Cochlear Implantation in Children with CHARGE Syndrome

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Introduction: CHARGE syndrome is a rare congenital condition that manifests with anomalies of coloboma, heart defects, choanal atresia, mental retardation, genitourinary and ear anomalies that can affect almost any part of the auditory pathway. In those patients with a significant sensorineural hearing loss, cochlear implantation has become a potential therapeutic option.

Methods: Chart review of three cases from the Southern Cochlear Implant Programme.

Outcomes: All patients met clinical diagnostic criteria of CHARGE syndrome, and had abnormal inner ear anatomy with profound sensorineural hearing loss. One child had previously undergone cochlear implantation which was unsuccessful due to increasing non-auditory stimulation. All patients had successful cochlear implantation with full insertion of a Nucleus Freedom Implant with contour Advance. All patients showed improvement in their audiological function; one child has high functioning verbal communication, one child uses both sign and verbal communication with improved speech quality and ability to speech read, and one child responds reliably to sound, understands short phrases and attempts to vocalize, but this is limited by tracheostomy.

Conclusion: Cochlear implantation faces numerous challenges in children with CHARGE syndrome, but with appropriate patient selection can result in successful audiologic and quality of life outcomes.
KEYWORDS CHARGE, cochlear, hearing loss, implant

Introduction

CHARGE syndrome is a rare congenital condition that manifests with anomalies of coloboma, heart defects, choanal atresia, mental retardation, and genitourinary and ear anomalies (Pagon et al., 1981). Almost any part of the auditory pathway can be affected resulting in a conductive, mixed or sensorineural hearing loss. In those patients with a significant sensorineural hearing loss, cochlear implantation has become a potential therapeutic option. There have only been a small number of case reports in the literature of cochlear implantation in patients with CHARGE syndrome, with variable anatomical anomalies, surgical challenges and audiological outcomes reported (Weber et al., 1998; Bauer et al., 2002; MacArdle et al., 2002; Lanson et al., 2007). This paper presents three more such cases and describes the relevant preoperative assessment, radiological and surgical findings, and outcomes.

Method

A review was carried out of cochlear implants performed by the New Zealand Southern Cochlear Implant Programme from 2003 to 2008. Three patients were identified as having CHARGE syndrome and all went on to receive cochlear implantation. All records were reviewed for diagnostic criteria and manifestations of CHARGE syndrome, preoperative audiology assessment, radiological findings on computer tomography (CT), surgical findings and their correlation with preoperative imaging, postoperative audiology assessment and functional outcomes.

Patients

Case 1

A 17-year-old male presented with progressive mixed hearing loss. A diagnosis of CHARGE syndrome was made at birth in the UK, the clinical records of which are unavailable for review. The known major criteria were:

- choanal atresia repaired at five days old;
- hearing loss, which was recognized early in life with hearing aids worn from the age of five months;
- abnormal pinna;
- right hemifacial microsomia with facial nerve palsy for which he had undergone cross-facial nerve grafting making the temporal portion of this facial nerve essentially nonfunctioning.

Known minor criteria include mild developmental delay. Audiologically he had been a consistent hearing-aid user, had used oral receptive and expressive language since the age of five and had attended mainstream schooling.
At the age of 16 his hearing on the right deteriorated to the extent that he was reliant upon his aided left ear and significant visual cues in order to communicate. He had a long history of middle-ear disease with multiple sets of ventilation tubes. At the time of his audiological assessment for cochlear implantation he had an unaided bilateral severe-profound sensorineural hearing loss with a significant conductive component (see Figure 1) and type-B tympanograms. Aided thresholds showed good levels up to 2000 Hz but above this hearing fell outside the speech spectrum. His speech discrimination assessment showed a binaural score of 45% in auditory alone hearing-in-noise testing (HINT-C) sentences, reaching current audiological cochlear implant criteria.

Preoperative imaging was performed with CT and showed a number of abnormal features (see Figure 2). He had bilaterally absent posterior and lateral semicircular canals with hypoplasia of the superior semicircular canals. The cochleae appeared slightly dysmorphic but still had two-and-a-half turns, with normal appearance of the IAC. Both oval windows appeared atretic and there was dehiscence of the tympanic portion of the facial nerve bilaterally. There was evidence of mastoid mucosal disease on the left. An anterior extension or diverticulum of the sigmoid sinus was apparent on the right.

