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Cochlear implantation in 3 adults with auditory neuropathy/auditory dys-synchrony

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Abstract. *Cochlear implantation in 3 adults with auditory neuropathy/auditory dys-synchrony.* We describe 3 adult patients with auditory neuropathy/auditory dys-synchrony (AN/AD) who underwent cochlear implantation. All patients had absent or poorly formed auditory brainstem responses (ABRs) in combination with preserved otoacoustic emissions (OAEs). They exhibited various aetiologies and a large variation in clinical features known to be consistent with AN/AD. Cochlear implantation was successful in 2 out of 3 cases. We conclude that AN/AD implantee candidates should be counselled with care.

Introduction

The term auditory neuropathy (AN) was first coined in 1996 by Starr *et al*.[1] Since then, a multitude of reports concerning this subject have appeared. Prevalence is estimated to range from 0.5% to 15% of all patients with sensorineural hearing loss.[2-5] AN is hearing loss characterised by absent or poorly formed auditory brainstem responses (ABR) in combination with robust otoacoustic emissions (OAE) and/or measurable cochlear microphonics (CM), despite normal radiographic findings. These features indicate a processing abnormality with preserved outer hair cell function.

There is considerable variation in clinical features. Typically, patients with AN show a discrepancy between the speech audiometric findings and their puretone audiometric data. Indeed, most patients complain of difficulties with understanding what they hear – especially in noise – notwithstanding the fact that they retain speech awareness. Patients can present varying puretone thresholds ranging from mild to severe uni- or bilateral hearing loss (permanent, progressive or fluctuating) with thresholds that are often poorer in the lower frequencies.

In most cases, the exact pathophysiological mechanism has not yet been revealed, and hypotheses concerning AN are intriguing. The cause is most probably to be found either in isolated inner hair cell damage, damage to the synaptic junction between the inner hair cells and the auditory nerve or the peripheral portion of the auditory nerve, or a combination of these lesions. It has been suggested that AN in fact implies a broad spectrum of heterogeneous disorders. The term AN may therefore be misleading and should perhaps be replaced by auditory neuropathy/auditory dys-synchrony (AN/AD).[6] AN/AD is a better description of what is happening in the auditory system and does not suggest a specific locus of pathology.

The aetiology of AN/AD continues to be unclear. Patients often have a history of a complicated perinatal course, such as hyperbilirubinaemia, prematurity, ototoxic drug exposure, neonatal ventilator dependence and cerebral palsy. Genetics, infections, metabolic disorders and other peripheral neuropathies also seem to be a predisposing factor for AN/AD. However, no known risk factors are detectable in 1 out of 4 AN/AD patients.[5,7-9] So far, several genes have been found to be associated with AN/AD.[10-12] Recently, a mutation in the *OTOF* gene was identified in some non-syndromic patients with AN/AD characteristics.[13]

In general, patients respond poorly to conventional amplification. In recent years, successful cochlear implantation in AN/AD patients has been reported.[7,8,14] Direct stimulation of the cochlear nerve can probably overcome problems with synchronisation and temporal processing typical in AN/AD patients.[15,16] However, in

some patients, cochlear implants yield disappointing results.[4,7] Most studies focus on a pediatric population with AN/AD. In order to delineate the spectrum of AN/AD further, we describe the pre- and post-cochlear implant results of 3 adult patients with various aetiologies of AN/AD.

Materials and Methods

Case 1

A 43-year-old man with motor sensory neuropathy since early childhood reported bilateral sensorineural hearing loss for the last 13 years. The neuropathy resembled Charcot-Marie-Tooth disease, but his family history was blank and no mutation in *Cx32* (associated with Charcot-Marie-Tooth) or *Cx26* and *Cx30* (associated with non-syndromal autosomal recessive sensorineural hearing loss) could be identified. Electromyography established indications of a demyelinating neuropathy. Twenty-one years previously, this patient had undergone a successful kidney transplant.

