Medical Diagnoses Driven by UNHS

Cheryl Edwards, AuD
Marilyn Neault, PhD
Laura Wheaton, ScD
Congenital Cytomegalovirus (CMV) and Hearing Loss

Laura Wheaton, ScD, CCC-A
What is Cytomegalovirus (CMV)?

- CMV is a type of herpes virus that often causes an asymptomatic infection in people who are otherwise healthy.
- After becoming infected, the virus remains in the body, dormant for the rest of the person's life.
Types of CMV

• Congenital CMV
  – Infected before birth from either a primary or recurrent maternal infection

• Perinatal CMV
  – Occurring during the periods before, during, or after the time of birth
  – Exposure to infected cervical secretions, breast milk, or blood products
Congenital CMV

- Most common congenital infection
- 40,000 children are born with CMV infection in the US each year.
- Contributes to approximately 400 deaths.
- 8,000 children are diagnosed with permanent disabilities (sensorineural hearing loss, vision impairment, and/or developmental delay).
Treatment

• Currently no cure for CMV.
• Antiviral drugs help with the progression of hearing loss, pneumonia, and retinitis.
• Two drugs commonly used
  – Valganciclovir (intravenous)
  – Ganciclovir (oral)
Children’s Hospital Boston Protocol

- **Newborn Hearing Screen**
  - Unilateral refer
  - Bilateral refer

- **Diagnostic ABR**
  - Newly identified hearing loss
    - Cheek swab for CMV testing
    - Consultation with Otolaryngology Team
    - Repeat ABR every 4 – 8 weeks
Case Study (HM)

• Born full term
• Healthy pregnancy and delivery
• Transferred to the NICU at 4 days of life due to petechiae involving head and trunk.
Case Study (HM)

- Thrombocytopenia
- Calcification throughout the brain
- Abdominal ultrasound revealed calcifications of the gallbladder.
- Congenital CMV was diagnosed.
NHS/ABR - First week of life

- Referred bilaterally on the Newborn Hearing Screen (NHS)
- Diagnostic ABR revealed a severe hearing loss bilaterally.
- Absent Distortion Product Otoacoustic Emissions (DPOAEs) bilaterally
Plotted thresholds are based on ABR findings.
ABR - 5 weeks of age

- Inpatient evaluation
- Hospitalized for anemia
- Currently taking Ganciclovir
- Parents report no concerns regarding hearing.
- Examination of the ears by an otolaryngologist was performed prior to this appointment.
  - Middle ears were clear.
ABR - 5 weeks of age

Testing Results/Impressions:
- ABR results revealed a moderately-severe hearing loss bilaterally.
- Limited testing as patient woke up
- Improvement in hearing thresholds
Plotted thresholds are based on ABR findings.
ABR – 9 and 17 weeks of age

- Outpatient visit
- Still taking Ganciclovir; began smaller doses at 17 weeks of age
- Doing well at both visits, per parent report
ABR – 9 and 17 weeks of age

Testing Results:

• ABR results:
  – Right ear: Mild high frequency hearing loss
  – Left ear: Normal hearing

• DPOAE results:
  – Right ear: Present 2K-3K Hz, absent 4K-8K Hz
  – Left ear: Present 2K-8K Hz

-Normal tympanograms for both ears
ABR – 9 and 17 weeks of age

Testing Impressions:

• 9 weeks: Significant improvement in hearing thresholds in comparison to previous testing
• 17 weeks: Noted stability in hearing sensitivity
Plotted thresholds are based on ABR findings.
Future Management

- Audiological follow-up via unsedated ABR testing to monitor hearing sensitivity
- Otologic care per managing otolaryngologist
- Medical management per Infectious Disease (ID) protocol
Conclusion

• Children diagnosed with CMV are at risk for permanent developmental delay and impairments, including hearing loss.
• Early identification of a CMV diagnosis is crucial so that treatment may be prescribed before irreversible damage occurs.
• Hearing loss associated with CMV can improve with appropriate treatment.
• Audiological follow-up is critical.
Questions to Consider

- Should all mothers be tested for CMV?
- Should CMV be a part of newborn screening?
  - Use of the dried blood spot
- Should we develop a universal CMV protocol for all babies who refer on the NHS?
- Need for future research
Profound bilateral sensorineural hearing loss: is that all? (Part 1)

Marilyn Neault, PhD
March 2, 2010

Thank you to Margaret Kenna, MD, Greg Licameli, MD, Heidi Rehm, PhD, and Jennifer Harris, AuD
Is that all?