Despite this finding it was decided to proceed with a cochlear implant on the right for multiple reasons: the left ear had known mucosal disease and had been infected recently; the left ear was also his better hearing ear, and the right facial nerve was known to be nonfunctioning in its tympanic segment due to the previous cross-facial graft. Intraoperatively a large sigmoid diverticulum that essentially obscured all

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**FIGURE 1**

[Diagram showing hearing thresholds pre-op and post-op]
passage to the mastoid antrum was found. This was managed by removing the overlying bone and decompressing the diverticulum with surgicel and bone wax to allow adequate exposure. The facial nerve was found to be dehiscent and ran inferior to the oval window and posterior to the round window niche. A cochleostomy was drilled anterior and inferior the round window and a Nucleus Freedom implant with contour advance electrode was advanced in the scala tympani with insertion of all 22 electrodes. The young man had an uneventful postoperative recovery.

Audiology assessment four months following implantation showed an excellent early result. He reported improved ability to listen in the classroom and being able to understand conversations without visual prompts. Sound-field audiogram showed thresholds between 20–30 dB across all speech frequencies (see Figure 1) and speech discrimination tests showed an average of 89% correct HINT sentences in quiet and 61% in noise (+5dBSNR) when testing his cochlear implant ear alone (see Table 1). Both the patient and his parents reported a significant improvement in his hearing.

TABLE 1

<table>
<thead>
<tr>
<th>Test material</th>
<th>CI ear alone in quiet</th>
<th>CI in noise (+5dBSNR)</th>
<th>CI and hearing aid in noise</th>
</tr>
</thead>
<tbody>
<tr>
<td>HINT sentences for adults in quiet</td>
<td>Average 89%</td>
<td>Average 61%</td>
<td>Average 84%</td>
</tr>
</tbody>
</table>

Figure 2: Axial CT showing a large sigmoid diverticulum obscuring the passage to the mastoid antrum.
Case 2

A 14-year-old male who had previously undergone left cochlear implantation nine years earlier at the age of four. His major criteria for CHARGE syndrome include:

- hearing loss;
- bilateral choanal atresia;
- pinna anomalies.

Minor criteria include:

- growth deficiency;
- gonadal hypoplasia requiring testosterone replacement;
- development delay;
- distinctive facies.

His previous left cochlear implantation was performed 10 years ago and he developed problems with nonauditory stimuli that led to progressively more electrodes being switched off. By the time of his cochlear implant assessment he had only seven electrodes switched on and received essentially no useful input from the implant. Sound-field audiometry showed moderate-to-profound thresholds in most of the speech frequencies (see Figure 3). He used a combination of sign and spoken language to communicate. His case was discussed by the cochlear implant programme team and the decision was made to reimplant him on the same side.

![Figure 3](image-url)
Preoperative imaging with CT showed the previous left cochlear implant with an artifact arising from this. The implant appeared to have migrated with no electrode array present beyond the basal turn. Bilaterally he had complete agenesis of the semicircular canals.

Intraoperatively the receiver/stimulator was found to have migrated anteriorly a significant distance and the electrode were embedded in newly formed bone in the mastoid cavity. The electrode was cut and the previous device removed. The facial nerve was found to be dehiscent and in an abnormal position running immediately superior to the promontory, over the oval window, then immediately posterior to the round window in a relatively anterior position. A new cochleostomy was made antero-inferior to the round window, and a Nucleus Freedom implant with contour advance electrode was fully inserted. He had an uneventful postoperative recovery.

Postoperative audiology assessment one-year post implantation showed him to be a good implant user. He was reported to have benefited from increased awareness of environmental sounds and ability to lip read since his reimplantation. There is a reported improvement in the clarity of his speech with increased use of voiceless sounds in speech. Sound-field audiometry showed thresholds between 45 dB and 70 dB across the speech frequencies (see Figure 3), which correlate with his ability to gain benefit from the implant but not to hear speech at conversational levels. To date he remains with a limited dynamic range. He has no significant nonauditory stimulation.

Case 3
A three-year-old female with multiple CHARGE-related disabilities. Major diagnostic criteria included:

- bilateral severe sensorineural hearing loss;
- bilateral coloboma with early glaucoma;
- left hemifacial microsomia with facial weakness but good eye closure.

