Ear and Hearing Problems in Fanconi Anemia

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Fanconi Anemia

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

<table>
<thead>
<tr>
<th>Nonhematologic Presentations</th>
<th>Frequency(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal (radial ray, hip, vertebra)</td>
<td>71</td>
</tr>
<tr>
<td>Skin Pigmentation (Café-au-lait)</td>
<td>64</td>
</tr>
<tr>
<td>Short Stature</td>
<td>63</td>
</tr>
<tr>
<td>Eyes (Microphthalmia)</td>
<td>38</td>
</tr>
<tr>
<td>Renal &amp; Urinary tract</td>
<td>34</td>
</tr>
<tr>
<td>Male genitalia</td>
<td>20</td>
</tr>
<tr>
<td>Mentally challenged</td>
<td>16</td>
</tr>
<tr>
<td>GI (duodenal, anorectal atresia)</td>
<td>14</td>
</tr>
<tr>
<td>Cardiac</td>
<td>13</td>
</tr>
<tr>
<td>Hearing</td>
<td>11</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>8</td>
</tr>
<tr>
<td>No Abnormalities</td>
<td>30</td>
</tr>
</tbody>
</table>

(Dokal, 2000)
Ear problems in FA

- Not much information in medical literature
  - Fanconi (1927)-Auricular deformity
  - Uehlinger (1929)-Ear canal narrowing
  - Emile-Weil (1938)-hearing loss

- Pubmed Medical literature search:
  - “Fanconi anemia”: 3194 articles
  - “Fanconi anemia and ears”: 14 since 1970

- Reasons:
  - Non-life threatening problem
  - Unawareness of healthcare providers
    - More common than we think
Hearing loss in FA

- A chart review study of 69 subjects from NYC

- Incidence:
  - Only 26 out 69 pts had audiograms
  - 12/69 (17%) with either subjective or documented hearing loss
    » Only 8 of 12 hearing loss had audiograms

- Type and degree of hearing loss
  - Primarily mild conductive hearing loss

(Santos et al, 2002)
Recent ear study on FA

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

- Previous studies were limited because
  - Many were either a brief single case report or a retrospective review

- Hearing loss is one of major factors correlated with a risk of bone marrow failure in FA
  - Rosenberg et al, 2004

- Description of typical ear findings & their prevalence in FA patients would be important

- May lead to early diagnosis of FA
  - Especially in absence of low blood counts or other typical physical features.
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-reinforced audiometry
Typical audiograms

Normal Hearing

Sensorineural HL
Conductive hearing loss

Conductive HL
Audiologic evaluation

- For younger pts
  - Otoacoustic emission (OAE)
  - ABER (Auditory brainstem evoked response)
  - ASSR (Auditory steady-state response)
  - Do not need patient’s cooperation
  - May require sedation
Imaging study

- CT/CAT (Computerized Axial Tomography) scans help to evaluate bony ear and middle ear bones.
CAT/CT scan
Normal CT of Temporal Bone
Normal CT of Temporal Bone
Magnetic Resonance Imaging (MRI) of brain and ear

- Not necessary unless sensorineural hearing is present

- Look for inner ear malformation, auditory nerve, and brain changes
NIH Experience:

- 31 pts
  - Age range: 3 – 56 yrs (Mean age=20)
- Total of 62 ears in 31 pts
  - Ear surgeries for conductive hearing loss (Ossicular chain reconstruction) and enlarging ear canal (Canalplasty)
  - pts excluded due to unavailable audio or CTs
  - No sufficient information
  - For audio date->58 ears (4 excluded)
  - For CT scan data->52 ears (10 ears excluded)
Degree of Hearing loss (n=58 ears)

- Normal: 67%
- MILD: 23%
- MODERATE: 8%
- PROFOUND: 2%
Types of hearing loss (n=24)

- Slight Conductive: 8
- Conductive: 9
- Mixed: 4
- Sensorineural: 3

Types of Hearing Loss:

- Slight Conductive
- Conductive
- Mixed
- Sensorineural
Case I

Left ear drum Normal

Left normal hearing
Case II

Left slight conductive hearing loss:

Left ear drum

Normal
Case III

Left slight conductive hearing loss:

Left ear drum

Normal
Case IV

Left ear drum

Normal

Left moderate conductive hearing loss
### Ear drum and middle ear abnormalities

<table>
<thead>
<tr>
<th>Ears (n=54)</th>
<th># ears</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>22</td>
<td>41%</td>
</tr>
<tr>
<td>Scar</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Abnormal</td>
<td>30</td>
<td>56%</td>
</tr>
<tr>
<td>Atresia (No ear canal)</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>
CT scans

- N = 52 ears when
  - Excluded due to a prior surgery; no or inadequate CT
- Middle ear bones
- Bony plates on ear drum
- Dimension of ear drum
**Middle ear bones (Ossicles)**

- Not well-formed: 6 (11%)
Ear drum structures

- Bony plates on ear drum: 24 (44%)
Size of ear drums at medial ear canal

• Grossly small ear drum/canal: 12 (23%)
Ear Atresia (absent ear canal)

- No ear canal development: 1 (2%)
Dimension of ear drums on CT

FA

Normal
Height of ear drum (Annulus)

- Control: 9.3 mm
- FA: 8.1 mm

Statistical significance: P<0.001
Width of ear drum (Annulus)

- Control: 8.8 mm
- FA: 6.8 mm

P < 0.001
Sensorineural hearing loss & Narrow internal auditory canal  \( n=2 \)

Abnormal Right side
Central nervous system Involvement
Common Ear manifestations

- Small ear drum with bony island and usually malformed middle ear bones (58%)
  - Rarely aural atresia (Absent ear canal)
- Hearing loss (33%)
- Conductive hearing loss
- Rarely associated with sensorineural hearing loss and narrow ear nerve canal
  - Perhaps associated with brain structural problems
Why Ear Problems in FA?

