Hearing Characterization in Oculoauriculovertebral Spectrum: A Prospective Study with 10 Patients

Thayse Bienert Goetze,1 Pricila Sleifer,2 Rafael Fabiano Machado Rosa,1,3,4 Alessandra Pawelec da Silva,1 Carla Graziadio,3 and Paulo Ricardo Gazzola Zen1,3,4*

1Graduate Program in Pathology, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil
2Speech Language Pathology, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil
3Clinical Genetics, UFCSPA and Complexo Hospitalar Santa Casa de Porto Alegre (CHSCPA), Porto Alegre, RS, Brazil
4Graduate Program in Biosciences, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil

Manuscript Received: 31 March 2015; Manuscript Accepted: 23 September 2016

Oculoauriculovertebral spectrum (OAVS), also known as Goldenhar syndrome, is considered a condition associated to failing of embryogenesis involving the first and second branchial arches, leading to structural abnormalities arising from it. The aim of this study is to verify the hearing features presented by patients with OAVS and provide additional information that may contribute to improvement of speech therapy. The sample consisted of 10 individuals diagnosed with OAVS and cared for by the Clinical Genetics Service. All patients underwent objective assessment of auditory function through tonal and vocal audiometry. This evaluation was completed using TOAE and BERA. The patient’s age ranged from 1 year and 9 months to 27 years and 4 months. At physical examination it was found that 10 had microtia, 7 preauricular tags, 6 low-set ears, 6 ear canal atresia, and 2 preauricular pits. Among the patients, five presented with abnormal hearing. Three patients had conductive hearing loss ranging from mild to moderate, and two patients had sensorineural hearing loss from mild to profound. Three patients had hearing loss in both ears. Speech-language disorders are common in children with OAVS. Thus, the referral to the audiologist and speech pathologist is indicated as soon as possible. Early recognition and detailed understanding of aspects related to the etiology, clinical features, and outcome of patients with OAVS are essential for their proper management.

Key words: Oculoauriculovertebral spectrum; Goldenhar syndrome; hearing sciences; audiology; speech; language

INTRODUCTION

Oculoauriculovertebral spectrum (OAVS) [OMIM 164210], also known as hemifacial microsomia and Goldenhar syndrome, is considered a rare condition which has been etiologically associated to different causes, which includes environmental factors that can result in a blastogenesis disruption. OAVS usually involves facial asymmetry and mainly affects the right side of the face [Rollnick et al., 1987; Cohen et al., 1989]. It has an estimated prevalence of one case in 5,600–26,550 live births, affecting more males than females at a ratio of about 3:2 [Grabb, 1965; Poswillo, 1973; Melnick, 1980; Cohen et al., 1989].

The features verified in patients with OAVS are characterized by a wide spectrum that ranges from mild to severe unilateral cranial, face, and neck congenital anomalies. Involvement of spine, heart, and kidney is also common [Cohen et al., 1989].

Anomalies associated with OAVS have been observed in children of mothers exposed to several teratogenic agents as thalidomide, primidone, retinoid acid, anticoagulants and salicylates, ethyl alcohol, folate antagonists, anticonvulsants, vasoactive drugs, and smoking [Kleinsasser and Schlothane, 1964; Cohen et al., 1989; Gorlin et al., 2001; Werler et al., 2004]. Other factors that have been related to OAVS include vaginal bleeding in 2nd trimester, which suggests abnormalities in the placenta and are likely to have a vascular nature [Werler et al., 2004]; twin pregnancies, in which anastomosis of vessels of the placenta can be observed both in

How to Cite this Article:
Goetze TB, Sleifer P, Rosa RFM, da Silva AP, Graziadio C, Zen PRG. 2017. Hearing characterization in oculoauriculovertebral spectrum: A prospective study with 10 patients. Am J Med Genet Part A 173A:309–314.
monozygotic as in dizygotic twins; hypoxia due to high altitude [Salvado et al., 2003]; intrauterine compression secondary to oligohydramnios [Cohen et al., 1989; Salvado et al., 2003] and hypertension [Salvado et al., 2003].