Minor criteria included:

- Cleft palate and lip repair with poor oral intake requiring long-term gastrostomy feeding. She had acute airway deterioration following cleft surgery resulting in tracheostomy placement, which has remained due to persistent supraglottic odema thought secondary to severe reflux.
- Cardiac anomalies consisting of a small patent ductus arteriosus and a right ventricular rhabdomyoma.
- Global developmental delay.

She was recognized early on as having hearing loss and was fitted with hearing aids at the age of six months. Her family reported little response to the hearing aids at home and she showed no apparent awareness of sound. She had middle-ear disease and three previous sets of ventilation tubes placed with no reported improvement in her hearing. Her other comorbidities and surgical requirements precluded active
management of her hearing loss earlier. Preoperative audiology assessment reliably showed a profound mixed hearing loss, which only improved to a moderate-severe loss with high-powered hearing aids (see Figure 4), insufficient to provide audibility for spoken language development, and a recommendation for cochlear implantation was made.

Preoperative imaging with CT scanning showed bilateral mucosal disease of the middle ear and mastoid cells. The ossicles appeared mildly dysmorphic. Bilaterally she had abnormal vestibular apparatus, with complete absence of the semicircular canals and a hypoplastic vestibule on the left and only a rudimentary posterior semicircular canal but normal vestibule on the right (see Figure 5). The internal auditory canal, cochlea and vestibular aqueduct appeared normal bilaterally.

The decision was made to implant her on the left, the side of her pre-existing facial weakness.

At surgery a moderately well pneumatized mastoid was found, lacking a lateral semicircular canal. The middle fossa dural plate was followed down to the antrum and the aditus ad antrum opened to display the short process of the incus. The tympanic segment of the facial nerve could then be seen through the aditus prior to opening of the facial recess, although the facial nerve was in an abnormal position. When this space was opened it was obvious that the facial nerve was following an abnormal position inferior to the oval window and immediately posterior to
the round window. The stapes footplate was in its normal position but had no connection to the stapes suprastructure, which was lying on the promontory. A cochleostomy antero inferior to the round window was then drilled. There was some difficulty in initial insertion of the electrode due to some mild rotation of the axis of the inferior segment of the basal turn of the cochlea requiring a more superior angle of insertion. Full insertion of the Nucleus Freedom device with a contour advance electrode was possible, however. Thresholds were recorded in five electrodes in theatre at completion of surgery. There were no perioperative complications.

Audiology assessment at three months postimplant found her to be a consistent implant wearer, becoming distressed if it was disconnected. She responds reliably to sound and understands short phrases. She is attempting to vocalize but this is clearly limited by her tracheostomy. She vocalizes intentionally and is able to produce appropriate pitch, intensity, and duration change of sounds. Sound-field audiometry six months after implantation shows thresholds between 30 dB and 45 dB across the speech frequencies in keeping with her ability to recognize speech at conversational levels (see Figure 4).

Discussion

The combination of symptoms now recognized as CHARGE syndrome was first alluded to by Hall (1979), who described choanal atresia in patients with other congenital abnormalities. Pagon et al. (1981) went on to describe 21 such patients, who had coloboma, heart defects, choanal atresia, developmental retardation, genital
hypoplasia and ear anomalies. They used the term CHARGE association to describe them. The diagnosis of CHARGE was made if the patient had at least four out of the seven most common findings, being those referred to in the acronym plus growth retardation. Pagon found development delay present in all patients, with retarded growth and ear abnormalities the second most common findings. The hearing loss varied from mild to profound and was found to be predominately sensorineural.

With increasing evidence of cases with the same features, the term ‘syndrome’ is now accepted (Thelin et al., 1986). Blake et al. (1998) revised the diagnostic criteria. The four major criteria are given the acronym CCCC, and stand for coloboma, choanal atresia, cranial nerve involvement and characteristic ear anomalies. Minor criteria, which are less specific, include genital hypoplasia, development delay, cardiovascular anomalies, growth deficiency, orofacial cleft, tracheoesophageal fistula and distinctive facies. The diagnosis of CHARGE syndrome is made if the patient has all four major criteria or three major and three minor. The term ‘CHARGE-like’ can be used for patients who have several features but do not fill the criteria. Recent research has identified a mutation in the CHD-7 gene on chromosome 8, which is present in 60% to 65% of patients with CHARGE. The mutation is thought to arise de novo, and is inherited in an autosomal dominant manner (Lalani et al., 2007).

