

Auditory Neuropathy/Dyssynchrony: A Retrospective Analysis of 15 Cases

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Abstract

Introduction Auditory neuropathy/dyssynchrony (AN/AD) comprises a spectrum of pathology affecting the auditory pathways anywhere from the inner hair cells to the brainstem. It is characterized by an absent or atypical auditory brainstem response (ABR) with preservation of the cochlear microphonics and/or otoacoustic emissions (OAEs).

Objective Retrospective analysis of patients with AN/AD.

Methods Fifteen patients with AN/AD were included in this study and their records were retrospectively investigated.

Results Possible etiology of AN/AD was neonatal hyperbilirubinemia in three patients, family history of hearing loss in three patients, consanguineous marriage in two patients, head trauma in two patients, mental motor retardation in one patient, cerebrovascular disease in one patient, and there was no apparent cause in three patients.

Conclusion Otolaryngologists should keep in mind the diagnosis of AN/AD especially in patients complaining of difficulty in hearing and speech and audiological evidence of disassociation between pure tone and speech audiometry. ABR and OAE testing is recommended in these patients for AN/AD diagnosis.

Keywords

- ▶ auditory neuropathy/dyssynchrony
- ▶ otoacoustic emission
- ▶ auditory brainstem response

Introduction

Auditory neuropathy/dyssynchrony (AN/AD) is a hearing disorder characterized by an absent or atypical auditory brainstem response (ABR), with preservation of the cochlear microphonics (CM) and/or otoacoustic emissions (OAEs).^{1,2} In 1996, Starr et al first described this rare entity, drawing on their observations in 10 patients.³ The authors suggested that these patients were probably similar to those previously reported cases with a paradoxical absence of ABRs and only a slight impairment of pure tone thresholds but in whom CMs or OAEs had not been recorded.^{3–5} Also In 1998, Doyle et al reported eight patients with normal transient evoked OAEs (TEOAEs) and distortion product OAEs (DPOAEs) combined with the absence or marked abnormalities of ABRs.⁶ Starr et al

suggested that this type of hearing impairment is due to a disorder that impairs auditory nerve function and may have as one of its causes a neuropathy of the auditory nerve, occurring either in isolation or as part of a systemic neuropathic process.³ Clinically, the diagnostic criteria of AN/AD is defined as (1) sensorineural hearing loss, usually bilateral, of any degree; (2) normal outer hair cell function as evidenced by the presence of OAEs and/or CM; (3) absent or atypical ABR; (4) understanding of speech worse than would be predicted from the behavioral or pure tone audiometry; (5) absent acoustic reflexes to the ipsilateral and contralateral tones a 110-dB hearing level.^{1,7–9}

In this retrospective study, we investigated the audiological findings, history, and clinical manifestations of patients diagnosed with AN/AD at our clinic.

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Patients and Methods

Fifteen patients with AN/AD were included in this study, and their records were retrospectively investigated. All of the patients' medical and otologic histories were recorded. A complete ear, nose, and throat examination was performed. Otoscopic examinations were done by an otolaryngologist before testing to rule out any external or middle ear pathology that could affect audiometric measurements. Then pure tone audiometry (250 to 8,000 Hz), tympanometry, and acoustic reflex measurement (500 to 4,000 Hz) were done in a standard fashion (Interacoustic AC 40 and AZ 26, Denmark, Assens). DPOAEs were measured at click levels of 65 (L1) and 55 dB (L2) peak sound pressure for the F1 and F2 components (Homoth Medizinelektronik GmbH&Co, KG, Germany, Hamburg). DPOAE-grams were recorded in one-quarter-octave steps over a frequency range of F2 from 0.5 to 6 kHz. DPOAE values were plotted on a DPOAegram, which shows the emission level as a function of the F2 frequency. ABRs were recorded using Homoth ABR equipment. Electrodes were placed on the forehead as a ground electrode and on both mastoids as active electrodes. The responses were filtered with a bandpass of 100 to 3,000 Hz. Alternate polarity clicks of 100-millisecond duration were presented monaurally with a repetition rate of 16.4/s. Each ear was tested separately, and all responses were replicated twice. Patients underwent assessment in a state of natural sleep. In this retrospective study, we did not include genetic research; we investigated only according to the history of patients.

