Current Understanding of Auditory Neuropathy

Nem-Yun Boo,[1] *FRCP (Edin & Glas), FAMM, FAMS*

Abstract

Auditory neuropathy is defined by the presence of normal evoked otoacoustic emissions (OAE) and absent or abnormal auditory brainstem responses (ABR). The sites of lesion could be at the cochlear inner hair cells, spiral ganglion cells of the cochlea, synapse between the inner hair cells and auditory nerve, or the auditory nerve itself. Genetic, infectious or neonatal/perinatal insults are the 3 most commonly identified underlying causes. Children usually present with delay in speech and language development while adult patients present with hearing loss and disproportionately poor speech discrimination for the degree of hearing loss. Although cochlear implant is the treatment of choice, current evidence show that it benefits only those patients with endocochlear lesions, but not those with cochlear nerve deficiency or central nervous system disorders. As auditory neuropathy is a disorder with potential long-term impact on a child's development, early hearing screen using both OAE and ABR should be carried out on all newborns and infants to allow early detection and intervention.

Ann Acad Med Singapore 2008:37(Suppl 3):60-2

Key words: Auditory brainstem responses, Cochlear implant, Otoacoustic emissions

Introduction and Definition

Until a decade ago, hearing loss was generally classified as either (i) conductive, due to pathologies in the middle ear and/or blockage to the external auditory canal, or (ii) sensorineural, due to abnormalities in the cochlea including the outer hair cells and the auditory nerve. In 1995, a new category of hearing loss termed auditory neuropathy (AN) was first reported based on a longitudinal study of 10 patients with absence of or grossly abnormal auditory brainstem responses (ABR), but preservation of otoacoustic emissions (OAE) and cochlear microphonics.[1] Eight of these patients subsequently developed clinical evidence of peripheral nerve neuropathy. As the ABR evaluates neural function of the auditory pathway (which includes the inner hair cell and spiral ganglion of the cochlea, the VIII nerve and brain stem), an absent or abnormal ABR indicates abnormalities in any part of this auditory neural pathway. The OAE evaluates the outer hair cell (OHC) function within the cochlea. The presence of a response to OAE indicates normal cochlear OHC function. The cochlear microphonic is a receptor potential displayed in the ABR, produced by polarisation & depolarisation of cochlear hair cells. The response is pre-neural with no latency delay on the ABR. The presence of cochlear microphonics in the ABR reflects the integrity of OHC. Based on these hearing test findings and the clinical features of this first reported series of patients, their investigators proposed the term "auditory neuropathy" for patients with this type of hearing impairment as they opined that it was due to a disorder of the auditory nerve with preservation of the cochlear hair cell function.[1,2]

Sites of Lesion

Subsequent studies in humans and animal models with characteristic electrophysiological features of AN, however, showed that various sites of the auditory pathway could be affected. These include the cochlear inner hair cells, spiral ganglion cells of the cochlea, synapse between the inner hair cells and auditory nerve, or the auditory nerve itself due to either a reduction of neural elements or disruption in the temporal integrity of the neural signals.[3-9] All these varieties share a relatively spared receptor function and an impaired neural response with diminished ability to follow fast temporal changes in the stimulus.[2] To reflect their concern that the term AN may be anatomically inaccurate for such a heterogeneous sites of hearing impairment, some

[1] Department of Paediatrics, International Medical University, Kuala Lumpur, Malaysia
Address for Correspondence: Professor Nem-Yun Boo, Department of Paediatrics, Clinical School, International Medical University, Jalan Rasah, 70300 Seremban, Negeri Sembilan, Malaysia.
Email: nemyun_boo@imu.edu.my

investigators have proposed "auditory neuropathy/dyssynchrony (AN/AD)" or "auditory synaptopathy (AS)" in place of "auditory neuropathy." [8,10-14]

Epidemiology

The actual prevalence of AN/AD is unknown as reports on population studies are lacking. Based on the result of a universal newborn hearing screening of 14,807 infants born in a large Singapore hospital where the prevalence of hearing loss was found to be 3.5 per 1000 infants (n = 52), the prevalence of AN/AD was reported to be 0.6 per 1000 (n = 9) infants.[11] Most of the studies reported on the prevalence of AN/AD were on patients with hearing loss. In children with hearing loss, the prevalence of AN/AD varied from 2.4% in school children with hearing loss[12] to 8.44% among profoundly hearing impaired children.[13] In adults, the prevalence of AN/AD was reported to be 1 in 183 adults with neural sensory hearing loss.[14]

Aetiologies

The etiologies of AN/AD have been identified to be due to numerous disorders. The most common ones can be classified primarily into one of 3 main groups: genetic, infectious or neonatal/perinatal insults.[10] Mutations of several genes which are important for the inner hair cell, spiral ganglion or peripheral nerve function have been found to be associated with AN in families with this type of hearing loss.[15-17] Perinatal hypoxia,[18] neonatal hyperbilirubinemia[6,8,10,19,20] and prematurity[4,10] have been identified to be the most common neonatal/perinatal insults associated with the AN/AD.