Preoperative audiological examination revealed a pure-tone average ($PTA_{0,5\text{-}1\text{-}2}$) of 83 dB HL for the right ear and of 65 dB HL for the left ear (Figure 1). Speech discrimination using standard, phonetically balanced French word lists (Fournier disyllabic words), was 0% at 90 dB SPL in both ears (Table 1). Conventional hearing aids resulted in little improvement because of extremely poor speech discrimination. The aided speech reception threshold was 0% at 90 dB SPL in both ears. The patient was barely able to communicate by means of lip reading. Sign language could not be taught because of the advanced status of his motor sensory neuropathy. Tympanometry showed bilateral normal middle ear pressure. Stapedial reflexes were present at 110 dB HL for 500 Hz in the right ear and at 90 and 110 dB HL for respectively 1000 Hz and 500 Hz in the left ear. They were absent at 2000 and 4000 Hz. Transient evoked otoacoustic emissions (TEOAE) were intact in both ears (Figure 2). Spontaneous OAEs were absent while provoked OAEs were present. There was a contralateral attenuation in both ears but this was most prominent on the right side. A better afferent route was therefore suspected and the implantation was planned in the right ear. ABR testing revealed

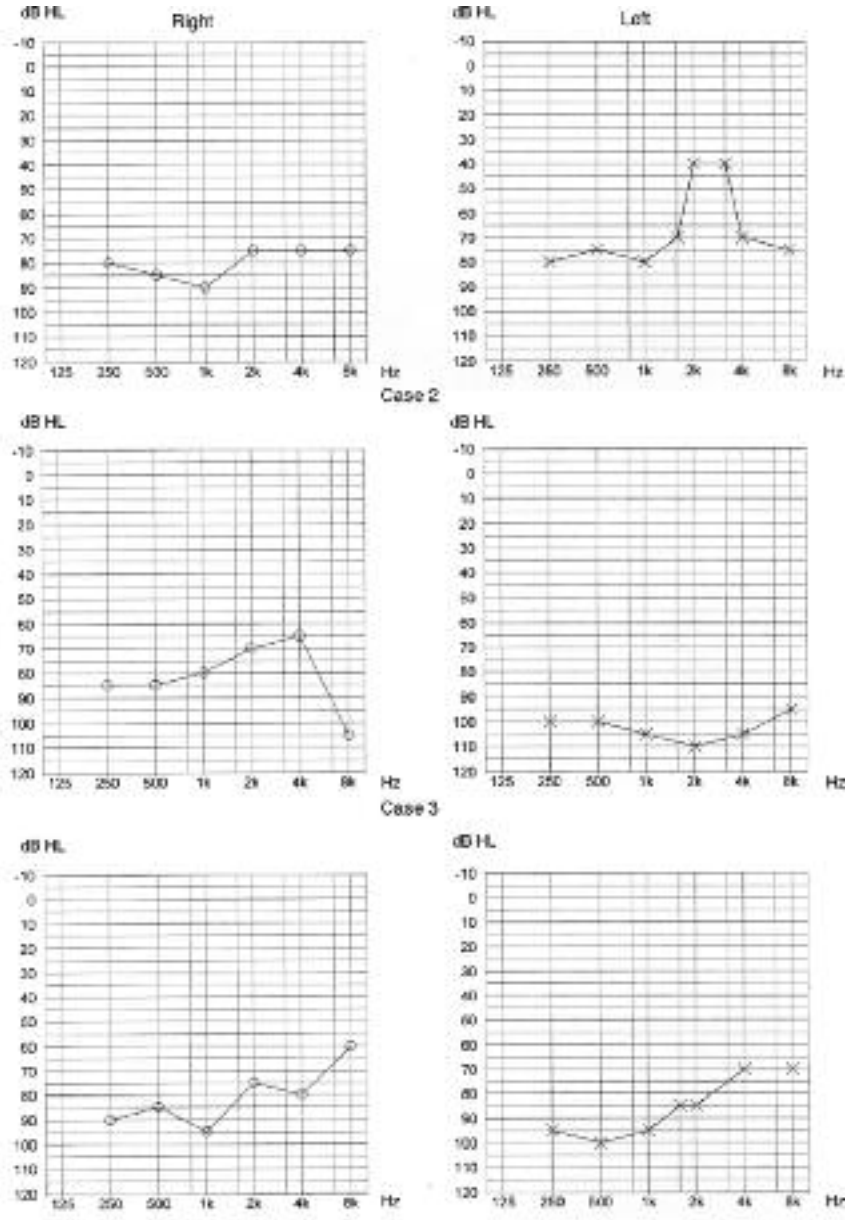

Figure 1
Last air conduction puretone threshold before implantation for Cases 1,2,3

