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Case Report

Cochlear implantation in pediatric patients with Cockayne Syndrome

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ABSTRACT

Cockayne Syndrome (CS) is a rare, autosomal recessive disorder characterized by a spectrum of phenotypic abnormalities, including progressive sensorineural hearing loss (SNHL) that involves both peripheral and central components. To date, a single series of CS patients undergoing cochlear implant (CI) placement has been reported; this study reports on additional previously unreported pediatric CI recipients. Subjective benefits were noted early after activation in both patients, and speech perception scores improved over time as well, varying from 42 to 70% (versus 0–12% previously). Thus, we report that cochlear implantation in pediatric patients with CS can be effective in the management of progressive SNHL.

1. Introduction

Occurring in approximately 2 per million newborns in the United States and Europe, Cockayne syndrome (CS) is a rare, autosomal recessive disorder characterized by short stature, progeria, photosensitivity, and impaired neurological development [1]. Mutations in the ERCC gene are the underlying cause, resulting in disruption of DNA repair. Other progressive symptoms include hearing loss, tooth decay, and eye and bone abnormalities. The disorder spans a phenotypic spectrum classified into four types: CS type I, CS type II, CS type III, and Xeroderma pigmentosum-Cockayne Syndrome (XP-CS). See Table 1 for a description of these different types.

To date, only one case series of two patients with CS who received cochlear implants represents the entirety of published literature on this topic [2]. The first patient exhibited a mild presentation suggestive of CS type III. The second patient had earlier neurological deterioration and handicap consistent with CS type I. Each was 36 and 21 years old, respectively, at the time of cochlear implantation. The former communicated great satisfaction with her improvement in hearing, while the latter did not experience significant benefit [2]. Herein, we present the first two cases of pediatric patients with "classic" CS type I who underwent cochlear implantation for progressive hearing loss with both conductive and sensorineural components. Both benefitted significantly from cochlear implant placement by both subjective and objective measures. Thus, we report that cochlear implantation can be an appropriate intervention for pediatric patients with CS despite both the peripheral and central auditory impairment that occurs in these patients.

2. Case 1

Patient 1 is an outgoing male that was diagnosed with Cockayne Syndrome at the age of 5. DNA sequence analysis of the ERCC6 gene identified seven separate mutations. Major limitations associated with his disorder included severe spasticity and contractures, impaired neurological development, and progressive hearing loss. At age 13, his language comprehension and expression were significantly delayed to a 3.5-year age level, and the Kaufman Brief Intelligence Test measured an overall IQ in the impaired range. Nevertheless, he functioned well in school with the help of a full-time aide and enjoyed socializing with his peers.

The patient demonstrated many of the physical characteristics of CS. He appeared older than his stated age with small, shrunken eyes, sparse scalp and eyebrow hair, and very fair skin marked by scattered café-au-lait spots. He was of short stature with a microcephalic head and a prominent nose and ears.

2.1. Investigations

At age 5, MRI revealed significant white matter abnormalities as well as cerebral and cerebellar atrophy in the setting of microcephaly. The optic apparatus appeared hypoplastic or atrophic (see Fig. 1).

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Table 1
Description of the different types of Cockayne Syndrome.

Type	Typical age at diagnosis	Common signs and symptoms
Type I	First 2 years of life	Microcephaly, failure to thrive, short stature, delayed development, photosensitivity, vision and hearing impairment, dental cavities
Type II	Birth	Severe growth failure at birth, impaired neurological development, congenital cataracts, congenital joint contractures, early postnatal contractures of the spine
Type III	After the first 2 years of life	Skin blistering, abnormal sense of smell, dental cavities, increased photosensitivity, vision and hearing impairment
Xeroderma-pigmentosum	First 5 years of life	Similar to Type I with an increased risk of skin cancers

