Auditory Neuropathy
History

• Sininger et al. (1995) --- 10 cases; presents OAE with absent / abnormal ABR; coin the term ”auditory neuropathy”

• Starr et al. (1996) --- neural auditory pathway dysfunction

• Berlin et al. (2001) --- suggest auditory dysynchrony
Synonym

- Auditory neuropathy (AN)
- Auditory dys-synchrony (AD)
- Auditory neuropathy/dyssynchrony (AN/AD) as the third term
Epidermiology

- Berlin et al (2001): 10% of diagnosed deaf patient
- 8%-10% of newly diagnosed children with HL per year
- Less than 10% of cases are unilateral
- Only 25% cases older than 10 years when the symptoms initially occur
Characteristics(1)

• Preserved otoacoustic emissions (OAEs) and/or cochlear microphonic potentials (CMs)
• Abnormal or absent auditory brainstem response (ABR)
• Speech discrimination scores are worse than predicted by pure tone audiogram, particularly in the presence of noise
Characteristics(2)

• Insidious beginning and a slow and progressive evolution
• Moderate-to-profound hearing loss and is centred in middle and high frequencies
• Hearing thresholds for pure-tone detection can range from normal to profound levels
Pathophysiology(1)

- A spectrum of pathologies that affect the auditory pathways:
  1. Desynchrony of neural discharges
  2. Impairment in the patients’ temporal processing abilities
  3. Without affecting the amplification function of the inner ear
- Idiopathic: approximately half of all cases
The pathway of the auditory system. The major pathways are indicated by heavy arrows.
Auditory pathway

- Inner hair cell ➔ Type I spiral ganglia cells ➔ Cochlear nucleus (ponto-medullary junction) ➔ Contralateral superior olivary nucleus (upper pons) ➔ Inferior colliculus (midbrain) ➔ Medial geniculate ganglia (thalamus) ➔ Auditory cortex (temporal lobe)
Pathophysiology (2)

- Genetic (mutations in several genes):
  1. MPZ, NDRG1, and PMP22---critical for peripheral nerve myelination and axonal survival
  2. OTOF---otoferlin, synaptic vesicle-membrane fusion
- Infectious (measles, mumps, meningitis)
- Immunologic (steroid treatment, Stevens-Johnson syndrome)
- Metabolic (diabetes, hyperbilirubinemia, hypoxia)
- Neoplastic (tumors)
- Prematurity
Pathophysiology(3)

• **Neonatal risk factors**
  1. Prematurity
  2. Hyperbilirubinemia (indirect)
  3. Hypercholesterolemia
  4. hypoxia
  5. neural ischemia
  6. central nervous system immaturity
  7. low-birth weight
  8. antibiotics and diuretics in NICU
Pathophysiology (4)

- Bilirubin neurotoxicity --- deposits in cochlea and vestibular nuclei, spiral ganglion
- Anoxia --- inner hair cell/cochlea afferent system vulnerable to hypoxia
- Cochlea nerve deficiency (18% children with AN/AD)
- Auditory nerve myelinopathy / axonal neuropathy --- generalized neuropathic disorder
Diagnosis(1)

- **Audiology**:
  1. Presence of normal OAEs and/or CMs
  2. Absence of ABR waveforms
  3. Impaired speech perception, disproportional to the pure-tone audiogram
Diagnosis(2)

- A more **even distribution** across the audiometric range
- **Fluctuations** in the audiometric findings during the course of the disease are not uncommon in AN/AD
Diagnosis(3)

• Approximately 20% of AN/AD subjects may have a low-amplitude wave V in their ABRs
• OAEs may be absent in up to 30% of ears with confirmed diagnosis of AN/AD
• OAEs may disappear during the course of AN/AD
Diagnosis(4)

- **Lab data**:
  1. Bilirubin
  2. Neuron-specific enolase --- higher; as a marker for close follow-up

- **Image**:
  1. HRCT --- IAC and cochlear morphology; an unreliable marker of CN integrity
  2. MRI --- 18% AN/AD children showed cochlear nerve disorders
BB = Bill's Bar (bony)
TC = Transverse Crest (bony)
MRI---normal
T2 weight image; axial and parasagittal view, left ear

**Axial view**

**Para-sagittal view**

- Cochlear n.
- Facial n.
- Anterior
- Superior
- Vestibular n.
- Cochlear n.
MRI---abnormal

T2 weight image; axial and parasagittal view, right ear

**Axial view**

- Absent Cochlear n.

