Case Report

Cochlear Implants in Alström Syndrome

Annals of Otology, Rhinology & Laryngology
2020, Vol. 129(8) 833–837

DOI: 10.1177/0003489420903061
journals.sagepub.com/home/aor
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Abstract

Objectives: Too little is known about hearing loss rehabilitation in patients with Alström syndrome (AS). Benefits of hearing aids (HA) have not been fully documented and only one case treated with a Cochlear Implant (CI) has been described in the proceedings of a conference. Furthermore, comorbidities and risk of complications following surgical intervention may contraindicate Cochlear Implant procedures in these patients.
The present case report concerns the first AS patient with CI in the literature.
Methods: After reporting a concise description of the audiological profile of patients with AS described in the literature, the case of a 22-year-old woman with genetically confirmed Alström syndrome who underwent a sequential bilateral CI (Bi-CI) rehabilitation is reported. Audiological results before and after cochlear implantation are described.
Results: The patient showed an excellent functional outcome with CIs, which enabled her to achieve communicative, social and academic results comparable with her peers, and no complications occurred.
Conclusions: AS is not necessarily an absolute contraindication to CI. For many AS patients, a good cognitive function and adequate life expectancy represent a clear indication to prompt and adequate hearing rehabilitation with CIs. The description of this type of clinical cases could in the future also generate indications for a tailored audiological treatment of patients with very specific needs, such as patients with Alström Syndrome.

Keywords
Alström syndrome, deafness, cochlear implant

Introduction

Alström syndrome (AS; OMIM 203800) is a rare autosomal recessive genetic disorder with a prevalence of 1-9 per 1,000,000 population. It is characterized by cone-rod dystrophy, gradual hearing loss, truncal obesity, insulin resistance, diabetes mellitus type 2, hypertriglyceridemia, short stature, cardiomyopathy and progressive renal, hepatic, and pulmonary diseases.[1] The syndrome is caused by mutations in ALMS1, a gene that encodes a ciliary protein. Many of the symptoms of this syndrome appears in infancy and early childhood, other signs may appear at a later stage. Seventy percent of patients progressively develop bilateral sensorineural high-frequency hearing loss in the first 10 years of life,[2-4] though the age of onset of their hearing loss and its severity can differ considerably, even in the same family.

A previous study[5] evaluated phonological working memory and executive functions (EFs) in 10 young adults with Alström syndrome. All patients had a moderate to profound hearing loss, and they were fitted with bilateral hearing aids (HAs). The limitations in executive functions found in AS patients compared to 20 aged-matched controls seemed to be related to early blindness and hearing loss, and maybe also to gene specific abnormalities.

In a 2015 study,[4] the authors have reported the histopathology of the inner ear of two patients affected by AS. Regarding the first case, a woman, dead at the age of 42, developed a hearing loss in the first 10 years and wore HAs throughout life. An audiometric test performed at age 41 showed a bilateral profound sensorineural hearing loss. The second case was a young man, dead at the age of 29, who developed a moderately severe bilateral sensorineural hearing loss during childhood and who wore HAs by the age of 7. In both patients, degenerative changes in the organ of Corti and spiral ganglion cells and atrophy of the stria vascularis and spiral ligament were found to be the predominant histopathologic correlates of the hearing loss.

A 2013 study[6] analysed the genetic and audiological findings in two family members with AS through a

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complete otorhinolaryngological assessment. Both patients suffered from bilateral sensorineural hearing loss since childhood. In the first case hearing loss has progressed to moderate loss, while it has progressed to the point of being profound in the second case. Normal auditory brainstem responses (ABR), normal tympanometry and absent otoacoustic emissions (OAEs) were found in both cases, and this suggests a cochlear origin of hearing loss.

