Auditory Neuropathy Spectrum Disorder

Yvonne S. Sininger PhD
Professor of Head & Neck Surgery
University of California Los Angeles
Financial Disclosure Information

I have no relevant financial relationship with the manufacturers of any commercial products and/or provider of commercial services discussed in this CME activity.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
What is it?

Audiologic Signs

- Hearing thresholds from normal to profound deafness
- Auditory Brainstem Response absent or abnormal.
- Present (prominent) Cochlear Microphonic.
- Otoacoustic Emissions usually present.
- Speech perception poorer than predicted by audiogram
- Absent middle ear muscle ear reflexes.
Auditory Neuropathy in Children < 2 Years of Age

---Mild--- Moderate--- Severe--- Profound
Female 16 months

COCHLEAR MICROPHONIC

Rarefaction & Condensation

Auditory Brainstem Response

Click 80 dBnHL
Speech Discrimination re PTA

![Graph showing the relationship between PTA 2 (1000, 2000, 4000 Hz) and Neuropathy Speech Discrimination Score. The expected speech discrimination score is also indicated.]
Potential Sites of Lesion in AN Based on Symptoms

- CM present from either IHC OHC or both OAE (outer hair cells) Functioning
- Inner hair cell function or synapse could be involved.
- ABR Wave I Abnormal- (Peripheral Auditory Nerve Involved ?)
Evidence of Auditory Nerve Involvement in Auditory Neuropathy

- Starr et al. found 30-40% of patients have evidence of other peripheral nerves disorders (absent deep tendon reflexes or poor nerve conduction).
- As many as 80% of adult AN patients have subtle or pronounced peripheral neuropathy (HSMN, Friedreich’s Ataxia).
- Sural nerve biopsy on 4 patients with AN shows peripheral nerve disease, primarily axonal.
Evidence of Auditory Nerve Involvement in Auditory Neuropathy

- Human temporal bone histology showing normal complement of hair cells with poor ganglion cell survival (Spoendlin, Nadol).
- Temporal bone histology on patient with documented AN shows axonal degeneration (95% loss of ganglion cells), with a normal complement of hair cells (30% loss of OHC in apical turn). Starr et al., Brain 2003
Auditory Nerve

Normal

Auditory Neuropathy
Inner Hair Cells from Temporal Bone of Auditory Neuropathy Patient
Mutations in the gene encoding pejvakin, a newly identified protein of the afferent auditory pathway, cause DFNB59 auditory neuropathy.
Nine (18%) of 51 children with ABR characteristic of AN have been identified as having small (N = 2; 4%) or absent (N = 7; 14%) cochlear nerves on MRI.

RESULTS: Of the nine children with cochlear nerve deficiency, five (56%) were affected unilaterally and four (44%) bilaterally.
Otoferlin involved in vesicle-membrane fusion.

OTOF mutations can explain 3.5% of non-syndromic deafness.

Summary of sites of lesion in ANSD with solid evidence

- Auditory Nerve neuropathy or insufficiency
- Inner Hair Cell/auditory nerve synapse
Consequences of Neural Involvement

- ANSD is known for fluctuations in symptoms: remission, true fluctuations, and/or progression.
- Poor and inconsistent encoding of temporal information lead to unusual temporal processing and poor speech perception.
- Noise is even more disruptive to auditory/speech perception than seen in other types of loss.
**History Factors in Auditory Neuropathy**  
*N=59*  
*(Sininger, Starr & Oba)*

<table>
<thead>
<tr>
<th>Count</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Dominant Family History</td>
</tr>
<tr>
<td>7</td>
<td>Multiple Risk Factors</td>
</tr>
<tr>
<td>7</td>
<td>Premature Birth</td>
</tr>
<tr>
<td>8</td>
<td>Hyperbilirubinemia</td>
</tr>
<tr>
<td>17</td>
<td>Recessive Family History</td>
</tr>
<tr>
<td>26</td>
<td>No Known Risk Factors</td>
</tr>
</tbody>
</table>
Management of Children with ANSD

Assistive Listening Devices
N = 140

- CI (49) 35%
- CI + HA (8) 6%
- HA (44) 31%
- NAD (39) 28%

From Pat Roush U. North Carolina

Complicated by difficulty in audiometrics
Half of Subjects with Hearing Aids show significant improvement. 
Rance et al., E&H 2002
T and C Levels and NRT Thresholds are the Same for AN Patients and Controls

Peterson, Shallop, et al.
Electrical stimulation “reintroduces” timing precision and synchrony, demonstrated in an electrical ABR.

Peterson, Shallop, et al.
UNC AN Children with CI N=49

Cl in AN EAR

From Pat Roush U. North Carolina
Rehabilitation Strategies for Children with ANSD

- Significant individual variability is seen across patients.
- Rehabilitation strategy may need to incorporate and emphasize visual information.
- Delays in obtaining audiometric information is common.
- Persistent, frequent monitoring of hearing and communication ability is recommended.
Thanks for Listening