Table 1

Pre- and postoperative speech recognition scores in Cases 1,2,3

Speech recognition scores					
	Preoperative		**Postoperative**		
	Unaided R,L	Aided R,L	Words		Sentences
			CI	LR & CI	CI
CASE 1	0%	0%	56%	86%	99%
CASE 2	25%	48%,27%	86.50%	np	np
CASE 3	0%	0%	48%	78%	68%

Preoperative speech recognition scores without (unaided) and with hearing aids (aided) in both ears (R: right, L: left). Postoperative speech recognition scores for words with the cochlear implant (CI) only and using lip reading (LR) in combination with the cochlear implant; and speech recognition scores for sentences with CI.

Legend: np: not performed.

no reproducible wave forms (Figure 3) and transtympanic promontory electrical stimulation of the left ear showed auditory perception, with train pulse ranging from 312 to 1000 µsec. Testing of the right ear and transtympanic electrocochleography (ECochG) failed.

A favourable psychological and speech therapeutical evaluation was obtained prior to implantation. Computed tomography (CT) of the temporal bones and magnetic resonance imaging (MRI) of the inner ear, ponto-cerebellar angle and brainstem did not reveal any abnormalities. Vestibular assessment was not performed because of the patient's critical physical condition.

The patient subsequently underwent right-sided cochlear implantation with a Nucleus device (Nucleus 24 Contour, CI 24R CS). Because of the high anaesthetic risk known in Charcot-Marie-Tooth patients the intervention was planned under local anaesthesia. During surgery, however, the patient had to be intubated because of imminent respiratory failure. Full insertion of the electrode array was accomplished and confirmed with a Stenvers radiography. Auditory brainstem responses (eABR) were electrically evoked intra-operatively (Figure 4).

Case 2

A 46-year-old female was referred to our department for hearing assessment. She developed progressive hearing loss at the age of 17 years. In early childhood she was diagnosed with bilateral optic nerve atrophy and chronic progressive external ophthalmoplegia. Her mother, a sister and both of her daughters had the same combination of ophthalmological and audiological symptoms.

The pure-tone audiogram showed a $PTA_{0,5\text{-}1\text{-}2}$ of approximately 78 dB HL and 105 dB HL for the right and left ears respectively (Figure 1). Speech audiometry using phonetically balanced Flemish (NVA) word lists (CVC, phoneme score), revealed a maximum speech discrimination score of about 25% at 105 dB SPL testing both ears separately. Using hearing aids, she achieved monaural maximum recognition scores of 48% and 27% at 70 dB SPL in respectively the right and left ear. Communication was extremely difficult and she was unable to use the telephone. Tympanometry showed bilateral normal middle ear pressure, and ipsilateral stapedial reflexes for white broadband noise inputs of 95 dB nHL were absent. TEOAE contained highly reproducible contiguous energy bands at strongly positive signal-to-noise ratios (Figure 2) whereas distortion product otoacoustic emissions (DPOAE) were clearly recordable in the 2.0 to 6.0 kHz bands in both ears. The patient had no discernable pattern with ABR testing at click levels of 95 dB nHL (Figure 3). Psychoelectric transtympanic electrical promontory stimulation using a pulse width of 2500 µsec at a frequency of 20 Hz produced an electrical threshold of 237 µA for the right ear but failed to produce any auditory sensation, other than pain, in the left ear. Electrical ABR prior to cochlear implantation using the same transtympanic promontory site revealed a dissimilar pattern, producing a more stable wave pattern at the level of the left nerve

