

Cochlear Implants in Waardenburg Syndrome

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Objective: Waardenburg syndrome is an autosomal-dominant syndrome characterized by dystopia canthorum, hyperplasia of the eyebrows, heterochromia irides, a white forelock, and sensorineural hearing loss in 20% to 55% of patients. This patient population accounts for approximately 2% of congenitally deaf children. The purpose of this retrospective case review was to describe the outcomes for those children with Waardenburg syndrome who have undergone cochlear implantation. **Methods:** Pediatric cochlear implant recipients with documented evidence of Waardenburg syndrome underwent retrospective case review. All patients received their cochlear implants at the study institution followed by outpatient auditory habilitation. Charts were reviewed for etiology and duration of deafness, age at time of cochlear implantation, perioperative complications, duration of use, and performance outcomes. Results of standard tests batteries for speech perception and production administered as a part of the patients' auditory habilitation were reviewed. **Results:** Seven patients with Waardenburg syndrome and cochlear implants were identified. The average age at implantation was 37 months (range, 18–64 months) and the average duration of use was 69 months (range, 12–143 months). All of these patients are active users of their devices and perform very well after implantation. There were no major complications in this small group of patients. **Conclusions:** Children with congenital sensorineural hearing loss without other comorbidities (e.g., developmental delay, inner ear malformations) perform well when they receive cochlear implantation and auditory habilitation. Patients with Waardenburg syndrome can be expected to have above-average performance after cochlear implantation. **Key Words:** Waardenburg syndrome, cochlear implant, pediatric.

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INTRODUCTION

Approximately one to three in 1,000 children are diagnosed with sensorineural hearing loss (HL) before age 2 and an additional one in 1,000 children become severely hearing impaired before age 18.¹ Thirty percent to 50% of congenital HL is thought to have a genetic basis, but this number is likely higher because a significant percentage of HL is attributed to unknown causes.² Approximately 75% of the genetic causes of HL are autosomal-recessive (AR), whereas 20% are autosomal-dominant (AD), approximately 5% are X-linked, and approximately 1% are mitochondrial.

Waardenburg syndrome (WS) is an autosomal-dominant syndrome characterized by dystopia canthorum, hyperplasia of the eyebrows, heterochromia iridis, a white forelock, and sensorineural HL (SNHL).³ This patient population accounts for approximately 2% of congenitally deaf children. Waardenburg syndromes I, IIA, IIB, IIC, III, and IV have been described (Table I).^{3–5} HL occurs in approximately 35% to 75% of patients with WS I and 55 to 91% of patients with WS II.^{6–9} Temporal bone abnormalities may be seen in patients with WS with HL.¹⁰ Temporal bone histopathology has shown atrophy of the organ of Corti and the stria vascularis.¹¹ The absence of melanocytes within the inner ear has been purported to contribute to the pathophysiology of HL in WS.¹² Spiral ganglion cell counts have been variably reported to be mildly reduced¹² to severely decreased.¹³ Cochlear implantation is a well-established method of auditory rehabilitation for children with severe to profound SNHL. Although severe to profound SNHL is frequently associated with WS, to date, few reports have focused on the outcomes of this subset of children after cochlear implantation.^{14,15} These reports suggest that patients with WS demonstrate a positive benefit from cochlear implantation. The purpose of this study is to describe the outcomes of pediatric patients with WS who underwent cochlear implantation at a tertiary referral center.

METHODS

A retrospective chart review was conducted of children with cochlear implants in the W. Paul Biggers, MD, Carolina Children's Communication Disorder Program (CCCDP), Department of Otolaryngology–Head and Neck Surgery, at the University of North Carolina at Chapel Hill (UNCH-CH). The Institutional Review Board at UNC-CH approved this study.

To date, 500 children have received cochlear implants at UNC-CH. Of these children, seven (1.4%) carried the diagnosis of WS and are the subject of this review. All children with WS who

TABLE I.
The Waardenburg Syndromes.

	Gene	Locus	Phenotype
WS I	PAX3	2q35	Dystopia canthorum, pigmentary disturbances (white forelock, heterochromia iridis, white eyelashes, leukoderma), SNHL
WS IIA	MITF	3p14.1-p12	Identical to WSI, but without dystopia canthorum
WS IIB		1p21-p13.3	Identical to WSIIA
WS IIC		8p23	Identical to WSIIA
WS III	PAX3	2q35	Klein-Waardenburg syndrome—WSI phenotype plus upper limb anomalies
WS IV	PAX3		Shah-Waardenburg WSI phenotype plus Hirschsprung disease

Dystopia canthorum = lateral displacement of medial canthi resulting in broad nasal dorsum; SNHL = sensorineural hearing loss.

received a cochlear implant had severe to profound SNHL and limited benefit from a trial of amplification.