Otological manifestations are a very common feature of CHARGE syndrome and can affect all segments of the auditory system. More than 90% of children with CHARGE syndrome have a degree of hearing loss (Blake et al., 1998), which may be mixed or predominately sensorineural. Typical anomalies of the external ear (see Figure 6) include a triangular concha, small lobule, and extension of the antihelical rim towards the helix which has a thinned lower fold (Blake et al., 1998). Middle-ear disease is common with children often requiring multiple sets of ventilation tubes, and ossicular chain abnormalities are reported (Blake et al., 1998). Common inner ear anomalies include absent or malformed semicircular canals, abnormal cochlear formation and Mondini deformity, aberrant course of the facial nerve, narrowed internal auditory canal and venous malformations.

In a thesis by Stjernholm, the temporal bone anatomy and outcomes of two cochlear implant patients with CHARGE syndrome were studied (Stjernholm, 2003). In addition, the dimension of their bony cochlear nerve canals was compared with 117 random temporal bone specimens. In both patients the well recognized abnormality of absent semicircular canals was identified, in addition to narrowed bony cochlear nerve canals with hypoplastic cochlear nerves seen bilaterally on CT and MRI, suggesting an abnormal cochlear nerve. This may be compared with our patients, all of whom had either absent or hypoplastic vestibular apparatus but no abnormality of the internal auditory canal was seen.

Thelin et al. (1986) described the hearing loss anomalies found in 15 patients with CHARGE syndrome. Firstly they highlighted the difficulty of performing a full and accurate audiological assessment in these patients due to other confounding influences such as impaired vision, mental retardation and young age. They also commented that auditory brainstem responses (ABR) contributed little additional
FIGURE 6  Typical pinna appearance.
information due to difficulty interpreting waveforms at the near limit thresholds required to evoked potentials. They reported an 85% prevalence of hearing loss in the group (similar to Pagon’s findings) ranging from mild to profound, but this was a mixed loss in all cases. Conductive losses were presumed due to middle-ear effusions and/or ossicular chain anomalies, the latter being a diagnosis of exclusion if an effusion was not present. The majority of sensorineural losses were sloping with the greatest losses in the high frequencies, and half the patients showed progression.

The role of cochlear implantation in patients with CHARGE syndrome is not well established. To our knowledge there are only eighteen reported cases in the English literature of patients with CHARGE syndrome who have undergone cochlear implantation.

The largest series reported by Lanson et al. (2007) describes ten cases, all of whom received implantation by age 3.5 years. Outcomes were measured by standard audiometry and the Infant Toddler Meaningful Auditory Integration Scale (IT-MAIS) with varying degrees of benefit reported. The mean preoperative IT-MAIS total score was 3.11 compared to a mean postoperative score of 14.22 out of a possible of 40 points. Four out of the ten children have developed some oral communication (only receptive), which they use in combination with signing. The remaining six vary from using sign to no communication. Due to the varying mental retardation present in patients with CHARGE syndrome, they concluded that the expectation of a ‘successful outcome’ with oral language development from cochlear implantation was limited. However with careful selection and parental counselling, implantation could result in increased connectivity to the environment and optimized development of these patients.

Weber et al. (1998) reported on 12 children with cochlear malformations who underwent cochlear implantation, one of whom had CHARGE syndrome. Radiologically she had a dysplastic cochlear similar to an incomplete partition, with a virtually absent vestibular apparatus. She had only be followed for five months postoperatively at the publication of the paper but at this stage had only inconsistent auditory perception with reaction to acoustic stimuli and no speech-production ability. This child and another with autism were the only two in the group not to achieve ‘acceptable’ postimplantation results.