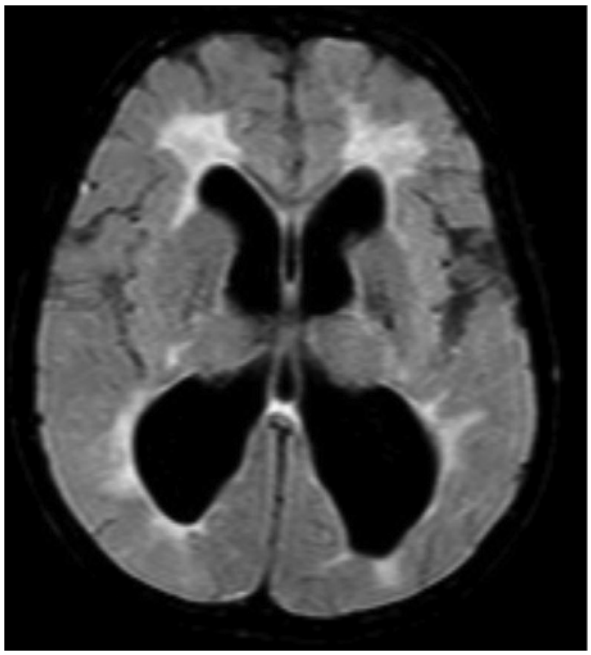

Fig. 1. MRI at age 16 revealed significant white matter abnormalities as well as cerebral and cerebellar atrophy in the setting of microcephaly.

At age 16, the patient experienced a sudden change in hearing despite his binaural hearing aids. He was doing well until two months prior, when his parents noticed that he had stopped responding appropriately. The hearing aids were checked and were found to be functioning normally. His hearing had decreased significantly, and he began using a desktop FM speaker and completing much of his classwork online.

Acoustic immittance testing indicated type A tympanograms bilaterally, suggesting normal middle ear pressure and compliance. Ipsilateral acoustic reflexes and distortion product otoacoustic emissions were absent in both ears, consistent with abnormal cochlear outer hair cell function bilaterally. Behavioral evaluation was completed using conventional audiometry. Responses to speech- and frequency-specific warbled tones, 250–8000 Hz, revealed profound hearing loss in both ears. There was no consistent response to stimuli at equipment limits in the left ear. The patient was conditioned using vibrotactile stimulation. Hence, profound sensorineural hearing loss was confirmed. After his rapid decline in auditory functioning, the patient became less talkative and more withdrawn socially. His propensity to engage others was proportional to his ability to communicate. Neuropsychiatric testing considered him a good candidate for cochlear implantation. An Advanced Bionics HiRes 90K Advantage CI was implanted in the right ear without complication (see Fig. 2).

2.2. Postoperative progress

After activation, the patient showed significant benefit from cochlear implantation, both socially and objectively in school. After one month, aided testing in the sound field revealed a speech reception threshold of 30 dB HL and responses to narrowband noise between 15 and 20 dB HL for the 250–6000 Hz frequency range indicating good detection of sound. On speech testing using (WIPI) Word intelligibility Using Picture Identification, the patient scored 84% at 60 dB HL in sound field, indicating significant benefit from his implant.

3. Case 2

Patient 2 was initially identified with a sensorineural hearing loss at age 10, and she started wearing hearing aids at 12 years old. Her hearing loss was essentially symmetrical until age 18, at which time testing revealed a complete loss of auditory function in the left ear. She was subsequently evaluated for cochlear implantation. Other limitations associated with her diagnosis of CS included growth and intellectual impairment, extreme photosensitivity, and a pigeon-toed, abnormal gait secondary to joint limitation and increased tone. She demonstrated relatively typical facies for a patient with CS, and her skin had a senile appearance for her stated age.

3.1. Investigations

At age 19, the patient completed evaluation for cochlear implantation. CT of the temporal bones revealed moderate cerebral and cerebellar atrophy as well as deep gray nuclear calcification. Hearing testing confirmed a severe sensorineural hearing loss in the right ear and a profound sensorineural hearing loss in the left ear (see Figs. 3 and 4). She continued to use a hearing aid in the right ear and maintained a remarkably high level of speech discrimination with amplification on that side. At that time, the patient was not considered to be an appropriate candidate for cochlear implantation, as she was benefitting significantly from amplification alone.

