

Best Practices for Medical Evaluation of Children with Hearing Loss:

Otolaryngology [ENT] Perspectives

R. Christopher Miyamoto, M.D., FACS, FAAP
Peyton Manning Children's Hospital at St Vincent
Pediatric Ear, Nose and Throat Center



Case 1

- 1 mos old infant, born 39 wk EGA
 - Failed newborn hearing screen at hospital;
 - Screening tests x2 failed = "refer"
 - Middle ears clear; no fluid
 - No family hx of deafness; 1 great-grandmother with hearing loss in old age
 - No pre/postpartum complications; no maternal infections—perfect pregnancy
 - Neonatal screen negative



Case 2

- 2 mos old corrected age, former 23 week premature infant
 - several weeks on ventilator, Pulmonary hypertension bronchopulmonary dysplasia
 - Required IV gentamycin for sepsis, necrotizing enterocolitis requiring bowel resection
 - Failed screen x2;



Case 3

- **2 year old male, former term infant, normal delivery**
 - Perinatal/birth history normal; postpartum hx normal----all the usual risk factors negative
 - Passed newborn hearing screen
 - Started to coo/babble early, now stopping with progress
 - No longer startles to loud noise, respond to name/sounds
 - Parents present for evaluation due to concern
 - No hx otitis, meningitis, other infections
 - Immunizations up to date



Developments

- **1) Universal Newborn Hearing Screening**
 - Healthcare providers must now screen & manage HL in infants—substantial pt population
- Joint Committee on Infant Hearing and AAP: endorsed UNHS revised guidelines 2000, Position update 2007
 - Confirm HL by 3 mos ---how to do/keep up?
 - Logistical issues:
 - Otolaryngology referral – time
 - Ability of otolaryngologist to confirm:
 - Middle ear fluid, audiological capabilities [OAE, ABR]
 - Intraoperative vs office sedation ABR capabilities
 - Intervention by 6 mos
 - Increased receptive/expressive language quotients



Significance of Hearing Loss

- Hearing impairment one of the most common sensory deficits in children & significant healthcare problem
- 1 - 2 infants per 1000 births have significant hearing loss [HL]
 - Bilateral severe-profound
- Up to 4/1000 births if mild-moderate or unilateral HL included
 - Steel KP *Science* 1998;279:1870-71
- = 40,000 infants born/year w/ significant HL;
- = 4000 profoundly deaf



Developments

- 2) Molecular/genetic understanding of hereditary hearing loss vastly enhanced over last 10 years
 - Genetic testing now integral for evaluation of hearing impairment in children
 - Expertise of Medical Genetic specialists invaluable
- 3) Early intervention [medical vs surgical] now standard of care



Categories of Hearing Loss

- 1) Congenital & noncongenital
 - Congenital: present at birth
 - +/- genetic/hereditary cause
- 2) Hereditary & nonhereditary
 - Genetic vs Non-Genetic [Dr Escobar]
 - May or may not be present at birth
 - ENT perspective here covers only small number of patients with genetic hearing loss
- 3) Syndromic & non-syndromic
 - Most syndromes are congenital & have hereditary basis [Waardenburg, etc]
 - Exceptions: Fetal alcohol syndr

Hearing Loss Breakdown

- Historically, infectious disorders [TORCH, meningitis], teratogens, ototoxic meds were primary causes of congenital & acquired HL
- Vaccines, abx, awareness of teratogens changed ddx
- Hereditary causes account for 50% childhood deafness
 - Morton NE *Ann NY Acad Sci* 1991;630:16-31
 - Over 150 loci [areas on genes] identified
- 70% hereditary hearing loss nonsyndromic
 - 75% of this autosomal recessive
 - Important for evaluation process
 - Autosomal recessive hearing loss locus DFNB1 found on Chromosome 13q—contains GJB2 gene
 - Mutations in GJB2 responsible for up to 50% severe-profound SNHL in autosomal recessive nonsyndromic HL in US & Europe

Hearing Loss Breakdown

- The Rest:
- 50% hearing loss NOT inherited
 - Acquired—ototoxics, risk factors, others
 - May have Genetic comp making susceptible
- 30% Syndromic
 - 823 syndromes linked to hearing loss
 - 150 gene loci linked to hearing loss
- Importance of Medical Genetics Evaluation
 - JCIH 2007 statement guidelines

