolerated and clinically appropriate.
- # Follow up should be sooner if clinically required.

Prevention

- Advice to pregnant women to avoid infected secretions from infants has shown decreased transmission in a research setting
- Hearing follow-up (every 6 months) in children with known congenital CMV
- No effective vaccine, but a few vaccine trials are performed
- Randomized trials in pregnant women (specific immunoglobulin, antiviral medicine)

Take home message

- In the future screening might be implemented
- New drugs (peroral treatment) –Valganciclovir
- Diagnosis
- Serology – two bloodtests taken some time apart or a good confirmatory test
- PCR on saliva or urin in neonates before two weeks to rule out congenital infection
- Wash hands and no kissing.....