The auditory profile of AS has been recently characterized in an interesting study[7] of 38 AS patients, aged 1.7-37.9 years. Audiometric assessments showed mean pure tone average of 48.6 dB HL in the right ear and 47.5 dB HL in the left ear. When analysing the right and the left ear separately, normal hearing thresholds were observed only in 11% of cases. The diagnosis of hearing loss (at an average age of 7.45, range 1.5-15) was preceded by the diagnosis of retinal dystrophy in all cases. Hearing loss was mainly sensorineural, occurred during childhood, and in more than half of the reported cases the degree was moderate. The audiometric results of more assessments over time, available for 33 patients, showed significant hearing loss progression with age of approximately 10-15 dB/decade. Predominantly normal ABR (80%), intact speech discrimination and the absence of OAEs in 71.2% of ears have suggested an outer hair cell site of lesion.

In our experience, a 31-year-old woman with genetically confirmed Alström syndrome attending department of medicine at Padua University Hospital suffered from mild sensorineural hearing loss, recurrent otitis, pulmonary infections and progressive visual loss since childhood, and she went totally blind before she was 30. She has developed congestive heart failure, hyperinsulinemia, diabetes mellitus and endocrine disturbances included hypothyroidism and hyperandrogenism from an early age. Inner ear damage or alterations in the central nervous system were excluded by magnetic resonance imaging. She began to wear hearing aids at the age of 10, with partial benefit, but information obtained through the audiometric examinations have become increasingly inconsistent over time, and the patient has become highly unreliable, mainly due to her reduced executive functions, attentive-cognitive deficit and depression.

Even though hearing loss is rather common in AS, the prevalence of AS patients with severe to profound hearing loss, and therefore suitable candidates for cochlear implantation, is estimated to be below 10%.[1] Furthermore, some comorbidities associated with Alström Syndrome, such as cardiomyopathy and renal, hepatic or pulmonary diseases, may imply an increased incidence of complications related to general anesthesia, and consequently a contraindication for cochlear implant (CI).[2]

There is a shortage of knowledge regarding hearing loss rehabilitation in this setting. Benefits of using hearing aids (HAs) have not been fully documented, and as for the CI outcome, it is hard to predict because of possible multiple comorbidities.

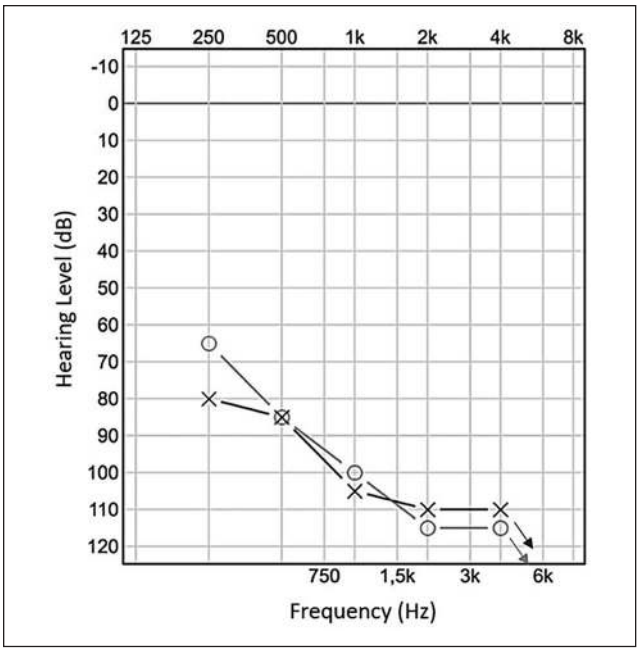

Figure 1. Pure tone air conduction thresholds, prior to cochlear implantation. X curve represent the thresholds for the left ear, O curve represent the thresholds for the right ear.

Only one case of treatment with cochlear implant has been reported in the proceedings of a conference.[8] The present case report concerns the first AS patient to be treated with CI in the literature.

Case Report

A 22-year-old woman with genetically confirmed Alström syndrome (genotype ALMS1: NM_015120.4: c.[6486_6489delAACT;6486_6489delAACT] NP_055935.4: p.[Thr2163Lysfs*4; Thr2163Lysfs*4]) had suffered from total blindness, non-alcoholic steato-hepatitis with increased transaminases, type 2 diabetes mellitus and hypertriglyceridemia since the age of 10 years; she also had an episode of heart failure when she was 8 months old, with residual mild dilation of right atria.

