Review

Auditory neuropathy—a rare condition where CI provides improved hearing and speech development

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Abstract  Auditory neuropathy (AN) was reported 30 years ago in 1979 when Davis and Hirsh presented the first case with normal or near normal hearing threshold but absent auditory brainstem responses. Many names have been given since then including paradoxical hearing loss, brainstem auditory processing syndrome, central auditory dysfunction, neural synchrony disorder or neural dyssynchrony. The term auditory neuropathy was first given by Sininger and colleagues in 1995. More and more AN articles have been published in recent years. The present short review and case report focus on the most important characteristics from a clinical point of view in order to let young physicians know AN, and consequently make correct diagnosis.

Introduction

Auditory neuropathy (AN) is characterized by congenital sensorineural hearing loss associated with absent or impaired auditory brainstem evoked responses and preservation of outer hair cell activity. Intact outer hair cell function is demonstrated by the presence of otoacoustic emissions and/or a measurable cochlear microphonic on electrocochleography, whereas no synchronous neural activity (absent action potentials) is seen on acoustically evoked brainstem auditory response testing. These patients demonstrate hearing loss for pure tones of varying degrees and impaired word discrimination out of proportion to pure tone loss. Speech development is severely impaired and amplification with hearing aids is often of limited value. An increasing number of AN patients now receive cochlear implants (CI) with good results.

Occasionally we meet children that despite, as it seems, enough hearing capacity don’t develop speech at expected rate. They have passed neonatal hearing screening when these programs use otoacoustic emissions (OAE), and come for hearing evaluation due to delayed or absent speech development. Hearing thresholds are elevated from mild to severe. These children can be difficult to test, showing varying results from test to test and they don’t respond to speech according to their pure tone thresholds [3]. Further investigation shows absence of auditory brainstem response and preserved OAE, indicating intact outer hair cell function [1, 2]. A measurable cochlear microphonic (CM) is also a positive sign of AN.

Definition of auditory neuropathy

◆ Mild to severe hearing impairment on air- and bone conduction pure tones audiometry.
◆ Absent or strongly deviating auditory brainstem response (ABR).
◆ Normal otoacoustic emissions with positive contralateral masking.
◆ Speech discrimination far below expected from pure
tone thresholds.
◆ Absent ipsi- and contralateral stapedius reflexes.
◆ Normal CMs

Pathology

The pathology of AN is not well known. Perisynaptic synchronization disorder is one of the possible pathogenesis underlying AN. The output synapses of the primary receptor neurons are marked by structures called synaptic ribbons, involved in the release of neurotransmitter glutamate in the cochlea, retina and vestibular organs. Abnormalities in a variety of functional aspects of the ribbon presynaptic terminal may underlie AN and retinopathy \[11, 12\]. It may also be a neural disorder. Cochlear nerve deficiency has been shown in one out of five subjects with AN (6). Children with cochlear nerve deficiency can present with similar symptoms as AN and electrophysiologic evidence with ABR testing shows a CM with absent neural responses. Starr et al found a more complex pattern with transient OAE absent in 30% and ABR present but deviating with a low amplitude wave V in 20% of the subjects (1). OAE may be absent or decline over time \[4, 5\]. Familial AN has been linked to the x–chromosome \[13\] and to gene DFNB59 \[15\]. Familial AN not connected with any of these genes has also been described \[14\].

Clinical signs of AN

◆ Speech development is impaired or absent, despite amplification with hearing aids and support from speech therapist.
◆ The Child’s ability to respond to speech is much lower than expected from the pure tone audiogram.
◆ Background noise disrupts speech understanding much more than expected.
◆ Hearing seems to fluctuate from day to day but also during the day.
◆ The presence of another neurological disease that affects motor function and coordination.

Similar symptoms can be seen with rapidly progressing hearing impairment. Young children are often hard to test and especially so when hearing is rapidly changing. Amplification may not be adequate which also affects speech development. Delayed speech development is seen also in normal hearing children and the explanation has to be found in areas related to speech and hearing in the central nervous system. Speech production can also be involved in other neurological conditions affecting motor function and coordination. Behavioral disorders within the autistic spectrum is another condition with impaired language development despite normal pure tone thresholds. AN may also be part of a general neurological disorder and investigation should always include pediatric and neurological consultation \[7\]. There is a considerable inter–individual variability in children with AN. Hearing can be fluctuating and may even show improvement over time \[2\].