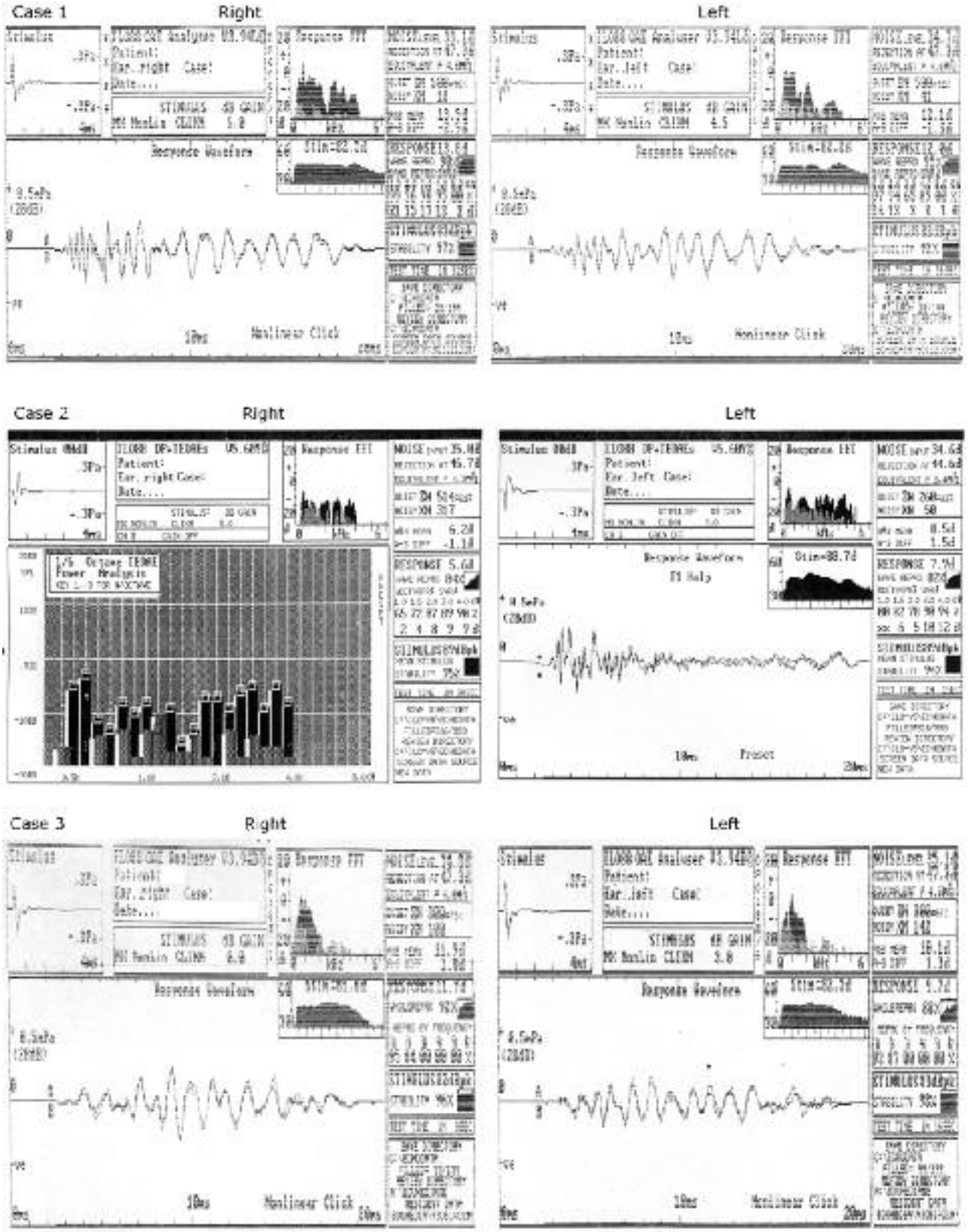

Figure 2
Preoperative transient evoked otoacoustic emissions (TEOAE) for Cases 1,2,3