A retrospective chart review was undertaken to investigate age of implantation, duration of use, operative and perioperative complications, as well as performance outcomes. Tests are administered in a standardized format and results recorded in a database. In general, the specific test administered is determined by patient age and expected performance ability. Thus, ceiling effects are avoided by the testing paradigm. For the purposes of this study, two primary measures are reported spanning the spectrum of speech perception testing. The Early Speech Perception (ESP) test assesses closed-set monosyllabic word ability. The Phonetically Based Kindergarten (PBK) test assesses open-set monosyllabic word ability. Radiologic studies, if available, were evaluated for the presence of inner ear malformations.

RESULTS

Seven pediatric patients with cochlear implants were identified as having WS. The average age at implantation was 37 ± 20 months (range, 16–64 months), and the average length of usage was 69 ± 42 months (range, 12–143 months). There were no major intraoperative or perioperative complications. One patient developed a wound seroma at the implant site that resolved without treatment or long-term sequelae. One child required reimplantation after experiencing a device failure, but quickly regained the prefail-

ure level of function. There were no cerebrospinal fluid gushers or cases of facial weakness.

Auditory performance outcomes are presented in Table II. All patients who have undergone testing for closed-set and open-set speech have obtained some degree of closed- and open-set speech. One patient has been unable to be tested with the ESP and PBK tests as a result of short duration of use (patient no. 2).

Radiologic studies were available on five of the seven patients. Three of the five had normal preoperative computed tomography scans without evidence of inner ear abnormalities. One patient (patient no. 4) had bilateral enlarged endolymphatic sac fossae but no visible vestibular aqueduct at the midportion of the posterior semicircular canal (PSC). Therefore, an enlarged vestibular aqueduct could not be diagnosed. The remaining patient (patient no. 5) had a significant inner ear malformation. This was characterized by bilateral horizontal semicircular canal dysplasia and bilateral PSC aplasia with a normal vestibular aqueduct.

DISCUSSION

P. J. Waardenburg first described the syndrome that bears his name in 1951. His investigation into families of

TABLE II.
Speech Perception Outcomes.

Patient No.	Age at CI (months)	Duration of Use (months)	ESP (%)	PBK (%)	Device	Comments
1	46	74	79	40	Advanced Bionics Corporation; Clarion	Wound seroma
2	19	12	NT	NT	Cochlear Corporation; Nucleus 24	
3	45	94	100	60	Advanced Bionics Corporation; Clarion	
4	16	37	100	52	MedEl; Combi 40+	Bilateral ELS enlargement
5	56	143	100	84	Cochlear Corporation; Nucleus 22	Bilateral HSC dysplasia and bilateral PSC aplasia
6	18	65	100	80	Advanced Bionics Corporation; Clarion	
7	64	59	100	80	Advanced Bionics Corporation; Clarion	

CI = cochlear implant; ESP = Early Speech Perception test (closed-set word ability); PBK = Phonetically Based Kindergarten test (open-set word ability); NT = not tested; ELS = endolymphatic sac; HSC = horizontal semicircular canal; PSC = posterior semicircular canal.

deaf patients with pigmentation abnormalities and dystopia canthorum led to the description of the syndrome that has since borne his name.³ Since his original description, four types and two subtypes of WS have been described. WS is inherited in an autosomal-dominant pattern, with the exception of some cases of WSII and WSIV, which may be autosomal-recessive.

Waardenburg syndrome I (WSI) is characterized by wide bridge of the nose owing to lateral displacement of the inner canthus of each eye, pigmentary disturbance (white forelock, heterochromia iridis, white eyelashes, leukoderma), and sensorineural HL. HL occurs in approximately 35% to 75% of patients with WSI. WSI has been linked to a deletion mutation in the PAX3 gene on chromosome 2q35.

Waardenburg syndrome II (WSII) is phenotypically identical to WSI with the exception of the absence of dystopia canthorum.⁵ Four subtypes of WSII (A, B, C, and D) have been described and differ in the location of causative mutations. HL occurs in approximately 55% to 91% of patients with WSII.

Waardenburg syndrome III (WSIII), also referred to as Klein-Waardenburg syndrome, has also been linked to the PAX3 gene. It carries the phenotype of WSI but is also associated with upper limb abnormalities. Patients with Waardenburg syndrome IV (WSIV, Shah-Waardenburg) have Hirschsprung disease with the addition of the features of WSI.

The incidence of WS in the general population is one in 4,000 live births. Among congenitally deaf children, the incidence is 1.4% to 2.3%. In Waardenburg's original description, he estimated an incidence of 1.78% among the deaf in his study population. Seven of the 500 (1.4%) pediatric cochlear implant patients currently followed at our institution have been diagnosed with WS, which correlates roughly with the previous studies.