Clinical Presentation

Children with AN/AD usually presents with delay in speech and language development.[21] Adult patients with AN/AD often complain that they can hear sounds but cannot understand speech. Difficulty in perception of speech both in quiet and background noise is a consistent feature in patients with AN/AD type of hearing loss.[2,22] In children with AN/AD, a high proportion (about 50%) show little or no ability to understand speech even in favourable (quiet) listening conditions.[23-25] Unlike the case of cochlear loss/damage which results in hearing loss of severity consistent with pure-tone audiometry, patients with AN/AD present with hearing loss with speech discrimination worse than that predicted by pure-tone audiometry. This is because AN/AD affects the timing of neural activity in the auditory pathway and disrupts the aspects of auditory perception based on temporal cues.

The clinical course of patients with AN/AD is variable, ranging from fluctuating hearing loss in some,[26-28] improvement over time in others,[29] or remain unchanged in others.[30] Transient hearing loss has been reported mainly in some children during febrile episodes.[27,28] Furthermore, infants with low birth weight (LBW) were identified to be a significant predictor associated with the subset of AN/AD which recovers over time, thus suggesting that in LBW infants the AN/AD may be due to a delay maturation of the auditory pathway.[29]

Investigation

As AN/AD is a disorder with potential long-term impact on a child's development, early hearing screen using both OAE and ABR should be carried out on all newborns and infants to allow early detection and intervention. In children and adults complaining of difficulty in understanding speech, both hearing tests should be similarly carried out. All patients with AN/AD have recordable OAEs and absent or abnormal ABR. Their hearing thresholds for pure-tone detection can range from normal to profound level. Majority of AN/AD patients (>90%) are bilateral.[9]

Once a patient is identified to have a recordable OAE but absence of or abnormal ABR, a thorough clinical evaluation, including history and neurological examination, should be carried out to exclude central nervous system (CNS) involvement before a definite diagnosis of AN/AD is made. Furthermore, other electrophysiological test should be carried out to locate the site of the pathology accounting for these electrophysiological changes. These should include testing for middle ear function, acoustic reflex studies, and electrocochleargraphy.[31] It is also crucial to obtain brain MRI with contrast enhancement in all patients with electrophysiological findings characteristic of AN/AD to exclude possible CNS lesions[26] and cochlea nerve deficiency.[32] This is because pathologies affecting the central auditory pathway up to the level of the brainstem can produce similar electrophysiological changes. The term "AN/AD" is anatomically appropriate only for lesions in spiral ganglion cells or their axons, or of the 8th nerve, but not lesions in the brainstem and brain.[33] It is important to differentiate between them as the management and outcome differ.[26,34,35]

Management

Cochlear implants is the treatment of choice[36,37] for patients with AN/AD in the absence of cochlear nerve deficiency and higher cortical deficiency.[32] Conventional amplification using hearing aids are rarely beneficial. Electric-ABR (EABR) testing at the time of implant surgery or in the immediate postoperative period has been shown to help predict success to cochlear implant in patients with AN/AD. Patients with robust brainstem potentials on EABR testing, thus suggesting normal cochlear nerve function, have good outcomes to cochlear implants.[38] As spontaneous recovery of useful hearing has been reported in subsets of children with AN/AD associated with prematurity and

hyperbilirubinemia,[29,30] serial clinical and audiometric evaluations should be carried out in young children before cochlear implantation be considered.

Although many investigators have reported significant improvement of speech perception in children with AN/AD following cochlear implants,[26,39] others found that the these children tend to be at the low end of post-implant performance range in speech perception when compared with children with sensorineural hearing loss.[32,37] Concomitant non-auditory factor such as CNS abnormalities could be one possible explanation for this poorer performance as many of these children were graduates of neonatal intensive care units. Hypoxia, prematurity and hyperbilirubinemia with resultant CNS damage are common problems present in this group of high risk infants.

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Financial disclosure: The author/s declare that they have no relevant financial interest in this manuscript.