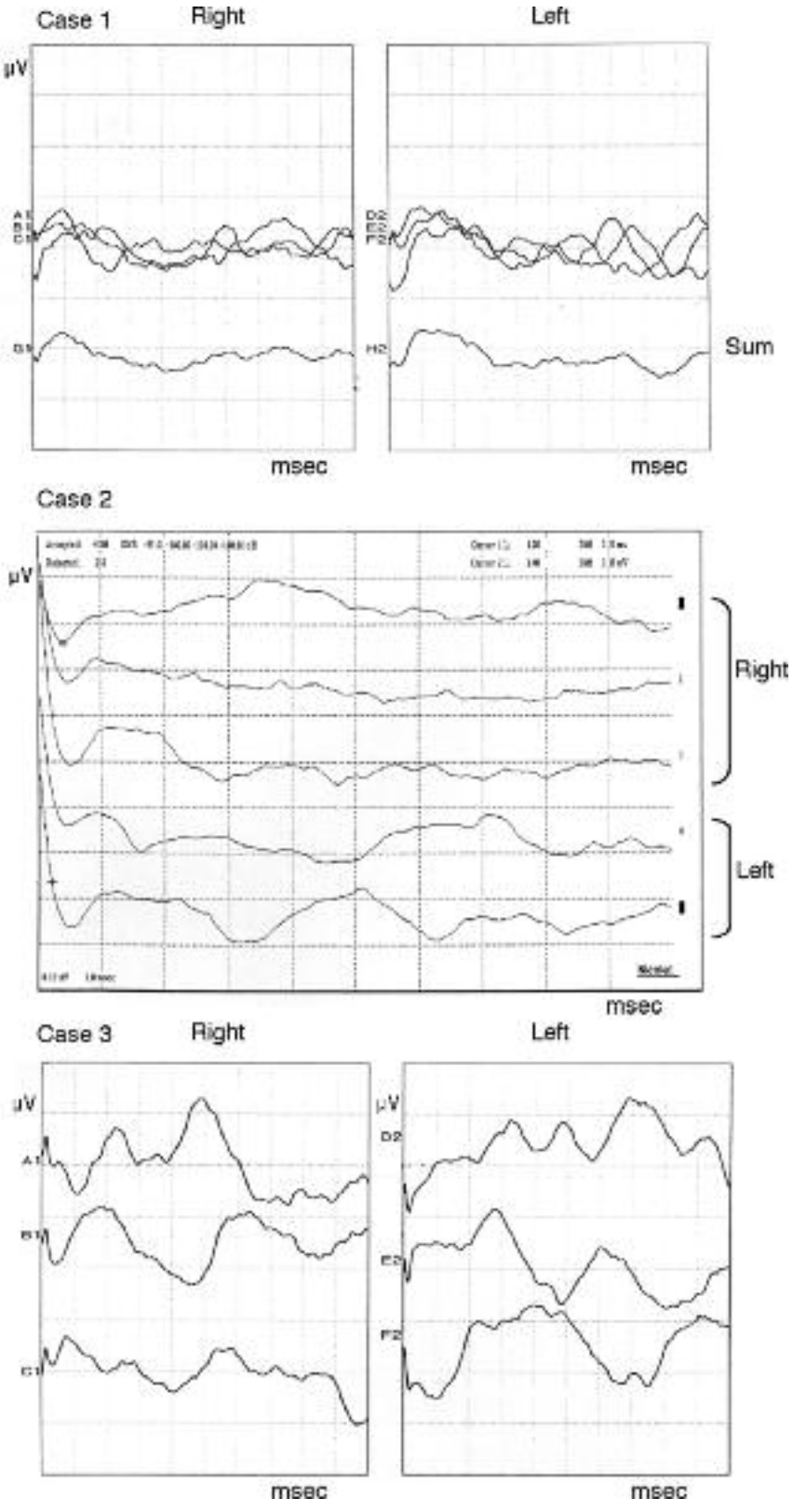

Figure 3
Preoperative auditory brainstem responses (µV) against time (msec) for Cases 1,2,3. Stimulus intensity was maximal (95dB nHL in Cases 1,2, and 100dB nHL in Case 3).

and non-reproducible activity for the right nerve.

A favourable psychological and speech therapeutical evaluation was obtained prior to implantation. CT of the temporal bones and MRI of the inner ear, pontocerebellar angle and brainstem did not show any abnormalities. The vestibular examination was normal.

The patient received a Med-El Combi 40+ cochlear implant in the left ear. Complete insertion of the electrode was confirmed with a Stenvers radiography. Impedance measurements performed intra-operatively resulted in normal values.