GJB2

- Gene in DFNB1 locus on chromosome 13
- GJB2 gene codes for connexin 26 protein
 - Expressed in nonsensory epithelium of cochlea
 - Membrane proteins that form gap junctions
 - Seem important in electrolyte, second messenger and metabolite exchange in cochlea
- Multiple mutations [60+ and counting] described
- 35delG mutation especially common [15-40%] [white/European descent, some hispanic, asian, african-american]

GJB2

- 35delG mutations usually cause severe-profound HL
- GJB2 mutations lead to range of hearing loss
 - Usually bilateral severe-profound range as with 35delG
 - Mild to moderate SNHL also reported
 - May be due to 35delG heterozygote, digenic inheritance of GJB2 and GJB6 [connexin 30]
 - other GJB2 mutation: M34T
- GJB2/DFNB1 HL usually nonprogressive
- Variations in mutations may lead to different hearing profiles [low or high freq losses]

Hereditary Syndromic Hearing Loss

- Most are congenital and some acquired
- 400 + syndromes associated w/HL
- Cause of HL: sensorineural, conductive, mixed
- Craniofacial & other features associated
- Findings may be subtle
- Dr Escobar

Hereditary Syndromic Hearing Loss

- Syndromes associated w/ SNHL:
- Autosomal recessive:
 - Pendred: most common syndromal deafness
 - 4-10%
 - Usher
 - Jervell & Lange-Nielsen
- Autosomal dominant:
 - Waardenburg
 - Alport
 - Branchio-Oto-Renal
 - Stickler

Hereditary Syndromic Hearing Loss

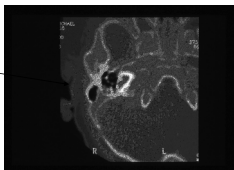
- Syndromes associated with conductive HL
- Examples:
 - Treacher-Collins
 - Apert
 - Crouzon
 - Goldenhar
- Delayed onset-CHL: associated w/ OM
 - Down, Turner, Velocardiofacial

Nonhereditary Congenital Hearing Loss

- TORCH:
 - Toxoplasmosis, Rubella, CMV, Herpes
- Syphilis
- CMV: most frequent cause nonhereditary HL in neonates
 - 40,000 CMV infected infants/yr; 4000 HL
 - 8-10% CMV-infected infants asx at birth can develop HL---need long-term f/u
- Perinatal risk factors [Joint Committee]
 - Low-birth wgt, mechanical ventilation, hyperbilirubinemia, meningitis, ototoxic meds, etc

Inner Ear Malformations

- CT visible
- Mondini spectrum: classic=
 - Only 1 ½ turns of cochlea, lacking apical turn and interscalar septum, enlarged vestibular aqueduct
 - Now, broad term applied to continuum of cochlear dysplasias [mild to common cochlear cavity]
- Michel aplasia: complete aplasia inner ear
- Enlarged Vestibular Aqueduct



Inner Ear Malformations

- Membranous labyrinth malformations:
- Alexander aplasia: cochlear basal turn aplasia
- Bing-Siebenmann: complete membranous cochlear aplasia, bony labyrinth intact
- Cochleosaccular dysplasia [Scheibe]: cochlea/sacculle membranous dysplasia

Autosomal dominant nonsyndromic deafness (ADNSD)

- Delayed onset hereditary hearing loss
- 10-20% of all nonsyndromic hereditary deafness
- 40+ genetic loci known to be associated with ADNSD
- Phenotype: variable; mostly moderate bilateral symmetrical SNHL
- often low-frequency HL [below 4 kHz] and normal high-frequency hearing

Evaluation of Hearing Loss in Infants & Young Children

- Thorough History/physical exam
 - Directed toward issues discussed earlier
 - Syndromic features—refer to Med Genetics
- Prenatal, perinatal, postnatal events
 - Prematurity
 - Teratogens
 - Perinatal maternal infections: TORCH
 - Low birth wgt <1500 g
 - Prolonged mechanical ventilation, hyperbilirubinemia, hypoxia

Evaluation of Hearing Loss in Infants & Young Children

- **Prenatal, perinatal, postnatal events**
- Cytomegalovirus [CMV]: 0.5 -2% live births
 - Congenital CMV infection:
 - 10% Symptomatic: 44% have HL by age 3yrs
 - 21% are delayed onset
 - 90% Asymptomatic: 7.4% have HL by 3yrs
 - 33% delayed onset
 - 50% of both groups w/progressive loss
 - Dahle A 1996; Pass RF *Pediatrics* 1980