- Baby girl born to 19 year old mother, healthy pregnancy, full-term birth
- Mother’s half-sibling has mild hearing loss
- Bilateral refer on newborn hearing screen
- Diagnostic ABR → profound bilateral sensorineural hearing loss
- Connexin 26 and connexin 30 negative
- Normal ophthalmology exam at 6 months, recheck recommended
Next chapter

- Parents begin using ASL with baby
- Right cochlear implant surgery at 12 months
- Parents requested test for Usher Syndrome at 17 months because the child was not walking well
- Result: two mutations in the myosin 7A gene (Usher Syndrome Type 1B)
Sister act

• At the time Usher Syndrome was diagnosed, baby sister had just been born
• Baby sister: bilateral refer on NBS, profound bilateral sensorineural hearing loss
• Autosomal recessive inheritance
• Genetic testing showed the same two mutations on the myosin 7A gene as her sister (F1963del and G1942X)
• G1942X is a novel mutation
Parental decisions

• Baby sister also received cochlear implant surgery at 12 months
• Parents considering 2nd implants for both girls
• Both use ASL and are developing spoken language
Usher Syndrome

• Hearing loss at birth
• Vision loss later from retinitis pigmentosa
• 3 - 6.2 per 100,000 in general population
• 0.6 - 28% in deaf population
• Still usually late diagnosis
• Limited availability of genetic testing
• Heterogeneous presentation
# Usher Syndrome

(3-6% of childhood deafness)

Traditional classification

<table>
<thead>
<tr>
<th>Type</th>
<th>Hearing Loss</th>
<th>Vestibular System</th>
<th>Retinitis Pigmentosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Congenital profound</td>
<td>Congenital balance problems; absent responses, late walkers (average 20 months)</td>
<td>Onset pre-puberty</td>
</tr>
<tr>
<td>Type II</td>
<td>Congenital mild-severe sloping</td>
<td>Normal</td>
<td>Onset in teens-20s</td>
</tr>
<tr>
<td>Type III</td>
<td>Progressive later onset</td>
<td>Variable, often progressive balance problems</td>
<td>Variable onset</td>
</tr>
</tbody>
</table>

Children's Hospital Boston
9 genes pinpointed for Usher so far, and there are more

- Type 1 Usher syndrome: 
  \textit{MY07A, USH1C, CDH23, PCDH15, SANS}

- Type 2 Usher syndrome: 
  \textit{USH2A, VLGR1, WHRN}

- Type 3 Usher syndrome: 
  \textit{USH3A}

Testing labs listed at \texttt{www.genetests.org}
Interventions

• Hearing aids
• Cochlear implants
  – Early diagnosis may tip the scales towards CI in families who might not have opted for it in other circumstances
  – Early bilateral CI gives chance for localization
• Physical therapy
• Mobility training
• Vision specialist if vision loss begins early
• Sunglasses, Vitamin A (for Usher Type 2), DHA (fish oil / flax) being studied
Genetic Testing for Usher Syndrome

- **Conservative approach**
  - HL with retinal abnormalities (positive ERG test, DAT or pigmentary changes)

- **Less conservative approach**
  - Profound congenital hearing loss with delayed walking

- **Even less conservative approach**
  - Test infants and children with moderate to profound SNHL if Cx26 (and possibly Cx30) negative
  - Test infants and children with any bilateral SNHL

- **No matter which approach, need genetic counseling**
Parental needs

- Genetic / medical explanations (available)
- Advice for daily living: when and what to tell the child? how make environment safe? (less available)
- Connections with other parents of young children with Usher (rarely local)
  - www.hearseehope.com
- Adult role models with Usher Syndrome and early cochlear implantation (rare)
Profound bilateral sensorineural hearing loss: is that all? (Part 2)