Results

Eleven male and four female patients diagnosed with AN/AD (age range: 2 to 52 years and median age: 19.3 years) were

included in this study. Possible etiology of AN/AD was neonatal hyperbilirubinemia in three patients. These patients had a history of exchange transfusion because of bilirubin levels over 20 mg/dL. Three patients had family history of hearing loss, two patients had consanguineous marriage, two patients had head trauma, one patient had mental motor retardation (psychomotor retardation), one patient had cerebrovascular disease, and there was no apparent causes in three patients.

Thirteen patients had bilateral and two patients had unilateral AN/AD.

None of the patients with AN/AD had middle or inner ear anomalies on computed tomography or magnetic resonance imaging. **Table 1** summarizes the patients' demographic, clinical, and audiological features (see also **Fig. 1** for a left and right ear ABR and DPOAE recording of a case of AN/AD).

Eight of 15 patients' pure tone audiometric results showed profound hearing losses; however, seven of them had mild to moderate hearing loss. Acoustic reflex tests were also absent in all of the patients.

Discussion

AN/AD is characterized by a unique pattern of hearing loss and distorted ABR with preservation of outer hair cell function.^{10,11} AN/AD comprises a spectrum of pathology affecting the auditory pathways anywhere from the inner hair cells to the brainstem. Thus it is difficult to define the disorder as cochlear or retrocochlear. Increased clinical suspicion supported by appropriate diagnostic tests is needed to establish an accurate diagnosis.^{12,13}

The clinical findings for auditory neuropathy are associated with several diagnoses including hyperbilirubinemia, neurodegenerative diseases, Charcot-Marie-Tooth syndrome, and other sensorimotor neuropathologies, mitochondrial

Table 1 Clinical and audiological features of the patients with AN/AD

Patient No.	Age (y)	Sex	ABR	DPOAE	History
1	2	M	Bilateral absent	Bilateral present	Consanguineous marriage
2	3y	M	Bilateral absent	Bilateral present	Mental motor retardation
3	52	F	Bilateral absent	Right ear (+)	Trauma
4	13	F	Bilateral absent	Bilateral present	Blood exchange due to hyperbilirubinemia
5	2	M	Bilateral absent	Right ear (+)	No apparent cause
6	2	F	Bilateral absent	Bilateral present	Blood exchange due to hyperbilirubinemia
7	7	F	Bilateral absent	Bilateral present	Family history of hearing loss
8	4	M	Bilateral absent	Bilateral present	No apparent cause
9	30	M	Bilateral absent	Bilateral present	Trauma
10	5	M	Bilateral absent	Bilateral present	Consanguineous marriage
11	2	M	Bilateral absent	Bilateral present	Blood exchange due to hyperbilirubinemia
12	52	M	Bilateral absent	Bilateral present	Family history of hearing loss
13	29	M	Bilateral absent	Bilateral present	No apparent cause
14	6	M	Bilateral absent	Bilateral present	Family history of hearing loss
15	50	M	Bilateral absent	Bilateral present	Cerebrovascular disease

Abbreviations: ABR, auditory brain stem response; AN/AD, auditory neuropathy/dyssynchrony; DPOAE, distortion product otoacoustic emission.