Case 3

A 35-year-old woman was diagnosed with sensorineural hearing loss at the age of 10 years. The hearing loss was most probably prelingual since she presented with typical speech characteristics, but she mentioned an additional decay in hearing at the age of 20 years. Hearing aids were fitted at the age of 10 years, but not beneficial. She had never received any therapeutical speech treatment and was raised bilingually (Arabic and French). She originated from a large Algerian kindred with consanguine parents. None of her siblings were known to suffer from hearing impairment. Her medical history was rather unclear. Nevertheless, at the age of 10 years, she underwent a paediatrical, endocrinological, nephrological, dermatological, cardiological, neurological and ophtalmological evaluation as part of an aetiological screening. No causal factor could be found. Recently, we checked for mutations in OTOF, *Cx26* and *Cx30*, but these were not found. The patient was

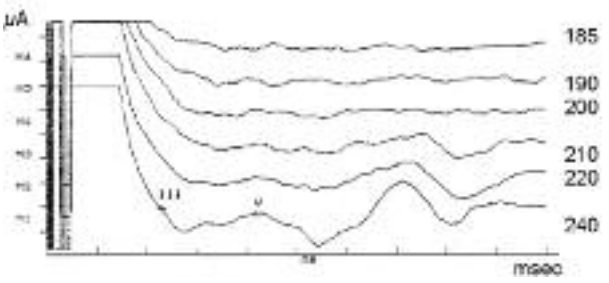

Figure 4
Auditory brainstem responses evoked electrically intra-operatively in current unit (μA) against time (msec) for Case 1 for electrode number 5.

very isolated socially apart from familial support. She was able to communicate with her family by means of lip reading and French sign language. However, this was not done consistently.

Audiological examination revealed a $PTA_{0,5\text{-}1\text{-}2}$ of 85 dB HL for the right ear and 93 dB HL for the left ear (Figure 1). In comparison with the audiograms obtained at the age of 10 years, her hearing had deteriorated by approximately 35 dB HL. Speech discrimination using standard, phonetically balanced French word lists (Fournier disyllabic words), was 0% at 100 dB SPL in both ears (Table 1). Tympanometry indicated bilateral normal middle ear pressure. Stapedial reflexes were absent in both ears for all frequencies. TEOAE (Figure 2) and DPOAE were intact in both ears. The efferent system was only functional in the right ear. It was concluded that the afferent system functioned better on the left side and implantation would be more favourable on this left side. ABR testing revealed no repeatable wave forms (Figure 3). She underwent vestibular testing which demonstrated bilateral vestibular areflexia.