Distortion product OAEs had been absent since birth, and she had worn HAs from the age of 10 months, when an audiological assessment confirmed a mild bilateral sensorineural hearing loss. Up until the age of 11 years, her hearing had benefited from using HAs. Then her hearing began to deteriorate rapidly and, by the age of 13, she had developed a profound bilateral symmetrical sensorineural hearing loss with a pure tone average (PTA_2) of 102.5 dB nHL for the left ear, and 103.7 dB nHL for the right. (PTA_2 consists of the average of threshold levels at 500, 1000, 2000, and 4000 Hz). (Figure 1). No ABR was detected at maximum

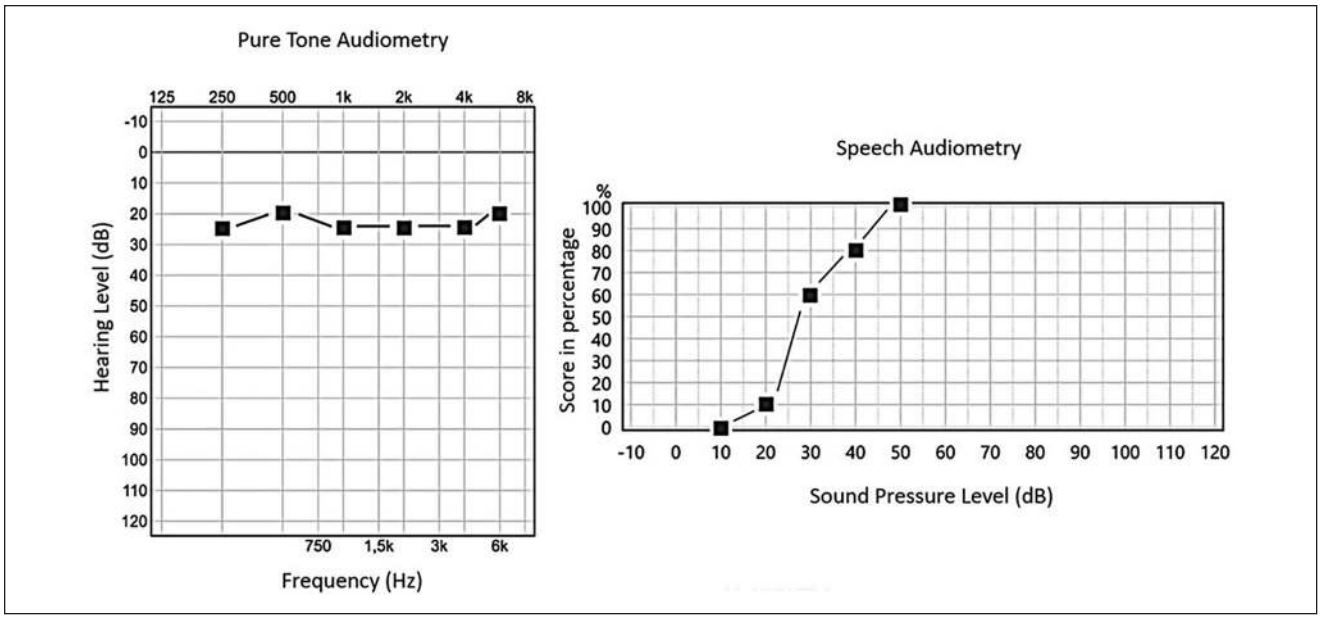

Figure 2. Free field pure tone threshold (left side of figure) and speech audiometry (right side) after cochlear implantation, left ear (at the follow-up 6 months after the second CI activation). Speech audiometry provides information about speech detection, identification and recognition. The values for three parameters were evaluated: Speech Detection Threshold (the lowest level sound at which the listener can hear the presence of a speech signal in 50% of the cases), Speech Recognition Threshold (the lowest level sound at which the listener can correctly repeat the speech stimuli 50% of the time), and word recognition score (the percentage of words correctly repeated by the listener).

intensity stimulation. Videonystagmography with caloric stimulation revealed a bilateral minimal canalar paresis of 24% in the right ear and 14% in the left. Speech perception with the HA was no longer adequate (word intelligibility in the better ear was 53%), and the patient began to refuse the HA in her right ear. Inner ear abnormalities or central nervous system alterations were ruled out on 3-Tesla magnetic resonance imaging. Cognitive assessment showed normal values for the patient's age, despite her multisensory deficit. She was strongly motivated and very well supported by her family.