Marilyn Neault, PhD
March 2, 2010
Baby Boy

- Full term healthy baby, bilateral refer
- Somalian parents, little English, interpreter used for all visits
- Diagnostic ABR at 7 weeks showed profound bilateral sensorineural hearing loss
- Parents: “We accept it. It is from God.”
Medical evaluation

• As part of routine workup for profound SNHL, otolaryngologist recommended an electrocardiogram
• Result: markedly prolonged QT interval
• Genetic testing: homozygous deletion in the LQT1 gene
• Diagnosis: Jervell and Lange-Nielsen Syndrome (JLN)
• Incidence 1 / 160,000 to 1 / 600,000
• Autosomal recessive inheritance
Interventions for hearing loss

• Audiogram showed no response to any sound
• Brief trial of loaned hearing aids, no response
• Family Sign Language Program
• Cochlear implant at 2 years 9 months (VERY difficult decision for parents)
• Child is a late walker (>24 months)
Importance of JLN diagnosis

• Long QT in EKG means high risk of fainting and even sudden death
• Caregivers must be aware
• Long QT should be known pre-anesthesia for CI
• Treatment: medication (beta blocker)
• Must avoid QT-prolonging medications
• Cardiologist recommended implanting a defibrillator (parents declined)
• Parents were tested for long QT → mother has it and is now medicated
Take-home messages

• Medical workup and genetic testing are good for more than satisfying curiosity
• Other important conditions can be found apart from the hearing loss
• Other family members may also have the related condition and be unaware
Results of an Atypical ABR:

Refer from UNHS

Cheryl Edwards, AuD
March 2, 2010
History

- Born full term, without complication
- Referred in left ear only on AABR screen
- Seen for Dx ABR at 7 weeks of age
- No parental concerns re: hearing
- No family history reported at that time
Results

- 1000 Hz tympanograms
  - Normal bilaterally
- Ipsilateral MEMR
  - Present 500 Hz – 2000 Hz, left
  - DNT, right
- DPOAEs
  - Present bilaterally
    - 1500 Hz – 8000 Hz, right; 2000 Hz – 8000 Hz, left
Right Ear

- Click stimuli at 50 dBnHL and 20 dBnHL
- Click rate decreased from 51.1/sec to 21.1/sec
- Tone Burst ABR elicited Wave V thresholds within normal limits from 1000 Hz – 8000 Hz.
Left Ear

- Wave I with latency-intensity function to 40 dBnHL.
- Comparison of condensation and rarefaction polarities did not yield an abnormal CM.
Follow-up

• Referred to Otolaryngology; imaging deferred until after second ABR
• Testing at 3 months:
  • Tympanograms: Normal
  • Ipsi MEMR: present, right; absent, left
  • ABR: Same responses, morphology worse
    • Slowed rate to 11.1/sec in the left ear
• Otolaryngology: recommended MRI
MRI – 3 months

0.6 cm x 0.6 cm x 0.9 cm
Radiology/Neurosurgery

- Unknown if mass is a tumor or vascular malformation (hemangioma)
- Felt that left ABR is affected due to involvement of the cerebellar peduncle
- Due to location, biopsy was deferred and monitoring via MRI recommended
Biopsy completed at 12 months

- Low grade pilocytic astrocytoma
  - Extends into cerebellum, dorsal pons and lower medulla
- Chemotherapy initiated at 14 months
  - Vincristine and carboplatin
- Mass has remained stable at 2.6 x 2.0 cm
Status: age 2 years

- Hearing
  - Evaluated every 3 months
  - Normal in sound field
  - SAT of 40 dB HL in the left ear
    - Not a big fan of the headphones
- Social and engaging
- 200 words, can sing ABCs
- OT/PT every 2 weeks
- Mobility increased, gait “unstable”
- Intermittent nystagmus, eye crossing
  - Using glasses
Conclusions

• What if OAEs had been used for screening …or follow-up
• Close collaboration with ORL, Genetics, Neurology, Neurosurgery, Ophthalmology, Radiology
Thank you!