**Para-sagittal view**

- Facial n.
- Anterior
- Absent Cochlear n.
MRI limitation

- Current MRI techniques alone are not sufficient in cases of small IACs
- Combine the MRI findings with functional assessments of hearing (ABR & behavioral audiometry) and facial motion (CN 7) may be helpful
Treatment

• Individualized and adjust according to the disease progress
  1. Auditory inputs (conventional amplification, cochlear implant)
  2. Visual language (baby signs, sign language, cued speech, or speech reading)
  3. Lip reading in adults and logopedic rehabilitation in children
Conventional Amplification(1)

• Potential noise-induced damages to cochlea
• No evidence of deterioration of hair cell function due to hearing aid use has been obtained so far
• No evidence that outer hair cells contribute to the hearing abilities of AN/AD patient
• For patients without or lost OAEs in the course of the disease? (miss early access)
Conventional Amplification(2)

- Only provide a louder, equally distorted signal?
- Poor acceptance among adult patient and some children---limited improvement
- Improve neural synchrony---recruiting all residual neurons available
- FM system; improve signal-to-noise ratio
- Benefit for a subpopulation: a management option or a trial period of candidature for C.I.
Cochlear Implantation(1)

- Increasing evidence suggests significant advantages for C.I. in the management of AN/AD
- Strategy---discrete, pulsatile signals better than high stimulation rates (increase synchronization of neural activity)
- Endocholelear lesion---by-pass the reduced number of inner hair cells
Cochlear Implantation (2)

- Factors favor better outcomes:
  1. Absence of medical co-morbidity
  2. Normal cognitive function
  3. Normal anatomy of inner ear structures and brain
  4. Present of cochlear nerve
Cochlear Implantation(3)

• Normal IAC demonstrated on CT does not ensure the presence of a cochlear nerve
• MRI is required to confirm before cochlear implantation
• Normal intraoperative EABR waveform indicates an intact auditory pathway to the level of the brainstem
**Cochlear Implantation (5)**

- Most cases (75%), the abnormality was *loss of IHC with survival OHC* causing abnormal tuning (*dys-synchrony*) of the basilar membrane.
- Other cases (25%) the hair cell dys-synchrony was associated with an abnormality of the neural pathway causing a ‘true auditory neuropathy’.

*Cochlear Implants Int. 2008; 9(1), 1–7*
Cochlear Implantation(4)

- Timing?
  1. AN/AD patient reach a stable audiogram---18 months of age
  2. Clinically meaningful improvement occurring since 12 months of age

Otol. Neurotol. 2002; March(23): 163—168
Conclusion

• Hyperbilirubinemia and hypoxia are major risk factors
• Auditory synaptic deficiency, auditory nerve myelinopathy and/or neural desynchrony are the most probable pathophysiologic mechanisms
• Combination of OAEs and CMs in patients with absent (or grossly abnormal) ABR waveforms
Conclusion

• Management should be individualized and modified
• Conventional amplification, intensive speech, and language therapy provide the mainstay of rehabilitation
• C.I. candidate selection should be cautious
• Universal newborn hearing screening protocols (solely OAE) may need to be revised
References


References


5. R. SANTARELLI et al. Cochlear microphonic potential recorded by transtympanic electrocochleography in normally hearing and hearing-impaired ears ACTA Otorhinolaryngol Ital 2006; 26, 78-95
Thanks for your attention!