The psychological report predicted a rather poor post-

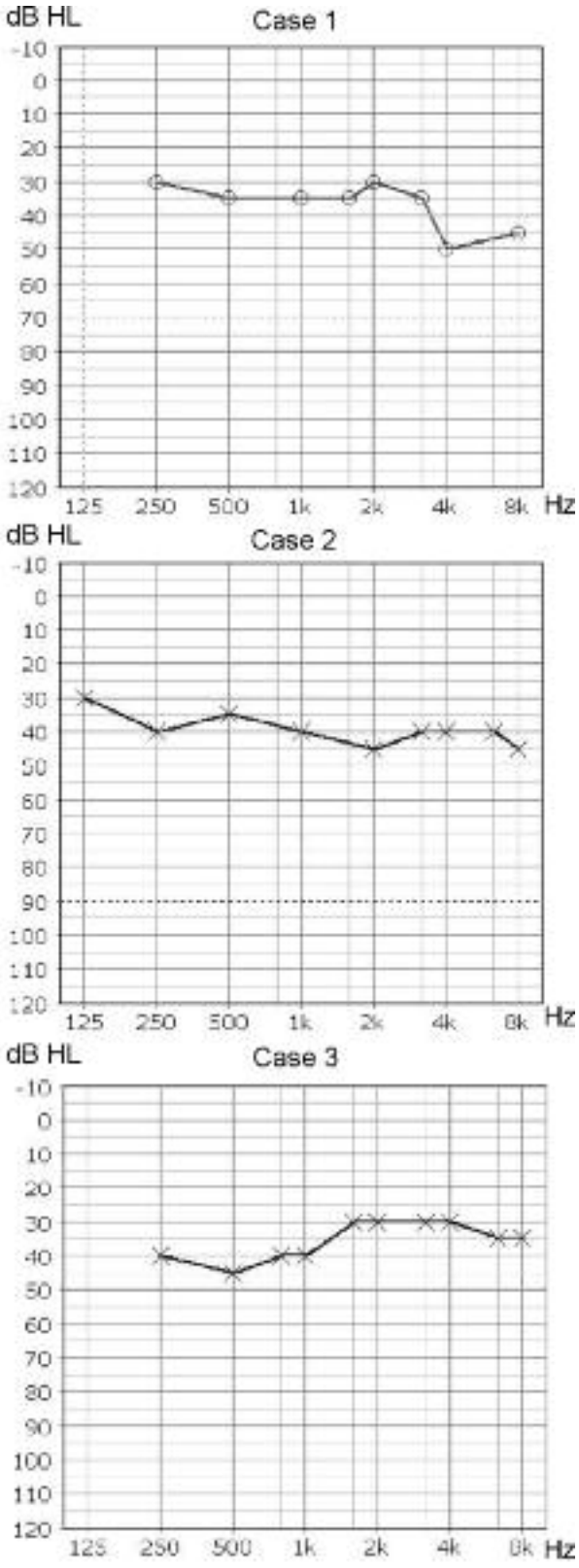

Figure 5
The most recent sound-field pure tone threshold obtained with the implant for Cases 1,2,3.

implantation outcome on the basis of the patient's relatively low motivation for rehabilitation. Furthermore, standard evaluation by the speech therapist indicated that intensive rehabilitation would be required because of very poor communication and very limited language skills. CT of the temporal bones and MRI of the inner ear, cerebello-pontine angle and brainstem were normal.

A Nucleus device (Nucleus 24 Contour, CI 24R CS) was implanted on the left side using standard surgical techniques. Full insertion of the electrode array was accomplished and confirmed with a Stenvers radiography. No postoperative complications were noted.

Results

Case 1

The implant was activated 1 month after surgery and the patient was enrolled in a standardised post-implant habilitation programme. The functional assessment involved a follow-up period of 24 months.

Postoperative sound field testing at 24 m showed a $PTA_{0,5\text{-}1\text{-}2}$ of 33 dB HL (Figure 5). His speech recognition score for disyllabic balanced words (Fournier disyllabic words) was 56% with the implant alone and 86% using lip reading in combination with the cochlear implant at 24 m after implantation (Table 1). With sentences (MBAA2) a speech recognition score of 99% was achieved with the implant only. The post-implantation communication mode was oral. The patient was able to use the telephone with his son only. Electrical ABR showed good results. The provoked OAEs were still present in the non-implanted ear 24 months after surgery.

Overall, the patient was extremely satisfied with the results.

Case 2

The implant was activated 1 month after surgery and the patient was enrolled in a standardised post-implant habilitation programme. The functional assessment involved a follow-up period of 24 months.

Postoperative sound field testing at 24 months found an average puretone threshold of 40 dB HL (Figure 5) and speech recognition score (NVA, CVC, phoneme score) of 86.5% at 70 dB SPL after implantation (Table 1). The post-implantation communication mode was oral. The patient was able to use the telephone with familiar voices. Overall, the patient was satisfied with the results.

Case 3

The implant was activated 1 month after surgery and the patient was enrolled in a standardised post-implant habilitation programme. The functional assessment involved a follow-up period of 24 months.

Postoperative sound field testing at 24 months showed an aided $PTA_{0,5\text{-}1\text{-}2}$ of approximately 38 dB HL (Figure 5). Her speech recognition score (Fournier disyllabic words) was 48% with the cochlear implant, and 78% using the cochlear implant in combination with lip reading for disyllabic balanced words at 24 months (Table 1). For sentences (MBAA2) 68% speech recognition with the implant only was achieved 24 months after implantation.

The post-implantation communication mode was oral and the patient was not able to use the telephone. Electrical ABR generated large and stable responses. However, the auditory origin of these potentials is questionable and may be of myogenic nature. NRT-derived potentials were absent. The provoked OAEs were still present in the non-implanted ear, but absent in the implanted ear 24 months after surgery.

Discussion

AN/AD was first described in 1996 and continues to generate conflicts and controversy among professionals. Fortunately, thanks to advances in otogenetics for one thing, the underlying pathophysiological mechanism is slowly being elucidated, and two distinct entities are being identified. One entity comprises lesions associated with the inner hair cells or synaptic junction, while the other involves the true neuropathies. Clinically, this is expressed in one group as mainly early-onset, severe to profound deafness, and in another group as late-onset, progressive forms of hearing loss. The three patients discussed clearly illustrate the variety of clinical findings that can exist in AN/AD. As in most adult patients with AN/AD described in the literature, concomitant peripheral neuropathies (motor sensory neuropathy in Case 1, and bilateral optic nerve atrophy and chronic progressive external ophtalmoplegia in Case 2) were found in two of our patients. We advise additional neurological examinations in all adult cases where there is a suspicion of AN/AD.