Cytogenetic abnormalities have been described in individuals with the phenotype of OAVS. Several chromosomal abnormalities have been detected and include deletion of the long arm of chromosome 5, trisomy 18, duplication of the long arm of chromosome 7, and supernumerary chromosome der(22)(11;22) (Emanuel syndrome) [Cohen et al., 1989; Rosa et al., 2010]. Patients presenting features of OAVS and mutations in the goosecoid, TCOF1 and GLI2 genes have been described. However, they usually have a more symmetric involvement than that seen in patients with OAVS [Rahimov et al., 2006].

Ear malformations in patients with OAVS can range from complete aplasia to deformities in the external, middle and inner ear which may result in hearing loss. The ear canal may be completely absent, resulting in deafness (unilateral) in approximately 40% of cases. It is known that exposure to sound stimuli is an essential factor for the child to develop the appropriate language and maturation of the central auditory system. This aspect emphasizes the importance of early detection and intervention of hearing disorders [Vinay et al., 2009].

Currently, it is known that any type of hearing loss can compromise language, learning, cognitive development, and social inclusion of children [Mondain et al., 2005]. Thus, a better understanding of abnormalities associated with OAVS will enable an earlier diagnosis and better planning and treatment approach.

**METHODS**

The sample consisted of patients with OAVS originated from the Clinical Genetics Service of Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)/Complexo Hospitalar Santa Casa de Porto Alegre (CHSCPA). Using the Hospital database, 23 patients were initially identified. Later, an active search was conducted by telephone or letter contact. Of 23 patients initially identified, 23 patients were initially identified. Later, an active search was conducted by telephone or letter contact. Of 23 patients initially identified, 23 patients were initially identified. Later, an active search was conducted by telephone or letter contact. Of 23 patients initially identified, 23 patients were identified. Later, an active search was conducted by telephone or letter contact. Of 23 patients initially selected, it was possible to contact 10 of them. All patients and their parents agreed to participate in the study. During the first contact, a protocol for the identification and the scheduled time of execution of speech therapy interventions were performed. All patients were re-evaluated to confirm the diagnosis of OAVS by medical geneticists. This followed the criteria suggested by Strömland et al. [2007]. Thus, we considered patients with OAVS those with clinical alterations in at least two of the following areas: (i) oro-craniofacial; (ii) ocular; (iii) auricular; and (iv) vertebral.

This is an observational, cross-sectional study, and all patients or guardians signed an informed consent form. The study was approved by the Ethics Committee of the institution. All patients had previously performed high-resolution GTG-banding karyotype in peripheral blood; fluorescent in situ hybridization (FISH) for 22q11 and 5p microdeletions, and search for chromosomal instability for Fanconi anemia. All presented normal results.

At first interview, it was asked information about auditory function, patient history, aspects of child development, and information about school performance. Abnormalities described in organs or systems, and results of ophthalmological, otorhinolaryngological, cardiological, and radiological evaluations were also registered. Anthropometric measurements of patients, such as weight, height, and head circumference, were verified. All patients underwent a speech-language study with the use of standard protocols, to assess auditory function and school performance for literate students (through the Academic Performance Test [APT]).

Audiological tests performed consisted of auditory brainstem audiometry or infant audiometry, speech audiometry, tympanometry, acoustic reflexes, and otocoustic emissions. All tests were conducted in the Audiology Clinic of Hospital de Clínicas de Porto Alegre (HCPA). Evaluations were performed with the AC40 clinical audiometer and the AD229 diagnostic audiometer (Interacoustics®) and TDH39 audiometric earphones (TDH Telephonic®) in sound booths. The pure tone audiometry at frequencies of 250, 500, 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz was performed in most patients. Bone conduction frequencies of 500, 1,000, 2,000, 3,000, and 4,000 Hz were tested. The descending method was used for stimulus presentation. The analysis of the results was performed by calculating the average of three frequencies: 500, 1,000, and 2,000 dB. For the classification of hearing loss, we selected the scale of Davis and Silverman [1970].

The speech audiometry was performed by investigating speech recognition index (SRT). For this evaluation, trisyllabic words were presented to the patient in audible intensity, 40 dB above the tone average of airway. This intensity was reduced to below the threshold. The patient was instructed to repeat the heard words. It was considered a proper SRT when the patient correctly repeat at least 50% of them.

