

Middle and Inner Ear Malformations in Two Cases of Velocardiofacial Syndrome

Alfredo Tabith Junior*, Rainer Guilherme Haetinger, Fernando Leite de Carvalho e Silva***, Monica de Castro Gudmon****.**

* Master's degree. General Director DERDIC_PUCSP.

** Doctoral Degree. Radiologist – Imaging Doctor - Hospital Beneficência Portuguesa de São Paulo.

*** Graduation in Medicine. Otorhinolaryngologist – Phoniatriest at DERDIC/PUCSP.

**** University Diploma in Phonoaudiology. Phonoaudiologist at DERDIC/PUCSP.

Institution: Divisão de Educação e Reabilitação dos Distúrbios da Comunicação da Pontifícia Universidade Católica de São Paulo - DERDIC/PUCSP Med Imagem - Hospital Beneficência Portuguesa de São Paulo.
São Paulo / SP - Brazil

Mail address: Alfredo Tabith Junior – Rua Dra. Neyde Aparecida Sollitto, 435 – São Paulo / SP - Brazil - Zip Code: 04022-040 – Fax: (+55 11) 5908-8009 – E-mail: alfredo.tab@uol.com.br

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SUMMARY

- Objective:** To describe audiometric characteristics and middle and inner ear malformations in two patients with velocardiofacial syndrome.
- Method:** Audiometric evaluation, computerized tomography of the temporal bones and analysis of DNA for multiple markers of 22q11 region were performed in two patients with clinical signs of velocardiofacial syndrome.
- Results:** Conductive hearing loss related to chronic otitis media and middle and inner ear malformations were found, the latter with the use of reformations based on multislice acquisitions on of the computerized tomography of the temporal bones.
- Conclusion:** We consider it to be highly important to carry out a thorough evaluation and monitoring of the hearing evolution, as well as the occurrence of symptoms related to the vestibular function in patients with velocardiofacial syndrome. From the radiological point of view, attention should be given to the use of high quality techniques for the tomographic study of temporal bones.
- Keywords:** ear, hearing loss, velocardiofacial.

INTRODUCTION

Characteristic facial features, congenital cardiac anomalies, cleft palate and learning disabilities, are all major characteristics of the velocardiofacial syndrome, described in some patients by SEDLÁČKOVÁ(1) and outlined by SHPRINTZEN et al (2). New phenotypic alterations of this syndrome have been described in the meantime (3-5). Although considered as one of the most frequent syndromes associated with cleft palate (6), it is not frequently recognized in the pediatrics practice. It's caused by deletion of the long arm of the chromosome 22 (22q11).

Recently, middle and inner ear malformations have been described in VCFS. Patients with hearing loss associated with otitis media and with external ear malformations are described (7-8). The first reference to a primary defect of the ossicular chain was made in 2003, in a child with signs of the VCFS and 22q11.2 deletion (9), from whom was found primary lung dysgenesis along with congenital conductive unilateral hearing loss, due to malformation and subluxation of the left stapes, therefore, a conductive hearing loss not related to otitis media, which is very common in this syndrome. Middle and inner ear malformations were found in two children with VCFS. One of them showed a Mondini type cochlear malformation, an abnormal shape of the ossicles, with fusion of the malleus with the incus and a monopodal stapes. The other child showed a congenital middle ear malformation with fixation of the malleus on the left annulus tympanicus, and a common cavity bilaterally between the vestibule and the lateral semicircular canal (10).

This article aims at describing and characterizing the middle and inner ear malformations found in two Brazilian boys with the VCFS.

METHOD

This paper was approved by Comitê de Ética em Pesquisa da PUCSP, protocol nº 261/2008.

Subjects: Two boys with clinical signs of VCFS, at the ages of 4.7 and 6.7 years old.

Procedures: Audiological evaluation, including pure tone audiometry, tympanometry, acoustical reflex, and Computerized Tomography (CT) of temporal bones. In both, analyses of DNA sample with markers of 22q11 region were performed. A Toshiba Aquilion-slice thickness 0.6mm tomograph, an Interacoustics AC33 audiometer, and an Interacoustics AZ-7 middle ear analyser were used.

RESULTS

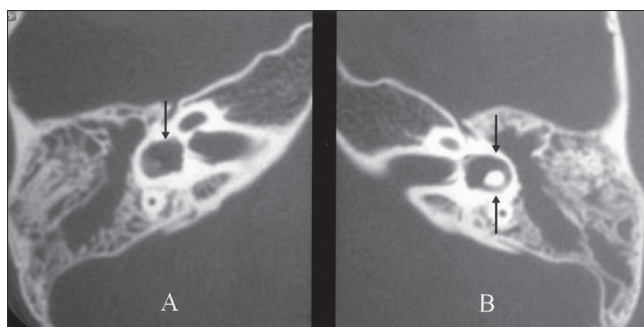
Patient 1 is a boy at the age of 6.7 years old, son of nonconsanguineous parents. He was born by cesarean, after a 41-week pregnancy. No family antecedents. He showed a submucous cleft palate, which was operated when he was 2.6 years, with good functional result. The neuropsychomotor development was normal. He shows clinical signs of VCFS, without cardiac defects. The DNA sample analyses from the patient and his parents, with five markers, revealed the deletion of, at least, one marker in the 22q11.2 region, which confirms the VCFS diagnosis.

