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Outcomes and Special Considerations of Cochlear Implantation in Waardenburg Syndrome

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Objectives: The objective of this study was a state-of-the-art analysis of cochlear implantation in patients with Waardenburg syndrome (WS).
Patients: Twenty-five patients with WS treated with cochlear implants in our department from 1990 to 2010.
Interventions: The 25 patients with WS underwent 35 cochlear implantations.
Main Outcome Measures: Hearing outcome was evaluated using HSM sentence test in 65 dB in quiet, Freiburg Monosyllabic Test, and categories of auditory performance for children and compared with that of a control group. Anatomic abnormalities of the inner ear were examined using magnetic resonance imaging and computed tomography of the temporal bones.
Results: The mean follow-up time was 8.3 years (range, 0.3–18.3 yr). The majority achieved favorable postimplantation performance with mean HSM scores of 75.3% (range, 22.6%–99%) and Freiburg Monosyllabic Test scores of 67.8% (range, 14%–95%). However, in 4 cases, the results were less satisfactory. The comparison with the control group did not reveal any statistical significance ($p = 0.56$). In 6 patients (24%), behavioral disorders caused temporary difficulties during the rehabilitation procedure. Except of isolated large vestibule in 1 patient, the radiological assessment of the 50 temporal bones did not reveal any temporal bone abnormalities.
Conclusion: Most patients with WS performed well with cochlear implants. However, WS is related to behavioral disorders that may cause temporary rehabilitation difficulties. Finally, temporal bone malformations that could affect cochlear implantation are notcharacteristic of WS. **Key Words:** Behavioral disorders—Cochlear implant—Hearing outcome—Inner ear malformations—Waardenburg syndrome.
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In 1951, ophthalmologist and geneticist P.J. Waardenburg investigated into families of deaf patients describing a syndrome that has since then borne his name. Waardenburg syndrome (WS) is an autosomal dominant disease, characterized by dystopia canthorum, hyperplasia of the eyebrows, heterochromia iridis, white forelock, and congenital sensorineural hearing loss (1). Forty years after its first description, WS was connected to genetic mutations in the *PAX3* gene (2). On the basis of genetic and clinical criteria, WS was divided into 4 types. However, the different combination of clinical characteristics, namely, presence (Type I) or absence (Type II) of dystopia canthorum, additional upper limp anomalies and more coarse facial characteristics (Type III) or Hirschsprung disease (Type IV), sensorineural hearing loss represents a common element in all types (1,3,4). Atrophy of the organ of Corti and stria vascularis, absence of melanocytes in the inner ear, and reduced spiral ganglion counts are believed to contribute to the pathophysiology of hearing loss (5).

Hearing loss in WS may vary in nature and severity, with different incidence depending on the WS type. Bilateral, profound sensorineural hearing loss is, however, the commonest type (5,6). Because of its usually bilateral, profound character, limited case series have already reported cochlear implantation as the suitable hearing rehabilitation method for patients with WS (5–8). Apart from these reports, further isolated cases were described, mainly focusing on the achieved hearing outcome (9–11). In general, the postimplantation performance was found to be favorable and, in some cases, even above the average (5). The aim of the present study was a state-of-the-art approach of WS cochlear implant recipients, evaluating the hearing outcome and any special considerations in an extended case series.

METHODS

A retrospective chart review was conducted on patients who underwent cochlear implantation in the Otorhinolaryngology

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TABLE 1. *Patients assessed with HSM and/or FMT*