Overall, the prevalence of AN/AD has been reported to be higher in paediatric populations, but AN/AD in adults is probably under-diagnosed. Adults with AN/AD may exhibit limited auditory problems with a relatively slow decrease in speech comprehension, and the tests to identify AN/AD (OAEs and/or CM in combination with ABR) are not routinely performed in adults. A discrepancy between the pure-tone audiogram and the speech recognition scores should alert the clinician to the possible involvement of AN/AD. Absent or elevated stapedial reflexes in combination with OAEs raise a strong suspicion of AN/AD and warrant ABR testing.[17] However, emissions can be lost over time, so an active search for cochlear microphonics recordings is necessary.[6]

The first papers looking at the potential benefits of cochlear implantation in AN/AD patients date from 1999.[4,7] Since then, a multitude of papers have been published, mainly reporting on children. Most of these reports have demonstrated that cochlear implantation is successful in AN/AD. As cochlear implants serve to activate the available nerve fibres, or to synchronise those neural elements that cannot discharge in a suitable manner,[8] effectiveness could be related to the site of lesion pathology. It is possible that children more often exhibit AN/AD caused by inner hair cell damage or synaptic junction defects. Adults, on the other hand, have genuine neuropathies more often. Moreover, in contrast to adults, children can benefit from early rehabilitation. In general, most AN/AD patients with implants have benefits consistent with their implanted sensorineural peers.[5,8,9,18]

The effectiveness of implantation has been shown on the basis of both objective (electrically evoked Compound Action Potentials and postoperative electrical ABRs) and subjective (pure-tone audiogram and speech recognition score) tests. Reports with less optimal results after cochlear implantation are scarce.[4,7] In addition, patients with (non-AN/AD) cochlear deafness whose eABRs are absent and whose speech perception benefits little from cochlear implantation have also been described.[19] In our three patients, the results were variable. Case 3 showed little benefit after cochlear implantation and exhibited poor audiological performance and electrical ABR responses. However, she already had a less favourable prognosis pre-operatively because of long-term deprivation from auditory stimulation, and because of the poor results of psychological and speech-therapeutical assessments. On the other hand, poor outcome could be caused simply by the site of lesion pathology and, more specifically, the degeneration of the auditory nerve.

The patient with a motor sensory neuropathy performed extremely well after implantation and electrical ABR showed good results. Postelmans *et al.*[20] have already described successful cochlear implantation in a patient with Charcot-Marie-Tooth and AN/AD. Demyelination is probably not as marked at the level of the auditory nerve as at the level of the long non-cranial peripheral nerves, and this could explain successful implantation in this patient. Zhou *et al.*[21] have reported electrical stimulation to produce synchronous ABRs in the presence of peripheral auditory nerve demyelination. Case 2, who has additional cranial neuropathies, is also a successful cochlear implant user.

Candidates considered appropriate for cochlear implantation need both a minimum number of functioning auditory nerve fibres and the ability to discharge these nerve fibres synchronously. In contrast to Case 3, cochlear implantation in Cases 1 and 2 led to encouraging results with improved audiological performance. Mason *et al.*[9] advise against cochlear implantation in AN/AD ears with no auditory perception in response to promontory stimulation. The favourable results obtained in Case 2, who only experienced pain on promontory stimulation, contradict this hypothesis. Unfortunately, in Case 2, no intra-operative eABRs or any other electrophysiological or postoperative measurements were performed.

Conclusion

AN/AD is a heterogeneous condition in terms of clinical features, audiometric findings, prognosis of aural rehabilitation, aetiology and pathophysiology. Cochlear implantation is currently the most successful rehabilitation strategy for patients with poor sensitivity and speech understanding caused by AN/AD. Most implantees with this form of hearing loss have good access to the normal speech spectrum and speech perception abilities comparable with their sensorineural counterparts. However, because isolated cases with poor results have been reported, candidates identified with AN/AD need to be counselled accordingly.

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