Bauer et al. (2002) reported the second largest series consisting of six children (aged 1.7 to 10.9 years) with CHARGE syndrome who received cochlear implantation (one child was not implanted due to an aberrant course of the facial nerve, making a total of five implanted patients). All six patients had abnormal temporal bones, with three patients having small internal auditory canals, findings in keeping with Stjernholm’s thesis. All patients had abnormal/absent vestibular apparatus and a facial nerve that coursed over the promontory, four had large vestibular aqueducts and three had dysplastic cochleae. All children were oral communicators preoperatively and were followed for an average of three years (range 0.6–10.3). After implantation four of the children had pure-tone threshold responses in the mild hearing loss range and the fifth child had speech awareness responses in the moderate hearing loss range. Three
of the five children had improved speech perception on Early Speech Perception testing; one had improved responsiveness and use of sound (as measured by the IT-MAIS) and one child had no measurable benefit but his parents reported improved environmental awareness. Due to the short duration of follow up for most of the children it is likely that further improvements could occur.

MacArdle et al. (2002) reported on two further CHARGE syndrome children in a review of children with craniofacial syndromes who received cochlear implantation. They reported both children post implantation had soundfield thresholds within the speech spectrum and improvements in their receptive language scores, and significant improvement in their awareness of environmental sounds. Both children had improvements in the speech intelligibility scores; however they remained with unintelligible speech and remained using sign language as their mode of communication.

The children in our case series contribute further important findings and information to the knowledge and literature about this small group of patients with CHARGE syndrome who have had cochlear implants. All three children had a positive outcome from their cochlear implant with a range of objective success shown. Case one, is a high-functioning child who had always used predominately oral receptive and expressive communication. This in combination with his slow postlingual decline in hearing and mild developmental delay predicted a high likelihood of him becoming a successful implant user. His has fulfilled these predictions and functions to such a high level that he is able to hear and understand telephone conversations with strangers. Case two has shown a more modest improvement. Postimplant thresholds fail to reach the conversational speech range, but he has shown improvement in his awareness of environmental sounds and ability to lip read and the clarity of his speech has been reported to have improved. Case three has shown an excellent audiological outcome from her implant, with postimplant thresholds in the conversational speech range. She is a continual user and is reported to respond reliably to sounds and understand short phrases. Her oral expressive ability is limited by her tracheostomy but she has attempted more vocalization since implantation.

Our patients are similar to the other reported cases in the literature in that they highlight the numerous challenges that children with CHARGE syndrome present when being considered for cochlear implantation. Full and accurate audiological assessment is not always possible due to confounding factors such as young age, impaired vision and mental retardation. Many of these children will have a mixed hearing loss and it is tempting to hope that improving the conductive component will be adequate surgical intervention. It is our experience that the conductive component is often multifactorial (poor Eustachian tube function, chronic infection and abnormal ossicles) and unlikely to improve significantly with surgical intervention (such as ossiculoplasty or tympanoplasty) and therefore recommend not delaying cochlear implantation by attempting these procedures. In the patient with a chronically discharging ear, blind sac closure can effectively be performed and followed by cochlear implantation.

Multiple anatomical abnormalities of the temporal bone can make surgery complex and challenging and the surgeon has to be prepared for the possibility of absent
usual anatomical landmarks, aberrant position and course of the facial nerve and the potential need to alter the cochleostomy site if abnormal anatomy is encountered. From our experience we would recommend an approach staying high on the middle fossa dura, following it down to the aditus ad antrum to expose the short process of the incus. With the absence of other usual anatomical landmarks, identifying the tympanic segment of the facial nerve can be a useful guide to finding its position in the vertical segment, allowing safe drilling of the posterior tympanotomy. Removal of the incus and the incus buttress will allow even further exposure if required. We would recommend the presence of a second otologist in the operating theatre to provide both support and exposure to a potentially complex and rarely performed procedure.

The surgeon also has to be aware of the other possible surgical procedures that the CHARGE syndrome child may require, and consider the most suitable timing for these to occur in relation to cochlear implantation. As with all children undergoing cochlear implantation, a thorough and complete assessment of the individual child in the context of its medical, developmental, and environmental issues needs to be undertaken in order to predict a realistic picture of what implantation could potentially achieve. The potential outcomes for children with CHARGE syndrome may not objectively measure as successfully when compared to other children but with realistic individual expectations the majority of cases reported have shown improvements that have been perceived as worthwhile. The results of our cases have certainly shown that the diagnosis of CHARGE syndrome does not negate the possibility of becoming a highly successful cochlear implant user.

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