Fanconi Anemia Research Fund
Annual Family Meeting 2010

Ear & Hearing Problems in FA

H. Jeffrey Kim, M.D. FACS
Georgetown University Hospital
Email: HK7@gunet.georgetown.edu
Fanconi Anemia

- Autosomal recessive disorder
- FANC B X-linked
- Incidence: 3 per 1,000,000
- Very heterogeneous condition
- A wide variety of clinical manifestations
  - Especially multi-organ congenital anomalies

<table>
<thead>
<tr>
<th>Nonhematologic Presentations</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal symptoms</td>
<td>71</td>
</tr>
<tr>
<td>Head/face anomalies</td>
<td>64</td>
</tr>
<tr>
<td>Renal symptoms</td>
<td>63</td>
</tr>
<tr>
<td>Eye (nystagmus)</td>
<td>30</td>
</tr>
<tr>
<td>Bone &amp; skeletal problems</td>
<td>34</td>
</tr>
<tr>
<td>Kidney deformity</td>
<td>20</td>
</tr>
<tr>
<td>Hair/eyelash changes</td>
<td>14</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>12</td>
</tr>
<tr>
<td>CNS</td>
<td>8</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>30</td>
</tr>
</tbody>
</table>

Ear and Hearing Problems in Fanconi Anemia

- Nicholas K. Kan, M.D.
- Hospital of the University of Pennsylvania
- National Institutes of Health
- National Cancer Institute
- Bethesda, MD 20892

- Not much information in medical literature
  - Futscher (1973) Aural atresia deformity
  - Lillicroft (1976) Ear canal narrowing
  - Ellis-Davis (1979) Hearing loss
- PubMed Medical literature search:
  - “Fanconi anemia” 254 results
- “Fanconi anemia and ear” 11 results

Hearing loss in FA

- A chart review study of 69 subjects from NYC

- Incidence:
  - Only 29 out of 69 had audiograms
  - 12/09/11X with either s/p or documented hearing loss
  - Only 8 of 12 hearing loss had audiograms

- Type and degree of hearing loss
  - Primarily sensorineural hearing loss

Fanconi Anemia Study at NIH

- Inheritable bone marrow failure disease protocol at NIH
  - Multi-disciplinary protocol
  - Systematically look at ear and hearing manifestations in FA
  - Comprehensive ENT evaluation, audiogram and CT of temporal bone

Outline of this Talk

- Anatomy and physiology of our auditory system
- Routine hearing & imaging tests
- Common ear findings in FA
- Consequences of FA ear problems
- Treatment options

Normal Ear Structures
**Examination of ears**

- Otoscope
- Microscope

**Normal tympanic membranes**

- Right
- Left

**Types of hearing loss**

- 3 types of hearing loss
  - Conductive hearing loss (CHL)
  - Sensorineural hearing loss (SNHL)
  - Mixed hearing loss (MHL)

**Audiologic evaluation**

- Behavioral audiologic test
  - Pure tone audiometry
  - Speech audiometry
- For children
  - Play audiometry
  - Visual reinforcement audiometry

**Typical audiograms**

- Normal Hearing
- Sensorineural HL
- Conductive HL

**Conductive hearing loss**

**Imaging study**

- CT/CAT (Computerized Axial Tomography) scans help to evaluate bony ear and middle ear bones
Magnetic Resonance Imaging (MRI) of internal auditory canal

- Not necessary unless sensorineural hearing is present
- Look for inner ear malformation, auditory nerve, and brain changes

NIH Experience:

- 32 pts
  - Age range: 3 - 60 yr (Mean age=23.5 SD 12.4)
  - 4 pts enucleated due to inadequate information
- Total of 56 ears in 28 pts
  - 4 pts with 5 main ear surgeries
- Ear surgeries for conductive hearing loss
  (Onset after brain re-structuring) and enlarging ear canal (Gouttner's Law)
- Examined non-operated 51 ears in 28 pts
  - 2 ears with middle ear fluid

Degree of Hearing loss (n=47 ears)

Type of Hearing loss (n=19 ears)

Case I
- Left ear: Normal

Case II
- Left ear: Normal
  - Left slight conductive hearing loss
Case III
Left ear drum: Normal
Left slight conductive hearing loss

Case IV
Left ear drum: Normal
Left moderate conductive hearing loss

TM/Middle ear abnormalities

<table>
<thead>
<tr>
<th>Ears (n=51)</th>
<th># ears</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>20</td>
<td>39%</td>
</tr>
<tr>
<td>Scar</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Abnormal</td>
<td>28</td>
<td>55%</td>
</tr>
<tr>
<td>Atresia (No ear canal)</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

CT scans
- N = 47 ears when
- Excluded 5 ears with prior surgery; no CT in 2 patients
- Middle ear bones
- Bony plates on ear drum
- Dimension of ear drum

Middle ear bones (Ossicles)
- Not well-formed: 4 (8%)

Ear drum structures
- Bony plates on ear drum: 21 (45%)