Patient No.	Sex	WS Type	Age (yr)	DOHL (yr)	CI Type	Bil/Uni	Follow-Up (yr)	HSM (%)	FMT (%)	Comments
1	M	I	1.1	0.4	Clarion	Uni	6.8	91.5	90	Bim
2	F	I	3.7	2	Nucleus 22	Bil	18.3	90.6	90	—
3	F	I	5	4	Nucleus RE-24CA	Uni	9.6	96.2	95	Bim
4	F	I	2.9	2.3	Nucleus RE-24CA	Uni	16.5	84.9	85	Bim
5	F	II	5	1.3	Nucleus RE-24CA	Bil	2.5	80	28.3	—
6	F	II	2	0.5	HiRes 90K	Bil	5.5	78.5	55	Reimplantation
7	F	II	8.9	8.9	Clarion	Uni	8	88.6	NA	Rehabilitation difficulties
8	M	II	11.2	9	Clarion	Uni	6.4	53.8	50	Bim
9	F	II	15	12.8	Nucleus M-24	Uni	5.5	94.3	80	Bim
10	M	II	1.2	1.2	Nucleus RE-24CA	Uni	4.3	94	90	—
11	F	III	2.2	0.6	Nucleus RE-24CA	Bil	5.5	60.3	45	—
12	F	Unknown	3.3	1	Nucleus M-24	Bil	9.5	99	95	Reimplantation
13	F	Unknown	2	0.8	Clarion	Bil	12.6	96.2	90	—
14	M	Unknown	3.9	3.9	Nucleus RE-24CA	Uni	17	90	80	Bim
15	*F*	*I*	*5.3*	*5.2*	*Nucleus RE-24CA*	*Uni*	*16.5*	*35.8*	*60*	—
16	*F*	*II*	*2.8*	*2*	*Nucleus RE-24CA*	*Uni*	*7.4*	*22.6*	*35*	*Rehabilitation difficulties*
17	*M*	*Unknown*	*3.5*	*2*	*Nucleus RE-24CA*	*Uni*	*6*	*24*	*70*	—
18	*M*	*III*	*10.1*	*6.5*	*Nucleus 22*	*Uni*	*15*	NA	*14*	*Long DOHL*

The hearing outcome refers to the scores of the last evaluation; the last 4 patients ("bad performers") are pointed with italic letters. In all other cases, the difference with the control group was not statistically significant ($p = 0.56$).

— indicates no additional comments; Bil, bilateral; Bim, bimodal; CI, cochlear implant; DOHL, duration of hearing loss; F, female; M, male; NA, not applicable; NGNS, non–German-native speaker; Uni, unilateral.

Department of Hanover Medical School, Germany, from June 1990 to January 2010. Of these cochlear implant recipients, 25 patients carried the diagnosis of WS, involving 35 cochlear implantations, as 7 patients underwent bilateral implantation and 3 underwent reimplantation. All patients with WS enrolled in this study fulfilled candidacy criteria for cochlear implantation. To identify the patients with WS, 2 independent databases, the medical databank and the database of the pedagogues and acoustic engineers, were thoroughly examined.

All patients received the same hearing rehabilitation protocol. The HSM sentence test in 65 dB in quiet and Freiburg Monosyllabic Test (FMT) were applied on adults and on cooperative children for the evaluation of the postimplantation performance. To assess the hearing outcome in younger children, categories of auditory performance (CAPs) were used. The results were compared with those of a control group involving 50 cochlear implant recipients, using SPSS Version 18 (SPSS, Inc., Chicago, IL, USA). A p value less than 0.05 showed a statistically significant difference. This group involved cochlear implant recipients without any syndromes, major anatomic anomalies, prelingual, or long duration of hearing loss or mental retardation, with cross-matching age and follow-up time. The cause of deafness in the control group was usually unknown, but hearing loss was, in all cases, progressive.

Factors further examined involved age of implantation, duration of hearing loss, use of hearing aids, follow-up period, any perioperative or long-term complications, surgical difficulties and anatomic abnormalities of the inner ear, or any additional handicaps. The duration of hearing loss was estimated according to the patients' feedback. To identify inner ear malformations, computed tomography of the temporal bones and magnetic resonance imaging of the inner ear canal (in most patients) were used.

RESULTS

Twenty-five patients with WS underwent 35 cochlear implantations during a 20-year period (Table 1). Females outnumbered males, 14 to 11. The mean implantation age was 5.9 years (range, 0.7–21.2 yr), and the mean follow-up time was 8.3 years (range, 0.3–18.3 yr).

The mean HSM and FMT scores were 75.3% (range, 22.6%–99%) and 67.8% (range, 14%–95%), respectively, and could be obtained from 18 patients (Table 1). The difference between the examined and the control group did not reach the level of significance ($p = 0.56$). In the remaining patients, CAP revealed satisfactory results (Table 2). In 2 cases, postimplantation results in numbers were not available (Table 3). In 1 case with non–promptly treated severe-to-profound hearing loss of long duration, the results were not favorable (Patient 18). In 3 more

TABLE 2. *Results of patients with WS assessed with CAP and with no data in numbers at all*

Patient No.	Sex	WS Type	Age (yr)	DOHL (yr)	CI Type	Uni/Bil	Follow-Up (yr)	CAP	Comments
19	F	I	13.9	10.5	Nucleus RE-24CA	Uni	1.8	4	Difficulties with CI acceptance
20	M	I	9.9	4.7	Clarion	Uni	10	4	Reimplantation Rehabilitation difficulties FF audio with CI: 35 dB XYY syndrome
21	M	I	6.9	5.9	HiRes 90K	Uni	14	2	NGNS good development
22	M	II	3	1.2	Nucleus RE-24CA	Bil Sim	1.5	4	Difficulties with the first fitting
23	M	Unknown	2.3	0.3	Nucleus RE-24CA	Uni	5.8	2	NGNS good development

FF Audio indicates free-field audiometry; Sim, simultaneously.