Several changes were attributed directly to her progressive hearing loss. Her articulation and intensity deteriorated over time, and it became increasingly more difficult to understand her on the telephone. The patient, once very social, became withdrawn as her hearing function declined. See Table 2 for test results measuring her language and cognitive ability. Her performance across measures of motor functioning, visual-motor integration, visual and verbal memory, and visual discrimination was consistent with the intellectual assessment results.

Due to the progressive nature of her hearing loss, the patient was deemed an appropriate candidate for cochlear implantation six months after her initial audiogram. A Med-EL device was implanted in the left ear without complications.

3.2. Postoperative progress

After activation, the patient noted an improvement in her hearing function after several device adjustments. At her four-month recheck, she noted an increase in awareness of environmental sounds. After one year, aided speech discrimination for phonetically-balanced words was 42%. The Synthetic Sentence Identification test was completed at 70% at a +10 message-to-competition ratio. She continued to report

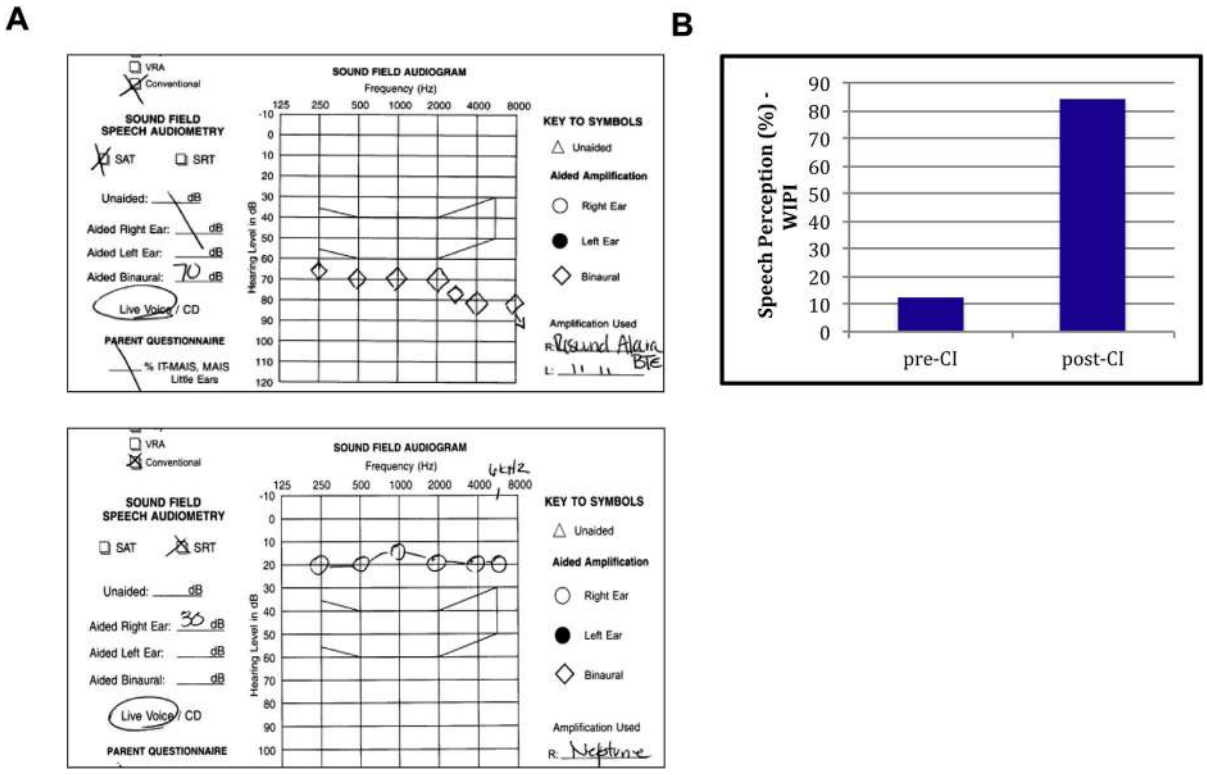

Fig. 2. A. Audiologic evaluation before (top) and after (bottom) cochlear implantation showing benefit with the CI. B. Speech perception improved as well.