Evaluation of Hearing Loss in Infants & Young Children

- Prenatal, perinatal, postnatal events
- NICU graduates
 - Persistent pulmonary hypertension of the newborn
 - Extracorporeal membrane oxygenation [ECMO]: [diaphragmatic hernia, heart disease, etc]
 - 20-25% with late-onset or progressive HL
 - = ABR at 6mos, audiogram 1 yr and annual x3yrs

Evaluation of Hearing Loss in Infants & Young Children

- Infections—neonatal meningitis
- Syncope [fainting]—Jervell & Lange-Nielsen
- Delayed walking/visual issues—Usher
- Family history



Evaluation of Hearing Loss in Infants & Young Children

- Physical Exam:
 - Check for craniofacial issues, subtle ear deformities
 - Check for ocular abnormalities: coloboma, hypertelorism, other abnormalities
 - Up to 50% severe-profound hearing impaired kids have eye issues
 - Armitage IM et al. *Arch of Dis Childhood* 1995;73(1):53
 - Pediatric Ophthalmology evaluation for all hearing impaired children recommended
 - JCIH 2007 statement

Evaluation of Hearing Loss in Infants & Young Children

- Confirm with OAE / ABR
- If bilateral SNHL and diagnosis not apparent [identifiable syndrome, meningitis, autosomal dominant SNHL, trauma] → check for GJB2 mutation/Connexin 26 testing, Cx 30
 - Potentially higher yield if HL >40dB
 - Can also send Mitochondrial 12sRNA mutation screen [aminoglycoside sensitivity]

Evaluation of Hearing Loss in Infants & Young Children

- If unilateral SNHL → CT scan
- If Cx26 positive: can stop
 - Rare to find other significant abnormalities
 - Few other significant CT or lab findings with DFNB1/Cx26
 - Some mild cardiac conductive defects anecdotally reported
 - Some CT scan abnormalities [EVA]
- Thus saves considerable costs and effort on family/health system

Evaluation of Hearing Loss in Infants & Young Children

- If Cx 26/Cx 30 negative:
 - Check CT temporal bone—look for inner ear malformations [next highest yield test]
 - If EVA, send Pendred gene mutation test [PDS]
 - Urinalysis or BUN/CR
 - EKG
 - Other tests per clinical suspicion
- Other gene mutation screens:
 - Myosin 7, Cadherin, Otoferlin
 - May detect another 10-12% etiologies
 - Expensive—gene chip arriving decreasing \$\$

Evaluation of Hearing Loss in Infants & Young Children

- If mild HL: consider Cx26 test vs just treating: amplification, f/u audiograms
- If unilateral HL: CT scan temporal bone
- If auditory neuropathy: present OAE, abnormal ABR/hearing loss
 - Close follow-up, repeated evaluations to confirm diagnosis
 - If cochlear implant candidate, MRI to eval for hypoplastic auditory nerve
 - Otoferlin gene mutation screen



Evaluation of Hearing Loss in Infants & Young Children

- Remains area of debate
- Thorough medical evaluation may still fail to reveal etiology in 30%
- Radiographic imaging useful in 30% cases
 - Billings KR, Kenna MR *Arch otolaryngol head neck surg* 1999;125(5):517
- Estimated that up to 90% congenital SNHL due to some type of membranous labyrinthine defect [ex Cx26 or others]
 - Lalwani AK, Grundfast KM *Pediatric Neurology*, 1995.



Evaluation of Hearing Loss in Infants & Young Children

- Moving away from shotgun approach with multiple labs
- Studies finding very low diagnostic yield, approaching 0%
 - Mafong et al. *Laryngoscope* 2002;112(1):1-7
 - 114 pts, 1 abnormal EKG = Jervell & Lange-Nielsen
 - Preciado et al. *Otolaryngology-HNS* 2004;131(6):804-809
 - 650 pts
- Use laboratory testing based on findings of history and physical exam findings



Conclusions

- Early identification allows early rehabilitation
 - Goal per JCIH: Start by 6 mos
- Audiologic monitoring and follow-up needed for at-risk patients
- Remainder of management/rehabilitation options covered elsewhere in conference
- Multi-disciplinary approach best for medical evaluation of children with hearing loss: primary care MD, otolaryngology, ophthalmologic, medical genetics