Size of ear drums at medial ear canal
- Grossly small ear drum/canal: 14 (30%)

Atresia (absent ear canal)
- No ear canal development: 1 (2%)

Dimension of ear drums on CT
Central nervous system involvement

- Small ear drum with bony island and usually malformed middle ear bones
  - Rarely neural atresia (complete closure of EAC)
- Conductive hearing loss
- Rarely associated with sensorineural hearing loss and narrow inner auditory canal
  - Perhaps associated with brain structural problems

Common Ear manifestations

- Small ear drum with bony island and usually malformed middle ear bones
  - Rarely neural atresia (complete closure of EAC)
- Conductive hearing loss
- Rarely associated with sensorineural hearing loss and narrow inner auditory canal
  - Perhaps associated with brain structural problems

Recent ear study on FA

- Vale et al, 2008
  - 8 subjects (age 3 to 13 years)
  - 4/8 (50%) hearing loss
  - Bilateral conductive hearing loss
  - 2 subjects with small ear canal

Why Ear Problems in FA?

- No one knows why
- Congenital problem
- Auricle, ear canal and middle ear bones are derived from 1st and 2nd branchial apparatus
- Prob due abnormal embryologic development

FA on ear development

- Knockout (Removal) of FancD2 in Zebrafish
  - Physical features include short body, small eyes and head
  - During development, many cells divide and proliferate, but without FancD2, cells mepropriately die
  - This results in congenital malformations

Hearing problems
Mild to Moderate Hearing Loss

- Mild to moderate hearing loss
  - Difficult to detect sounds with background noises
  - Decreased interactions with and responsiveness to environment (e.g., school, work)
  - Difficulty to hear certain sounds
    ("th", "s", "sh", "z", and "w")
  - Can affect language development, especially when mentally challenged

Mild to Moderate Hearing Loss

- Mild hearing loss effects from chronic ear infection cases:
  - A study of 207 children with prolonged ear infections from Boston
    - Followed from birth to age of 7 years
    - Treated with GYME, especially during first three years of life
    - Associated with lower scores on tests of cognitive ability, speech, and language, and school performance at age of 7

Management for hearing loss

- Early detection
  - Newborn hearing screening program very helpful
  - Monitored by NIDCD and others in Children
  - May not detect slight to mild hearing loss
- Need formal audiologic evaluation by audiologists for all FA cases

- Early Intervention
  - Auditory rehabilitation
  - Auditory language skills if intervention prior from 6 months of age
  - Speech therapy

Management options

- Auditory amplification
  - Hearing aids
  - Assistive listening device (FM system)

- Surgical correction to widen ear canal and middle ear bone problems

- Implantation hearing device (BAHA*)

Conventional hearing aids

- Devices designed to amplify sound
- Can be fitted for different hearing loss levels

FM auditory trainer

- System used to train individuals with hearing loss
- Helps improve listening and speech skills

Surgical Treatment

- Surgery through ear canal or behind the ear
- Usually after age of 7 yrs
- Laser technique is less traumatic
- Argon laser
  - CO2 laser

Middle ear exploration

- Pre-Op
- Post-Op

Audiograms

- Average Threshold = 72 dB (PTA)
- Average Threshold = 12 dB (PTA)
Risks of BAHA®

- Infection
- Bleeding
- Extraction of the implant
- Daily care of implant site

Practical communication tips

- Help your child to make a habit to watch the speaker
- Inform your child to let the speaker know when he/she is aware of something that was said or missed, and to ask for it to be repeated
- Reduce or move away from background noises. Help to manipulate the environment to allow communication in as noise-free an atmosphere as possible.
- Do not over-articulate and speak clearly and slowly.

Ear and hearing evaluation

- For individuals with FA
  - Auditory and Ota test
  - Pure tone auditory
  - Speech discrimination test
  - Full range audiometry
- For children with deafness
  - Comprehensive ear exam and hearing test
  - Otoacoustic emissions test
  - Manual acoustic stapedial test
  - Full range audiometry
Conclusion

- Hearing loss and congenital anomalies are more common than previously reported.
- Ear drum and middle ear bony problems.
- Commonly mild and moderate conductive hearing loss.
- Good ENT evaluation.
- Non-invasive examination.
- Auditory evaluation.
- Hearing aids helpful for moderate HL in NID.
- If speech and hearing loss, can be costly treated with assistive hearing devices, amplification, and/or surgery.

Collaborators at NIH

National Institute on Deafness and Communication Disorders (NIDCD)
- D. C. Brenner, Ph.D.
- D. M. (Debra) Researchers, M.D.
- F. J. J. K. A. (Christopher) Sakowski, M.D.
- A. C. (Andrew) Griffith, M.D., Ph.D.

National Cancer Institute (NCI)
- W. H. (Wanda) Alley, M.D., MPH
- W. J. (Wendy) Simpson, M.D., PH.D.

Radiology Department of Clinical Center, National Institutes of Health
- J. A. (John) Roman, M.D.

All the present authors are at NIH.