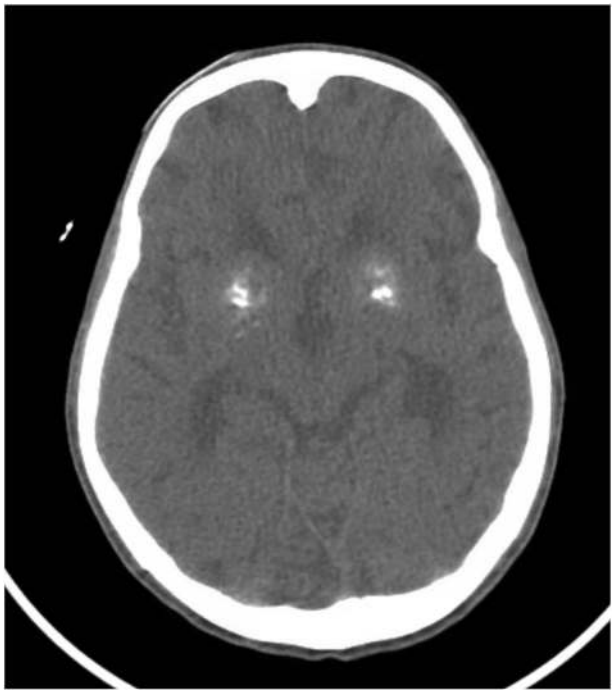

Fig. 3. CT scan at age 19 revealed moderate cerebral and cerebellar atrophy as well as deep gray nuclear calcification.

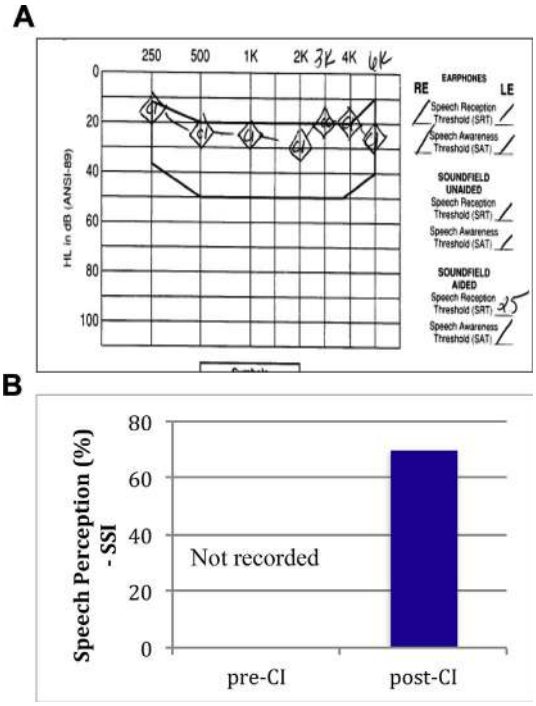

Fig. 4. Audiologic evaluation after cochlear implantation demonstrating benefit in both sound detection (A) and speech perception (B).

subjective benefit from the implant.

4. Discussion

4.1. Cockayne Syndrome

London physician Edward Alfred Cockayne first described CS in 1936. He recognized two siblings that exhibited “dwarfism with retinal atrophy and deafness” and followed up on their progress ten years later. The largest series published in 1992 reviewed 140 cases and described in detail the complications of condition [3]. Most recently, Wilson et al. identified 102 affected individuals and reported the prevalence and onset of clinical features, achievement of neurodevelopmental milestones, and guidelines for patient management [4]. All types are caused

Table 2
Test results measuring language and cognitive ability of Patient 2.