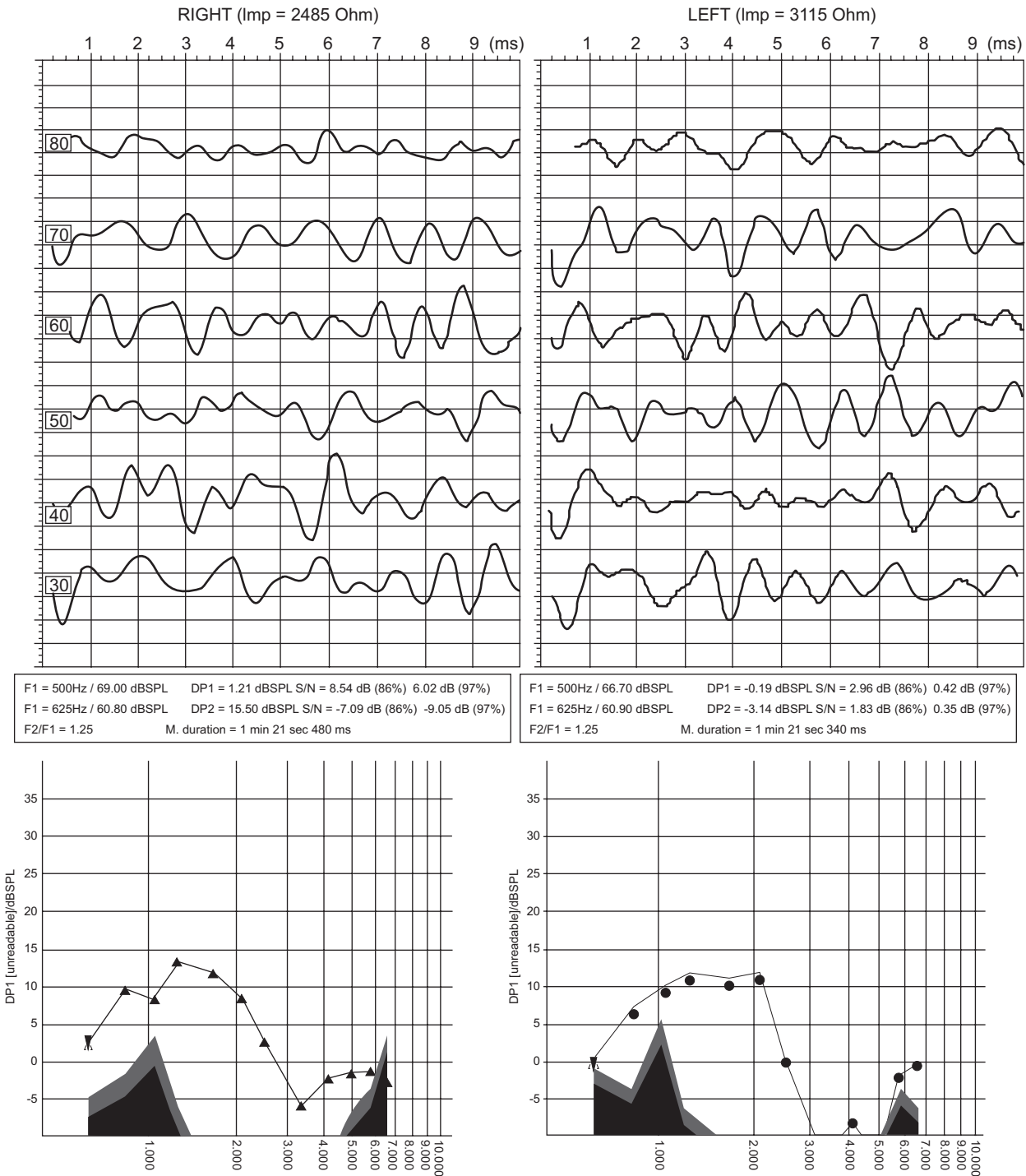


Fig. 1 Left and right ear auditory brain stem response and distortion product otoacoustic emission recording of a case of auditory neuropathy/dyssynchrony. Abbreviations: dBSPL, decibels sound pressure level; DP, distortion product; F1 and F2 used as formulation markers.

disorders, and ischemic-hypoxic neuropathy resulting from asphyxia.¹⁴ Also, experimental animal models for auditory neuropathy have been proposed using the carboplatin ototoxicity and ischemic-hypoxic neuropathy methodologies.^{12,15,16} In our series, three patients with AN/AD had neonatal hyperbilirubinemia, three patients had family history of hearing loss, two patients had consanguineous marriage, two patients had head trauma, one patient had

mental motor retardation, and one patient had cerebrovascular disease. We did not find any specific etiology in three patients.

Recently two mechanisms have been proposed for explaining the abnormalities of auditory function: (1) impaired synchrony among nerve fibers and/or (2) reduced neural input.¹⁷⁻¹⁹ It is generally thought that absent or severely distorted ABR is highly likely to be related to impairment of

neural synchrony in the auditory pathways. Similar to the previous reports, we could not obtain any response to the click stimulus.

The prevalence of AN/AD in patients with hearing loss ranged from 0.5 to 15% according to studies in literature.^{10,11} Because there are so many possible causes for AN/AD, it is difficult to estimate its exact prevalence.¹⁴ Davis and Hirsh suggested that 1 in every 200 hearing-impaired children had ABR findings inconsistent with pure tone findings.²⁰ Permanent bilateral hearing loss is seen in 1.4 per 1,000 live births. Therefore the incidence of AN/AD is likely to be 1.4 per 10,000 live births. According to Rance et al, AN/AD would be present in 2.3 per 1,000 infants with risk factors for hearing loss. Thus, if OAE tests alone are used for hearing screening of infants with risk factors, 11% of infants with permanent hearing loss will be missed.^{14,21} These data are important for designing the newborn hearing screening protocols especially in developing countries.

