CONGENITAL CMV INFECTION; A NEW ERA OF DIAGNOSIS AND TREATMENT

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WHAT IS CONGENITAL CMV?

• CMV infection that occurs in utero

• Incidence of cCMV is 0.6% of all live births in developed countries

• Most common non-genetic cause of childhood hearing loss

• Leading cause of intellectual disability, second only to Down syndrome

• Most pregnant women have never heard of CMV...

Kenneson Rev Med Virol 200
cCMV disease is common!

Griffiths Lancet Infect Dis 2012
Causes of deafness at birth and 4 yrs


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HOW DO NEWBORNS WITH CCMV PRESENT?

• ~10% are symptomatic at birth
  – Most develop neurologic deficits
  – Wide range of severity (can be mild)
  – Diagnosis frequently missed, delayed

• ~90% “asymptomatic” at birth
  – 15% develop permanent hearing loss

Boappana CID 2013; Fowler CID 2013
cCMV rarely looks like this.
Usually it looks like this…
HOW DO YOU DIAGNOSE CMV?

- Requires viral culture or PCR of saliva or urine at <3 weeks of life
  - Very high viral loads in saliva and urine
  - Dried blood spot PCR insensitive (~30%)
  - No role for infant serology

- At ≥3 weeks old, can not determine if infection was congenital or not

- Often suspected too late to definitively diagnose (or treat)

Adler PIDJ 2005; Pass J Peds 2010; Din Pediatrics 2011
Saliva testing for cCMV is easy!

Use of oral swabs is much more convenient than urine and equally sensitive

Boppana NEJM 2011
PROCEDURE

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WHY DOES DIAGNOSING CMV MATTER?

• Treatment of symptomatic neonates with oral antiviral medication is beneficial
  – Improved hearing, cognitive outcomes
  – Safe and well tolerated

• Close follow up for asymptomatic neonates

• Early diagnosis and support for hearing loss
WHAT DOES FOLLOW UP LOOK LIKE?

- Audiology every 3-6 months
- Early speech and occupational therapy
- Hearing aids/cochlear implants for SNHL
- Trials ongoing for treatment of late onset disease

Kimberlin J Peds 2003; Kimberlin IDSA 2013; Fowler CID 2013
6 Weeks vs. 6 Months Oral Valganciclovir Change in Hearing Between Birth and 12 Mo

6 Weeks of Treatment

- 57% Improved or Remained Normal
- 43% Worse or Remained Abnormal

6 Months of Treatment

- 73% Improved or Remained Normal
- 27% Worse or Remained Abnormal

P = 0.01
A TYPICAL CASE

• Newborn boy fails hearing screen through the BC Early Hearing Program

• ABR at 3 months old shows hearing loss

• No risk factors identified by history

• Physical exam is normal

• Could the hearing loss be due to cCMV?
  – Too late to diagnose (except by blood spot?)
  – Too late to start antiviral treatment based on current studies
CCMV TESTING - CURRENT STATE

• CMV testing currently only done if there is clinical suspicion (i.e., “TORCH” infection)
  – Diagnosed in only 10% of symptomatic cases in Canada in a recent national study
  – BC is not any better

• Universal screening requires testing every newborn, not yet standard of care

• Testing of infants with hearing loss
  – Recommended by US Joint Committee on Infant Hearing (2007 Position Statement)
  – Now state law in Utah, Connecticut, others...

Vaudry Peds Child Hlth 2014; Sorichetti J Peds 2015
FUTURE STATE

PROCESS

Screening for CCMV at BC Women’s

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INDICATIONS FOR SCREENING

• Failed newborn hearing screen (unilateral or bilateral).

• Delayed newborn hearing screening for >1 week after birth:
  – All NICU admissions
  – IN admission and <34 weeks gestation at birth

• Symptoms or signs not otherwise explained:
  – Intrauterine growth restriction, small for gestational age, or microcephaly

• Other:
  – Suspicion of primary CMV infection during pregnancy
  – CMV seen on placental pathology
HEARING SCREENING AND IDENTIFICATION

Indications for CMV testing:
1. Failed 2nd stage Hearing screen
2. Delayed Hearing screen:
   - NICU Admission
   - IN admission (<34 weeks)
3. Symptoms of CMV
FOLLOW-UP AND TREATMENT

2-3 weeks

Refer to:
- Audiology
- Pediatrics
- Ophthalmology

Paediatrics:
- Evaluation
- Urine CMV
- lab tests (BUN/CR, Serum CMV PCR, CBC-Diff, LFT)
- cranial ultrasound

Audiology:
- ABR testing
- close follow up

ENT:
- Evaluation (if ABR abnormal)

Ophthalmology:
- Evaluation

>4 weeks

Discuss treatment options with infectious disease based on ABR SNHL and follow up evaluation

All confirmed CMV cases require diagnostic ABR and medical evaluation without delay. To be completed <3 weeks of age where possible.
EDUCATION AND COMMUNICATION

- Education Days
- Admission Order Set (NICU)
- Eduquick
- Policy
- Patient Pamphlet
- Hearing Screeners
- Care Providers
EVALUATION

• Process Evaluation
  – At 3, 6 and 12 months
• Feedback from staff re: logistical issues
• Assess number of swabs received by lab from:
  • NICU
  • IN
  • Postpartum
• Failed hearing screens
• Positive CMV results.
TAKE HOME MESSAGES

• CMV is a common cause of hearing loss

• Need to diagnose affected newborns early to give appropriate treatment and care
  – Effective, safe oral treatment available

• Testing is simple, accurate and inexpensive
  – Saliva CMV PCR at <3 wks of life

• Targeted testing to go live at BCWH
  – Plan to expand province-wide

• Universal screening may be warranted

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