Her general state of health, corresponding to an ASA physical status III, was acceptable for the purposes of CI surgery. At age 13, she underwent right ear cochlear implantation.

No abnormalities occurred at the time of surgery, and a standard surgical technique was used with mastoid tympanotomy and a round window approach to fit an Advanced Bionics, HiRes CI with the full insertion of the 1J, and an array of 16 electrodes. There were no anesthetic or surgical complications despite the patient's many comorbidities. Good functional results were achieved with the CI and 6 months after its activation, the patient also rejected the contralateral HA. At 12-month follow-up, vestibular function examination ruled out any worsening of the patient's caloric vestibular reflectivity (particularly in the implanted ear). Vestibular-evoked myogenic potentials (VEMPs) were still bilaterally present, allowing for a second CI in the left ear 16 months after the first in the right ear.

At the follow-up 6 months after activating the second CI, PTA_2 was 23.75 dB nHL for the left ear, and 26.25 dB nHL for the right.

Sound detection thresholds did not differ across different frequencies (250, 500, 1000, 2000, 4000, and 6000 Hz), neither between the two ears. (Figures 2, 3) Speech detection threshold (SDT, the lowest level sound at which the listener can hear the presence of a speech signal in 50% of the cases) and speech recognition threshold (SRT, the lowest level sound at which the listener can correctly repeat the speech stimuli 50% of the time) were 10 dB and 30 dB, respectively, for both ears. The patient reached a word recognition score (WRS) of 100% in either ear at 50 dB SPL stimulation level (free-field presentation of a list of words). (Figures 2 and 3) Vestibular caloric function follow-up further excluded any deterioration, and the patient's balance and postural assessments were normal, while VEMP responses were bilaterally absent.

Free field hearing threshold and WRS with the CIs remained unchanged over time at subsequent follow-ups. At the latest visit one year ago, PTA_2 was 18.75 dB and 23.75 dB, for the left and the right ear, respectively; and 100%-word recognition was reached at 40 dB SPL (there was no difference between ears).