Patients with AN/AD complain of hearing disability, especially in the presence of noise, and tend to have word-recognition scores that are disproportionately poorer than would be expected by audiometric thresholds. In our series, all of the patients were admitted to our department with the complaint of hearing and speech disability. Only one of them had understandable speech. Pure tone audiometric thresholds are variable in patients with AN/AD, and the degree of hearing loss can range from mild to profound sensorineural type. Eight of our patients' pure tone audiometric results showed profound hearing losses, and seven had mild to moderate hearing loss. Acoustic reflex tests were also absent in all of the patients. Because OAEs and CM are dependent on the integrity of cochlear outer hair cells and are "preneural" events, they may be present and normal in AN/AD; however, absent or grossly abnormal ABRs are seen.^{14,22} Similar findings were observed in our cases.

The hallmark of AN/AD is an abnormal ABR reading together with a normal OAE reading. However, there is a lack of actual diagnostic procedures for AN/AD. Other tests may also be used as part of a more comprehensive evaluation of an individual's hearing and speech-perception abilities. Electrocochleography (ECoG), which objectively assesses cochlear potentials, is the indicated clinical procedure to analyze CMs. Although transtympanic ECoG yields recordings with higher amplitudes and lower test-retest variability, it has the disadvantage of being an invasive procedure. Extratympanic ECoG, therefore, is clinically more useful in this context, supporting an audiological diagnosis and increasing knowledge about cochlear function in AN/AD. ECoG is the most appropriate procedure for assessing cochlear function and helping identify CMs. CMs play an important role in the diagnosis of AN/AD. It is necessary and helpful to diagnose the sites of lesion in patients with AN/AD by analyzing the patterns of CM amplitudes. Therefore, recently ECoG has been used for diagnosing AN/AD.^{8,23}

Some patients with AN/AD lost their OAE over the period of time but there was no associated change in pure tone thresholds. It has also been reported that some patients with AN/AD do not have OAEs but rather evidence of hair cell

function was evident from CM. Therefore these authors suggested that presence of CM with absent ABR seems to be reliable criteria for diagnosing AN/AD.^{24,25}

There has been controversy regarding whether to provide hearing devices (hearing aids, personal radiofrequency [frequency modulation] systems, or cochlear implants) to children with AN/AD and whether to offer aural-oral or visual-manual modes of habilitation.^{14,26} Berlin et al suggested that conventional amplification has little beneficial effect on AN/AD patients.²⁷ On the contrary, Cone-Wesson et al concluded that nearly 50% of children demonstrate some benefit from the use of conventional hearing aids and that a trial of amplification is warranted.^{14,21} Cochlear implantation may also be an option for hearing rehabilitation. Although the outcome of cochlear implantation in children with AN/AD might vary, it is favorable in most cases. Cochlear implantation seems a justified hearing rehabilitation option for children with AN/AD and limited benefits from conventional hearing aids.²⁸⁻³⁰ In our series, we obtained some development in hearing and speech abilities using a conventional hearing aid in one case.

The current position statement of The Joint Committee on Infant Hearing (2007) calls for (1) physiological hearing screening of all infants before they are 1 month old, (2) confirmation of the hearing loss before 3 months of age, and (3) commencement of an interdisciplinary intervention program before the infant is 6 months old. Moreover, the scope of disorders targeted for identification has been expanded to include neural hearing loss (especially AN/AD) in addition to sensorineural and permanent conductive hearing loss.³¹

Conclusion

Although AN/AD affects only a small portion of all persons with hearing loss, the infant, child, or adult with AN/AD is often most disabled by the hearing disorder because of the lack of knowledge about its cause and, more importantly, its treatment. Continued research regarding the causes and pathologies underlying this disorder is needed.¹⁰ However, it is also necessary to develop methods to reduce false-negative screening results and to provide accurate diagnosis for the disorder.² A combined OAE and ABR screening procedure may be considered to overcome the limitations of OAE-only procedures especially in high-risk infants. Also, it should be kept in mind that adult AN/D cases may be related with systemic neurological diseases.

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