TABLE 3. *Patients that could not be assessed with HSM, FMT, or CAP*

Patient No.	Sex	WS Type	Age (yr)	DOHL (yr)	CI Type	Uni/Bil	Follow-Up (yr)	Comments
24	F	III	21.2	21	Nucleus RE-24CA	Uni	0.3	Long DOHL Rehabilitation difficulties
25	M	Unknown	0.7	0.7	Nucleus RE-24CA	Uni	1.2	Concentration disorders

Only comments of the pedagogues are available.

patients, low HSM and/ or FMT scores were documented (Patients 15–17). In 2 more case of a long duration of hearing loss and short follow-up time, the outcome is not displayed in numbers because such tests could not be applied. However, the first comments of the pedagogues were positive (Patient 24; Figs. 1–3).

Difficulties were observed in 6 patients (24%) during the postimplantation rehabilitation, namely, concentration disorders, problematic acceptance of the cochlear implant, and limited cooperation with the pedagogues. It is worth mentioning that, in 2 cases, the patients changed cochlear implant centers, repeatedly, interrupting the rehabilitation procedure (Patients 16 aznd 20). However, at the time of the last evaluation in our department, all 25 patients were active users of their devices.

Apart from an enlarged vestibule in 1 patient, without any clinical or surgical significance, the radiological studies did not reveal any inner ear anatomic anomalies in any case. Cochlear obliteration or cerebrospinal fluid gusher was not observed, and the electrodes could be fully inserted without difficulties. Finally, major complications, additional handicaps, or mental retardation were not observed in any case.

DISCUSSION

The initially estimated incidence of WS among congenital deaf children was 1.78% and correlated with the one described in later reports (1,5). In particular, a recent study showed that the incidence among cochlear implant recipients was 1.9% (6). In our study, this percentage seems to be lower because cochlear implantations in patients with WS comprised only 35 of the total implantations in the 20-year examined period (approximately 5,000 cochlear implantations). However, there are more patients with WS experiencing less severe hearing loss and are treated with hearing aids that undergo controls

FIG. 1. A young patient with small blue eyes, dystopia canthorum, hyperplasia of the eyebrows, and white forelock, typical for Waardenburg syndrome Type I. The speech processor of the cochlear implant on the right side and the hearing aid on the left one can be recognized.

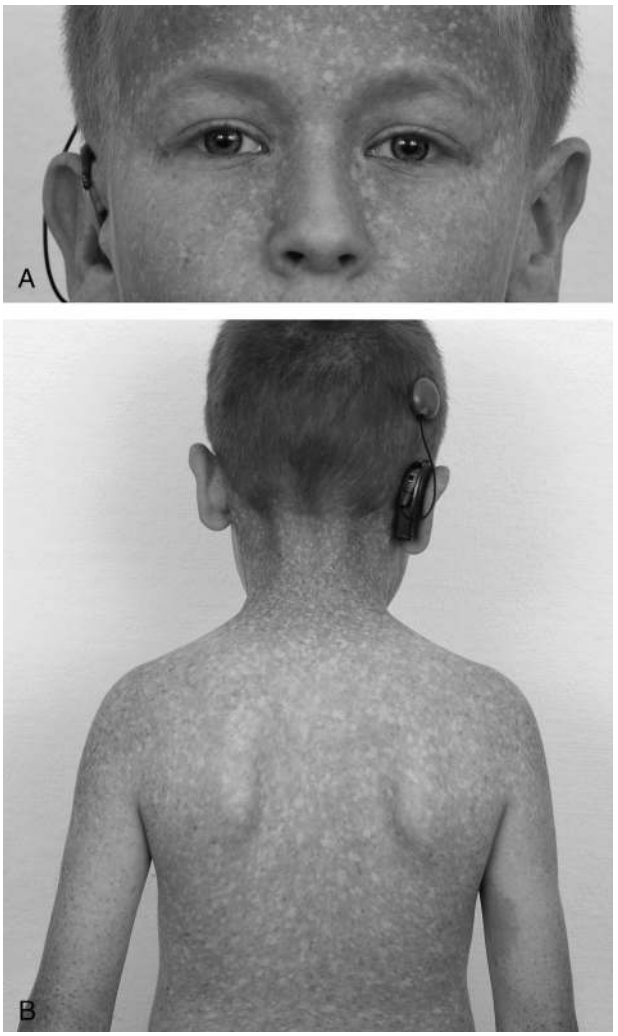

FIG. 2. Patient with Waardenburg syndrome Type II without any dystopia canthorum (*A*) but with extended skin pigmentary disturbances (*A, B*).