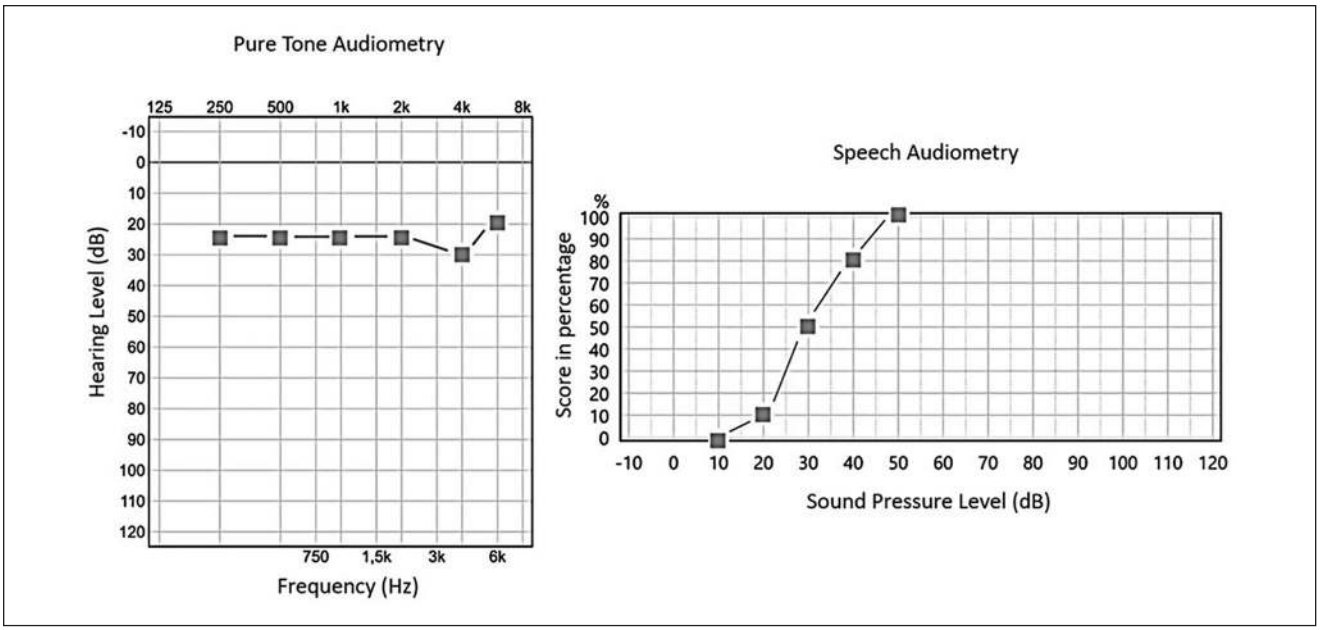

Figure 3. Free field pure tone threshold (left side of figure) and speech audiometry (right side) after cochlear implantation, right ear (at the follow-up 6 months after the second CI activation).

The patient was not able to perform the word recognition test in free field before cochlear implantation, while she obtained a good WRS score with the CIs since the early follow-ups after activating the second implant, and there was an increase in speech audiometric outcomes over time.

Speech intelligibility in noise was also assessed using the Italian Matrix Sentence Test (an adaptive method aiming for the 50% threshold of speech intelligibility [SRT] with a background noise level of 65 dB). The patient's SRT score was 1.8 (signal-to-noise ratio), a very good result for patients with CIs.

At the last follow-up visit patient was 22 years old. She showed normal scoring in the Verbal Comprehension Index (VCI = 92); Moreover, she had a good level of autonomy included the activities of daily living (ADL) (6/9) and instrumental activities of daily living (IADL) (9/14). She had no difficulty listening to television, talking on the phone or listening to music. She has also earned a bachelor's degree.

Discussion

These excellent results suggest a cochlear origin of hearing loss, most likely caused by alterations of outer hair cells and alterations in the stria vascularis, not involving central auditory pathway.

Data from published studies confirm how AS patients with hearing loss would benefit from HA, or in the case of severe to profound hearing loss, from CI surgery.

It is difficult to standardize auditory rehabilitation for patients with AS, which may be particularly challenging in cases not adequately benefiting from the use of HAs. Anesthesiological and infectious risks may contraindicate CI procedures but being blind and deaf is likely to severely impair a patient's ability to communicate and quality of life.

Most AS patients demonstrate normal cognitive functions, but vision and hearing loss occurring in childhood may cause impairment of the executive functions. In some cases, depression and anxiety disorders has been also reported.

Cochlear implantation restores one of the missing sensory modalities and it is a huge opportunity for communication.

The development of language functions can be significantly improved through an early rehabilitation of hearing loss.[6]

The potential gains in life quality from CI surgery could be great for AS patients. The possibility of improving verbal ability and executive functions, through the implementation of specific cognitive methods and adequate treatment and rehabilitation programs, may be essential for this type of patients.[5]

A good cognitive function and adequate life expectancy represent a clear indication to prompt and adequate hearing rehabilitation with CIs.

In the case reported here no surgical or post-operative complications have occurred and the patient achieved excellent results with CIs, which enabled her to achieve communicative, social and academic results comparable with her peers.

Conclusion

Comorbidities and risk of complications following surgical intervention may contraindicate CI procedures in AS patients, but Alström syndrome is not an absolute contraindication to CI providing the anesthetic, surgical and vestibular risks associated with the procedure are adequately assessed by a multidisciplinary team. An adequate preoperative evaluation and an experienced anesthesia team are crucial. Specific counseling should inform patient and families of the variable functional results. Communicative rehabilitation after surgery should consider the specific needs of AS patient. In future, multicenter data on more cases of CI in AS patients could help to generate indications for a tailored treatment.

Acknowledgments

The authors thank Dr. Favaretto Francesca and Dr. Lorusso Riccardina for their contributions.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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