We also carried out the research of speech recognition index (SRI). The SRI was obtained using the presentation of a list of 25 monosyllabic words in intensity audible to the patient, 40 dB above the tone average of airway. This intensity was fixed during the whole test. It was demonstrated to the patient that he should repeat the heard word. If the patient responded 92–100%, the assay was considered unchanged; but when he answered values less than 88%, he underwent to more 25 two-syllable words and it was registered the percentage of correct reproduction. When the patient was unable to perform the SRT and SRI, due to problems as inability to repeat words (usually three syllables) or to perform simple orders, threshold of detection of voice (TDV) was used.

**RESULTS**

The final sample consisted of 10 subjects, five males, with age ranged from 1 year and 9 months to 27 years and 4 months, with a median of 4.5 years. Their birth, family, and clinical features can be seen in Table 1. In only one pregnancy was reported twin pregnancy. One patient had no information about pregnancy, because the child was adopted (Table 1).

Three patients presented a family history of hearing loss in individuals before 50 years of age. Regarding to auditory function, five patients complained of hearing loss in the right ear and three in both ears. Among these patients the greatest commitment was on the left.
**TABLE I. Clinical Features Verified in the OAVS Patients**

| OAVS features | Preauricular pits, microtia, low-set ears, facial asymmetry, cleft lip/palate, abnormal vertebrae |
|---------------|-----------------------------------------------------------------------------------------|
| 1             | Preauricular pits, microtia, low-set ears, facial asymmetry, cleft lip/palate, abnormal vertebrae |
| 2             | Preauricular tags, microtia, facial asymmetry, anophthalmia, epibulbar dermoid, eyelid coloboma, low-set ears, abnormal vertebrae |
| 3             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 4             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 5             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 6             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 7             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 8             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 9             | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |
| 10            | Microtia, ear canal atresia, low-set ears, facial asymmetry, anophthalmia, epibulbar dermoid, low-set ears, abnormal vertebrae |

**Birth weight (g)**
- 2,800/AGA
- 4,900/LGA
- 2,950/AGA
- 2,755/AGA
- 3,125/AGA
- 3,350/AGA
- 3,700/AGA
- 2,365/AGA
- 1,580/AGA
- 3,150/AGA
- 3,500/AGA

**Birth height (cm)**
- 12 y 6 m
- 2 y 8 m
- 7 y 4 m
- 11 y 2 m
- 9 y 7 m
- 5 y 6 m
- 10 y
- 9 y 1 m
- 1 y 9 m

**Age (year/month)**
- 1 2 y 6 m
- 2 y 8 m
- 7 y 4 m
- 11 y 2 m
- 9 y 7 m
- 5 y 6 m
- 10 y
- 9 y 1 m
- 1 y 9 m

**Sex**
- M
- M
- F
- M
- F
- M
- F
- F
- F
- 5 M/5 F

**Weight (Kg)**
- 55 (P90–97)
- 10 (<P3)
- 60 (P50–75)
- 48 (P90–97)
- 40 (P90–97)
- 26 (<P97)
- 34 (<P97)
- 36 (P90)
- 40 (P90–97)
- 48 (P90–97)

**Height (cm)**
- 148 (P25–50)
- 148 (<P3)
- 148 (<P3)
- 148 (P50)
- 148 (P50–97)
- 148 (P75–90)
- 148 (P90–97)
- 148 (P90–97)
- 148 (P90–97)
- 148 (P90–97)

**Head circumference (cm)**
- 58 (>P98)
- 50 (P50–98)
- 60 (>P97)
- 60 (>P97)
- 55 (P90–98)
- 53 (P2–50)
- 53 (P98)
- 53 (P98)
- 54 (P50–98)
- 48 (P90–97)

**History of hearing complaint**
- ++
- +
- +
- +
- +
- +
- +
- +
- +
- +
- 8/10

**Parents/guardians find that patients listen well**
- ++++
- ++
- +
- +
- +
- +
- +
- +
- +
- +
- 8/10

**Reason Ear and foot surgeries**
- Appendicitis, aesthetic plastic surgery and infections
- Corrective surgery on spine, eyes, jaw, spine and feet
- Hand fracture
- Jaundice
- Asthma
- Seizures, pneumonia and intestinal infection
- Bronchiolitis
- Asthma
- 4/10