Because patients with WS are of normal intelligence and have been shown to have cochlear (sensory) HL on temporal bone histopathology, it would be expected that these patients would perform well after cochlear implantation when involved in an intensive rehabilitative program. In fact, the results of the present study show these children can achieve exceptional levels of speech perception using cochlear implants. When compared with other groups of children implanted at our institution with either GJB2 mutations¹⁶ or a variety of inner ear malformations,¹⁷ this small group of Waardenburg children appears to exceed the performance of these selected subgroups of patients. Although these results are encouraging, the number of patients in this study is too small to generalize WS as a positive prognostic indicator. Our results are consistent with those reported by other investigators.^{14,15}

Radiologic studies of patients with WS have variably reported the incidence of inner ear malformation from 0% to 100%. Five of the seven patients in our study had temporal bone computed tomography scans available for review. Two of the five had inner ear malformations as outlined previously. This may be the result of differing definitions of inner ear malformation, differing subtypes

of WS, or variable expressivity of the phenotype. Further studies with larger number of children will be important to determine these issues.

CONCLUSIONS

Waardenburg syndrome is a relatively uncommon cause of severe–profound SNHL in the pediatric patient population. In our small group of patients, no major complications were encountered. One patient required reimplantation after a device failure and has subsequently done well. Overall, this group of patients has performed extremely well on standardized tests of both closed- and open-set speech. When identified as a cause of SNHL, this diagnosis appears to carry an excellent prognosis for auditory habilitation with a cochlear implant.

BIBLIOGRAPHY

1. Morton NE. Genetic epidemiology of hearing impairment. *Ann N Y Acad Sci* 1991;630:16–31.
2. Marazita ML, Ploughman LM, Rawlings B, Remington E, Arnos KS, Nance WE. Genetic epidemiological studies of early-onset deafness in the US school-age population. *Am J Med Genet* 1993;46:486–491.
3. Waardenburg PJ. A new syndrome combining developmental anomalies of the eyelids, eyebrows and nose root with pigmentary defects of the iris and head hair and with congenital deafness. *Am J Hum Genet* 1951;3:195–253.
4. Arias S. Genetic heterogeneity in the Waardenburg syndrome. *Birth Defects Orig Artic Ser* 1971;7:87–101.
5. Klein D. Historical background and evidence for dominant inheritance of the Klein-Waardenburg syndrome (type III). *Am J Med Genet* 1983;14:231–239.
6. Hageman MJ, Delleman JW. Heterogeneity in Waardenburg syndrome. *Am J Hum Genet* 1977;29:468–485.
7. Liu XZ, Newton VE, Read AP. Waardenburg syndrome type II: phenotypic findings and diagnostic criteria. *Am J Med Genet* 1995;55:95–100.
8. Newton V. Hearing loss and Waardenburg's syndrome: implications for genetic counselling. *J Laryngol Otol* 1990; 104:97–103.
9. Oysu C, Baserer N, Tinaz M. Audiometric manifestations of Waardenburg's syndrome. *Ear Nose Throat J* 2000;79: 704–709.
10. Madden C, Halsted MJ, Hopkin RJ, Choo DI, Benton C, Greinwald JH Jr. Temporal bone abnormalities associated with hearing loss in Waardenburg syndrome. *Laryngoscope* 2003;113:2035–2041.
11. Takasaki K, Balaban CD, Sando I. Histopathologic findings of the inner ears with Alport, Usher and Waardenburg syndromes. *Adv Otorhinolaryngol* 2000;56:218–232.
12. Merchant SN, McKenna MJ, Baldwin CT, Milunsky A, Nadol JB Jr. Otopathology in a case of type I Waardenburg's syndrome. *Ann Otol Rhinol Laryngol* 2001;110:875–882.
13. Fisch L. Deafness as part of an hereditary syndrome. *J Laryngol Otol* 1959;73:355–382.
14. Daneshi A, Hassanzadeh S, Farhadi M. Cochlear implantation in children with Waardenburg syndrome. *J Laryngol Otol* 2005;119:719–723.
15. Migirov L, Henkin Y, Hildesheimer M, Muchnik C, Kronenberg J. Cochlear implantation in Waardenburg's syndrome. *Acta Otolaryngol* 2005;125:713–717.
16. Cullen RD, Buchman CA, Brown CJ et al. Cochlear implantation for children with GJB2-related deafness. *Laryngoscope* 2004;114:1415–1419.
17. Buchman CA, Copeland BJ, Yu KK, Brown CJ, Carrasco VN, Pillsbury HC 3rd. Cochlear implantation in children with congenital inner ear malformations. *Laryngoscope* 2004; 114:309–316.