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

- Knockdown (Removal) of Fancd2 in Zebrafish
  - Physical features include short body, small eyes and head
  - During fetus development, many cells divide and proliferate. But without Fancd2, cells inappropriately die
  - This results in congenital malformations

(Liu et al, 2003)
3 Types of hearing loss situations in FA

- The most common type of hearing loss is mild & moderate conductive hearing loss
- Rarely, absent ear canal and maximum conductive hearing loss
- Rarely, complete nerve hearing loss due to absent hearing/auditory nerve
Hearing problems

Socializing in a restaurant

Group situations
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 ("f", "s", "th", "v", and "z")
    » 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
    » Time spent with OTME especially during first three years of life was associated with lower scores on tests of cognitive ability, speech and language, and school performance at age of 7
Management options

- Auditory amplification (hearing aids)
  - Conventional hearing aids
  - FM assistive listening device

- Traditional ear surgery to widen ear canal and correct middle ear bone problems

- Other hearing devices (BAHA® and SoundBite®)
Conventional hearing aids

- CIC
- OTE
- ITC
- HS
- ITE
- RIC

- Completely-in-the-Canal (CIC)
- Mini-Canal (MC)
- In-the-Canal (ITC)
- Half-Shell (HS)
- In-the-Ear (ITE)
- Behind-the-Ear (BTE)
FM auditory trainer

FM-based system
Surgical Treatment
Middle ear exploration

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

Pre-Op

Post-Op

Average Threshold = 32 dB (PTA)

Average Threshold = 12 dB (PTA)
Middle ear bone (Ossicular Chain) Reconstruction
Risks of Operation

- Minor complications (<5%)
  - Infection
  - Bleeding
  - Ear drum perforation
  - Metallic taste in tongue—only transient

- Major complications (<1%)
  - Profound hearing loss
  - Imbalance/vertigo
  - Facial nerve injury
    » Uncommon unless congenital facial nerve anomaly present
    » Intraoperative facial nerve monitoring and CT scan helps

- No improvement in hearing
  - Usually can still wear hearing aids
BAHA® (Implantable Bone Anchoring Hearing Device)
Risks of BAHA®

- Infection
- Bleeding
- Extrusion of the implant
- Daily care of implant site
SoundBite® Hearing System
Absent Ear Canal
Absent Ear Canal

- Maximum conductive hearing loss
- Difficult with localization of sound
- May or may not need an intervention
- Usually can not wear traditional hearing aids
- Surgical ear canal reconstruction
- BAHA®
- SoundBite®
Absent or narrowed ear canal
BAHA® and SoundBite®
Absent Hearing/Auditory Nerve

- No hearing -> Unilateral profound sensorineural hearing loss
- A problem with localizing sound
- Traditional hearing aids are not helpful
- CROS hearing aids
- BAHA®
- SoundBite®
CROS/BiCROS hearing aids
BAHA® and SoundBite®
Practical communication tips

- Help your child to make a habit to watch the speaker.
- Instruct your child to let the speaker know when he/she is aware something that was said was 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.
**Recommendations**

- **For individual with FA**
  - Comprehensive ENT and audiologic evaluation
  - Audiogram every 2 to 3 yrs?
  - More frequently, if exposed to medications that can cause hearing loss
    - Deferoxamine (Iron-chelating agents)
    - Aminoglycosides (Antibiotics)
    - Cisplatin (Chemotherapy agents)

- **For siblings of FA**
  - Comprehensive ear exam and hearing test
  - Further genetic evaluation to rule out FA
    - Look for somatic mosaicism in fibroblast culture
**Conclusion**

- Hearing loss and congenital ear anomalies are more common than previously reported
- Ear drum and middle ear bone problems
- Commonly mild and moderate conductive hearing loss
- Good ENT evaluation
  - Microscopic ear examination
  - Audiologic evaluation
  - Imaging study-helpful for moderate HL or SNHL
- If significant hearing loss, can be easily treated with assistive-listening devices, amplification, and/or surgery
Collaborators at NIH

National Institute on Deafness and Communication Disorder (NIDCD)
   Carmen Brewer, Ph.D.       Christopher Zalewski, M.A.
   Susan Rudy, BS, NP         Andrew Griffith, M.D., Ph.D.

Georgetown University Medical Center
   Adediyun O Kalejaiye, MD

National Cancer Institute (NCI)
   Blanche Alter, M.D., MPH   Neelam Giri, M.D.
   Lisa Leathwood, RN, BSN

Radiology Dept of Clinical Center, National Institutes of Health
   John A Butman, MD PhD

All the Fanconi Anemia patients at NIH