**AGA, appropriate for gestational age; LGA, large for gestational age; SGA, small for gestational age; NICU, neonatal intensive care unit; y, year; m, month; d, days; +, present; −, absent; NA, not applicable; ?, unknown.**
| Patients | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|----------|---|---|---|---|---|---|---|---|---|----|
| **Tonal and Vocal Audiometry** | | | | | | | | | | |
| **Right ear** | Normal | Normal | Profound sensorineural | NA | Normal | Moderate conductive | Moderate sensorineural | Moderate conductive | NE | Normal |
| SRI | 55 dB | 65 dB | NA | NA | NE | 100 dB | NE | 90 dB | NE | NA |
| SRT | 20 dB | NE | NA | NA | 45 dB | 70 dB | 65 dB | 45 dB | NE | NA |
| **Left ear** | Normal | Normal | Profound sensorineural | NA | Normal | Normal | Mild sensorineural | Moderate conductive | NE | Normal |
| SRI | 55 dB | 45 dB | NA | NA | NE | 50 dB | NE | 90 dB | NE | NA |
| SRT | 15 dB | 15 dB | NA | NA | 25 dB | 35 db | 30 db | 50 dB | NE | NA |
| **TOAE** | | | | | | | | | | |
| Right ear | NE | NE | NA | + | NE | -- | NE | NE | + | + |
| Left ear | NE | + | NA | -- | NE | + | NE | NE | + | + |
| **BERA** | | | | | | | | | | |
| Right ear | NE | 35 dB | NA | 30 dB | NE | 65 dB | NE | NE | NE | NA |
| Left ear | NE | 20 dB | NA | 60 dB | NE | 20 dB | NE | NE | NE | NA |
| **IMITANCIOMETRY** | | | | | | | | | | |
| **Right ear** | | | | | | | | | | |
| Tympanometric curves | NE | NE | NE | Type A | NE | Type A | NE | NE | NE | NA |
| Acoustic reflex | NE | NE | NE | NE | NE | + | NE | NE | NE | NA |
| **Left ear** | | | | | | | | | | |
| Tympanometric curves | NE | Type A | NA | Type A | NE | NE | NE | NE | NE | NA |
| Acoustic reflex | NE | + | NA | NE | NE | NE | NE | NE | NE | NA |

SRI, Speech Recognition Index; SRT, Speech Recognition Threshold; TOAE, Transient Otoacoustic Emissions; BERA, Brainstem Evoked Response Audiometry; dB, decibel; NE, not evaluated due to lack of cooperation from the patient for examination; NA, not applicable; +, present; --, absent.

*Test used to assess compliance (greater or lesser rigidity or laxity) of the tympanic membrane and middle ear ossicles (malleus, incus and stapes).
Audiological evaluation of OAVS patients

In the present study, five children had language delay. These observations are consistent with those described by Brosco et al. [2004]. Any type of hearing loss can compromise language, learning, cognitive development, and social inclusion of children. These aspects reinforce the need for referral OAVS patients to the audiologist as soon as possible.

The effects of unilateral hearing loss are smaller than those caused by bilateral losses; however, they may also cause problems. In the presence of environmental noise, children with unilateral hearing loss may present greater difficulties than normal listeners to understand speech, even when the ear is positioned toward the sound source [Brosco et al., 2004]. Furthermore, it is thought that even with mild hearing losses, intelligible speech, and reading skills may be delayed or impaired [Yule and Rutter, 1987].

Early recognition and detailed understanding of aspects related to the clinical features and outcome of patients with OAVS are essential for their proper management. Usually, it is carried out in a multidisciplinary way due to the wide spectrum of clinical findings observed in OAVS. Therefore, several specialties, as Pediatrics, Medical Genetics, Otorhinolaryngology, Ophthalmology, Neurology, Psychiatry, Pediatric Surgery, and Speech Therapy, are frequently involved.

Thus, there is obvious need for further studies to investigate speech pathology associated with OAVS. This will delineate more clearly what abnormalities are associated with this syndrome and may indicate what type of radiological and laboratory investigation are the most appropriate. As a result, this will allow the early identification and intervention of these changes.

REFERENCES

Brosco KC, Zorzetto NL, Costa AR. 2004. Audiology profile in patients with Goldenhar’s syndrome. Rev Bras Otorrinolaringol 70:645–649.