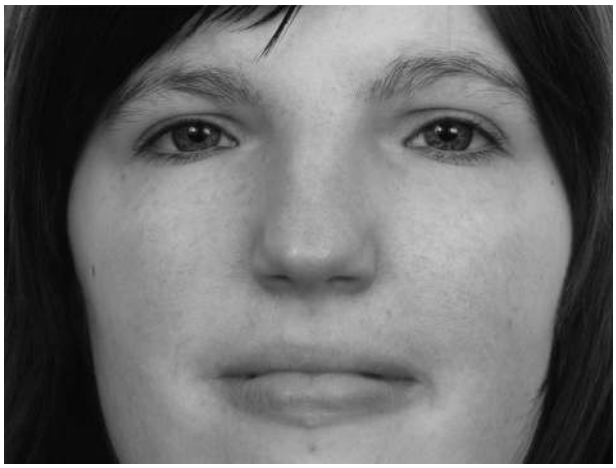

FIG. 3. Female patient with Waardenburg syndrome Type III. Apart from hypoplastic blue eyes and dystopia canthorum, coarse facial characteristics can be identified. The patient had also upper limp anomalies.

regularly in our department. The number of these patients is unknown.

On the basis of the above demographic observation, WS is a relatively uncommon cause of profound hearing loss. Thus, the already existing studies were conducted on small groups of WS cochlear implant recipients. We describe the hearing outcome in the largest series reported, presenting some difficulties during the rehabilitation procedure, which, to our knowledge, have not been reported until now.

Patients with WS usually experience bilateral profound hearing loss and are of normal intelligence (5). For that reason, WS cochlear implant recipients are expected to perform well. Past studies involving small groups reported above-average outcome (5–8). However, if we critically examine these results, we will realize that the performance of patients with WS is not always as favorable as described. In a group of 5 patients, low monosyllabic speech perception scores (25% and 40%) were observed in open set in 2 patients (6). Moreover, in the same study, 1 more patient did not achieve any open recognition of monosyllabic words. Most of the 25 patients reported in our study performed well with the cochlear implant. In particular, in many cases (n = 9), the cochlear implant recipients achieved monosyllabic scores better than 80%, pointing out an excellent hearing performance. The HSM and FMT scores indicate cochlear implantation as the proper hearing rehabilitation method for patients with WS and agree with most of the already existing studies.

On the other hand, in 4 cases, the results were less satisfactory. In Patient 18, the long duration of deafness that was not properly treated with adjusted hearing aids seems to be the main cause. In the remaining 3 cases, the HSM scores of 22.6% to 35.8% and the analogous low FMT scores may be related to WS because no other relevant factor can be held responsible. A previous electrophysiological study conducted on 20 patients with WS showed poor outcome in 4 cases with abnormal electric-evoked auditory brainstem responses, a sign of auditory neuropathy (12). Most of the patients in our study did not undergo a similar electrophysiological assessment. Therefore, auditory neuropathy cannot be proven as the cause for poor performance. Although these cases seem to be the exception of the satisfactory postimplantation performance achieved, a less favorable hearing result may be expected in a minority of patients with WS.

The difficulties during the hearing rehabilitation procedure represent another point worth mentioning. Problems either with the acceptance of the device or with the cooperation of the pedagogues were observed in 24% of the patients with WS in the present study. In 1 case (Patient 4), the coexisting XYY genotype can be held responsible fo the attitude problems (13). In the remaining 5 patients, however, such behavior was related to WS (14). Although more effort and energy was required during the rehabilitation appointments, these difficulties were temporary without any significant consequences.

Regarding imaging studies, previous works, involving small samples, reported heterogeneous results of inner ear malformations in patients with WS with variability from 0% to 100% (5). In particular, the radiological evaluation of 6 patients identified inner ear anomalies in all temporal bones and enlargement of vestibular aqueduct in 50% of the cases (15). On the other hand, an imaging study involving 8 WS cases revealed abnormalities of the inner ear bony architecture in only 17% (16). The present study involving the largest cohort did not identify any inner ear malformations that could impede cochlear implantation. Such temporal bone anatomic anomalies are rather sporadic findings rather than part of WS.

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