Test	Score	Description
Peabody Picture Vocabulary Test	50 (Extremely low)	Measures receptive vocabulary
Expressive Vocabulary Test and Comprehensive Assessment of Spoken Language	40 (Mean score 100, SD 15)	Measures comprehension, expression, and retrieval in four language categories: lexical/semantic, supralinguistic, and pragmatic
Goldman-Fristoe Test of Articulation	3 years, 7 months	Measures the articulation of consonant sounds
Leiter-R Full IQ test	42 (Mean score 100, SD 15)	Measures overall intelligence

Abbreviations: SD, standard deviation.

by mutations in *CSB/ERCC6* (65% of individuals) and *CSA/ERCC8* (35% of individuals), resulting in the production of malfunctioning proteins that disrupt DNA repair. Molecular genetic testing or a specific DNA repair assay on fibroblasts can confirm the diagnosis [5].

4.2. Cockayne Syndrome and hearing loss

According to Laugel et al., CS patients almost always exhibit progressive sensorineural hearing loss when appropriate hearing tests can be performed, although it may not be clinically significant until later in the disease process [6]. Audiograms of affected individuals detected hearing loss greatest in the high frequencies, while temporal bone pathologic findings revealed hair cell losses in the basal turn of the cochlea with corresponding neuron losses in the spiral ganglion, similar to presbycusis [7]. Auditory brainstem responses (ABRs) measured in two patients over time suggest that the disease progresses from the brainstem to the cochlear nerve. In two more cases, however, ABRs were absent at first examination. Hence, cochlear degeneration cannot be ruled out as a possible etiology [8].

In the Cockayne Syndrome Natural History study, hearing loss presented in 21% of CS patients neonatally and 84% by age 10 years. Interestingly, however, where detailed assessment of hearing loss was available, 44% had conductive or mixed hearing loss [4]. Thus the mechanism of hearing loss varies significantly among CS patients, much like the spectrum of disease.

4.3. Cockayne Syndrome and cochlear implantation

CS presents unique challenges to the cochlear implant team, as the variable association of profound hearing loss, visual impairment, and progressive intellectual deterioration must be managed. Furthermore, both peripheral and central changes in the auditory system are typically present in patients with CS. Given the wide phenotypic spectrum of CS, cochlear implant candidacy must be determined on a case-by-case basis.

In one case series of two adult patients with CS types I and III, substantial and marginal benefits with CI were observed, respectively. For the patient with CS type III, it was unclear whether or not her lack of response was secondary to auditory system deficits or to progressive cognitive impairment, however [2]. Both pediatric patients presented here are characteristic of the Type I, or the “classic” form, of CS, and they benefited substantially from cochlear implantation, by both subjective and objective measures. Patient 2 required several adjustments throughout the course of the year. She was monitored closely at one-month intervals, and her device was remapped and made louder several times to address any deficiencies. This close follow-up allowed for maximal functioning of her CI. Thus, we report that pediatric patients with CS can achieve improvement in auditory function despite both peripheral and central impairment.

Cochlear implantation is especially beneficial in patients that are unable to wear both hearing aids and glasses at the same time. However, both patients presented here maintained use of their hearing aids after cochlear implantation, so their need may not be eliminated entirely. Multidisciplinary, coordinated care between the patient (and family), the physician, implant audiologist, and other members of the CI team is especially important to optimize benefit in patients with CS, particularly given the central auditory changes that are part of the disease spectrum.

5. Conclusions

Cochlear implantation in pediatric patients with CS can be effective in the management of progressive SNHL. Subjective and speech-perception benefits can occur, despite both peripheral and central auditory impairment that occurs in these patients.

COI disclosure

The authors have no potential conflicts of interest to disclose.

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