Cohen MM, Rollinck BR, Kaye CI. 1989. Oculoauriculo-vertebral spectrum: An updated critique. Cleft Palate J 26:276–286.

Cohen MS, Samango-Sprouse CA, Stern HJ, Custer DA, Vaught DR, Saal HM, Tifft CJ, Rosenbaum KN. 1995. Neurodevelopmental profile of infants and toddlers with oculo-auriculo-vertebral spectrum and the correlation of prognosis with physical findings. Am J Med Genet 60:535–540.

Davis H, Silverman SR. 1970. Auditory Test Hearing Aids. In: Davis H, Silverman SR, editors. Hearing and Deafness. Holt: Rinehart and Winston.

Engiz O, Balci S, Unsal M, Ozer S, Oguz KK, Aktas D. 2007. 31 cases with oculoauriculo-vertebral dysplasia (Goldenhar Syndrome): Clinical, neuroradiologic, audiologic, and cytogenetic findings. Genet Couns 18:277–288.

Gerlin JJ, Cohen MM, Hennekam RC. 2001. Syndromes of the head and neck. London: Oxford University Press. pp 790–797.

Grabb WC. 1965. The first and second branchial arch syndrome. Plast Reconstr Surg 36:485–508.

Kleinasser O, Schlothane R. 1964. Ear malformation in the framework of thalidomide embryopathy (Based on a survey of 70 infants born during 1959–1962). Z Laryngol Rhinol Otol 43:344–367.
Melnick M. 1980. The etiology of external ear malformation and its relation to abnormalities of the middle ear, inner ear and other organ systems. Birth Defects Orig Artic Ser 16:303–331.

Mondain M, Blanchet C, Venail F, Vieu A. 2005. Classification et traitement des surdités de l’enfant. Oto-rhino-laryngologie (traité) 20:190C–120C.

Poswillo D. 1973. The pathogenesis of the first and second branchial arch syndrome. Oral Surg Oral Med Oral Pathol 35:302–328.

Rahimov F, Ribeiro LA, de Miranda E, Richieri-Costa A, Murray JC. 2006. GLI2 mutations in four Brazilian patients: How wide is the phenotypic spectrum? Am J Med Genet Part A 140A:2571–2576.

Rollnick BR, Kaye CI, Nagatoshi K, Hauck W, Martin AO. 1987. Oculo-auriculo-vertebral dysplasia and variants: Phenotypic characteristic of 294 patients. Am J Med Genet 26:361–375.

Rosa RFM, Pfeil JN, Zen PRG, Rosa RCM, Grazia C, Paskulin AG. 2010. Phenotypical variability in supernumerary chromosome der(22)(11;22) syndrome (Emanuel syndrome). Rev Paul Pediatr 28:367–371.

Rosa RFM, Silva AP, Goetze TB, Bier BA, Almeida ST, Paskulin GA, Zen PRG. 2011. Ear abnormalities in patients with oculo-auriculo-vertebral spectrum (Goldenhar syndrome). Braz J Otorhinolaryngol 77:455–460.

Salvado A, Rodriguez K, Guarisco JL. 2003. Hemifacial microsomia. J La State Med Soc 155:136–141.

Strömland K, Miller M, Sjögren L, Johansson M, Joelsson BME, Billstedt E, et al. 2007. Oculo-auriculo-vertebral spectrum: Associated anomalies, functional deficits and possible development risk factors. Am J Med Genet Part A 143A:1317–1325.

Van Lierde KM, Van Cauwenberge P, Stevens I, Dhooge I. 2004. Language, articulation, voice and resonance characteristics in 4 children with Goldenhar syndrome: A pilot study. Folia Phoniatr Logop 56:131–143.

Vinay C, Reddy RS, Uloopi KS, Madhuri V, Sekhar RC. 2009. Craniofacial features in Goldenhar syndrome. J Indian Soc Pedod Prev Dent 27:121–124.

Werler MM, Sheehan JE, Hayes C, Padwa BL, Mitchell AA, Mulliken JB. 2004. Demographic and reproductive factors associated with hemifacial microsomia. Cleft Palate Craniofac J 41:494–500.

Yule W, Rutter M. 1987. Language development and disorders. Oxford: MacKeith Press/Blackwell.