Risk factors

The cause of AN is not well known. Heredity, trauma or other medical conditions are possible predisposing conditions. AN is more often seen in combination with one of the following conditions.
◆ Neonatal anoxia
◆ Hyperbilirubinemia requiring blood transfusion.
◆ Prematurity especially in combination with low birth weight (4).
◆ Infections
◆ Immunologic deficiency
◆ Family history
◆ Neurological diseases, e.g. Friedreich’s ataxia and Charcot–Marie–Tooth syndrome

The rate of sensorineural hearing loss (SNHL) in high–risk nursery infants is 10 times greater compared with normal term newborns. Hearing screening of newborns with OAE will miss AN and should be complemented by ABR in high–risk groups \[2, 4\].

Investigating AN

Deviating or absent ABR in combination with preserved OAEs are the key indicators for AN. While cochlear hearing loss can affect ABR because stimulation of the nerve becomes weak, it also affects the outer hair cells and thereby abolishes OAEs. Also in AN, OAEs may disappear over time and the diagnosis has to rest on the clinical symptoms \[5\]. CT and MRI may show a deficient or absent cochlear nerve. The condition may be
unilateral or bilateral.

**Rehabilitation in children with AN**

Children with AN need a lot of support for speech development. It is difficult to predict the benefit of hearing aids. Some children are helped and others not. Amplification can even be hard with respect to fluctuating hearing thresholds. Sign language often works well in these children and can be a good support for language development when the goal is to provide the child not only with spoken but also written language. There is however an increasing body of evidence that a CI can help these children \(^7\text{-}^9\). The electrical stimulation is apparently capable to evoke a synchronized response in the auditory nerve and there are several reports of significantly improved hearing and speech development. The number of subjects is still small, but most children show a significant improvement after implantation. The decision to perform surgery in a cochlea with preserved outer hair cells and the possibility of spontaneous recovery seen in some subjects \(^2\) may seem controversial and raises questions regarding implantation before one year of age. Preoperative MRI is recommended to rule out any cochlear nerve deficiency. Although children who have a small nerve may benefit from cochlear implantation, this is obviously contraindicated in children with completely absent cochlear nerves. Auditory brainstem implantation (ABI) has been described in a few subjects with AN \(^{10}\).

All children consistently used their devices and had environmental sound awareness and utterance of words and simple sentences.

**Case history 1**

A two year old boy was referred to our department for hearing test because of impaired speech development. He had passed newborn hearing screening with OAE. He had recently received ventilation tubes due to otitis media with effusion without any improvement of hearing or speech. Play audiometry showed a moderate hearing loss of 40–50 dB bilaterally. Hearing aids were adapted with good improvement in the test situation with responses to warble tones at 10 dB (nHL). The reaction to speech improved but with very low rate. He rarely showed any reaction when his parents called his name and he seldom responded to speech. His communication strategies were based mainly on vision and context. He was referred to a pediatric neurologist with a question of autistic behavior or some neurological disorder. Parallel with that consultation hearing tests suddenly showed responses at 70–80 dB (Fig 1). ABR under anesthesia was performed showing no evoked neural responses but a large cochlear microphonic. Transient OAE tested with tubes in both ears were negative. CT and MRI of the brain and temporal bone were normal. Hearing aids were adjusted showing aided thresholds at 30–40 dB. He is regularly seeing a speech therapist where he can produce single words in respond to a question but communication is totally inconsistent. The alternative diagnosis in this case is rapidly progressive hearing loss and a behavioral disorder in the autistic spectra. The present question is whether this boy should benefit from a CI.

**Case history 2**

A 15-year-old girl presented with increasing hearing problems since two years ago. She complained of difficulties to hear in noisy environments and also to hear TV at home (big family). Development had been normal including speech and language. After four years in Sweden she had learned to speak Swedish. Hearing test (the first in her life) showed a mild to moderate hearing loss of 50 dB in the low frequencies and 30–40 dB in the middle to high frequencies. (Fig2). Transient OAE were
normal while ABR was absent. MRI of the brain was normal. Hearing aids give good result and she is wearing them all day, also for telephone calls. Test results and symptoms confirm the diagnosis of AN but the background is not clear. There is no history of previous disease or medication but further investigation may give a better clue.

**Summary AN**

Taken together the term AN probably represents a spectra of peri- and postsynaptic abnormalities presenting with similar clinical symptoms and a common test pattern defined by today’s available tests. More specific diagnostic tools are needed to understand the underlying pathophysiology and predict the outcome of different rehabilitation strategies. To help understand AN, figure 3 shows peripheral and central auditory anatomy. Figure 4 shows ABR testing in an infant in a Swedish hospital (figure 4). The author hopes that this short review and case report will provide basic information on AN for young otolaryngologists, which may help them diagnose AN in the clinic.

**References**

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