The audiogram shows air tone thresholds of 15dB HL at 250, 500, 1000 Hz, 20dB HL at 2000 and 4000Hz and 25dB HL, 60dB HL and 70dB HL (respectively at 4000, 6000 and 8000 Hz) in the right side. Air tone thresholds of 15dB HL at 250 and 500 Hz, 20 dB HL at 1000 and 2000 Hz, 25dB HL at 4000 Hz and 40dB HL at 6000 and 8000 Hz in the left side. Bone tone thresholds of 5dB HL at 500 e 1000 Hz, 0dB HL at 1000 Hz and 10 dB HL at 2000 and 4000 Hz. SRT was 35 dB HL in the right and 30 dB HL in the left. WRS was of 100% at 60 dB bilaterally. Tympanometry was of type B and the acoustical reflex was absent bilaterally. The CT of temporal bones shows signs of bilateral inflammatory otomastoidopathy, a common cavity between the vestibule and the lateral semicircular canal on the right side and an asymmetry of the lateral semicircular canal on the left (Picture 1). Ossicles had a normal configuration.

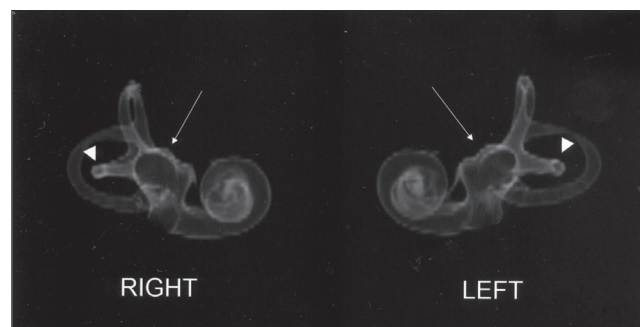
Patient 2 is a 4.6 year-old boy, son of non consanguineous parents. He has a third degree cousin from his mother branch, which bears a cleft palate. Born by cesarean he developed respiratory infection, hyperbilirubinemia and hypoglycemia in his 4th day of life, treated for 10 days.

He had a minor delay in his motor development and a heart murmur dysfunction that was monitored by a cardiologist. He had a delay in language development and, currently, shows a hypernasal voice and compensatory articulation errors. The oral examination shows a hypoplastic uvula, a short palate with reduced elevation movements. He has clinical signs of the VCFS. The analyses of DNA samples from him and his parents revealed that the patient shows deletion in, at least, four markers in the region 22q11.2, which confirms the VCFS diagnosis.

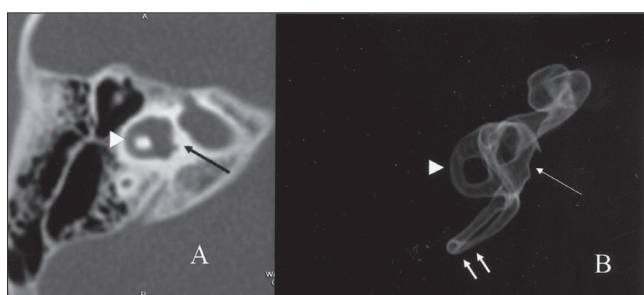
The audiological evaluation shows a conductive hearing loss, with air thresholds around 40 to 50dB HL on the right side and 25 to 30dB HL on the left, with normal bone thresholds, between 0 and 10 dB HL bilaterally. SRT was of 50dB HL on the right side and 30 dB HL on the left



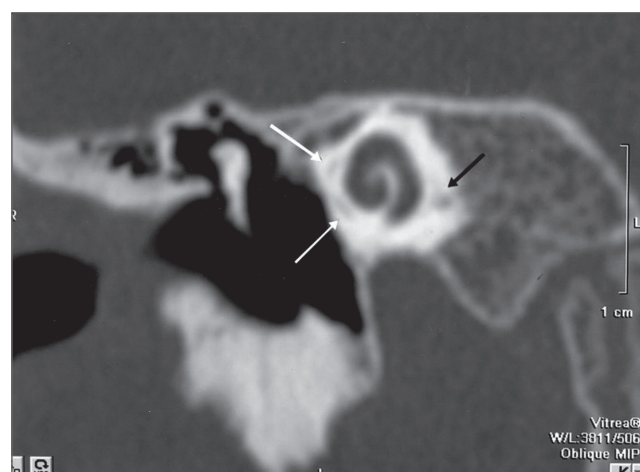
Picture 1. Patient 1: CT showing bilateral inflammatory otomastoidopathy and a common cavity between the vestibule and the lateral semicircular canal at right (arrow in A). Asymmetry of the lateral semicircular canal at left (arrows in B).



Picture 2. Patient 2: 3-D images from the osseous labyrinth based on CT showing bilateral displasia of the lateral semicircular canal (arrowheads) and globosity of the vestibules (arrows).



Picture 3. Patient 2: Axial and 3-D reconstruction showing displasia of the lateral semicircular canal (arrowheads in A and B) in comparison with the posterior semicircular canal (double small arrows in B) and globosity of the vestibule (long arrows in A and B).



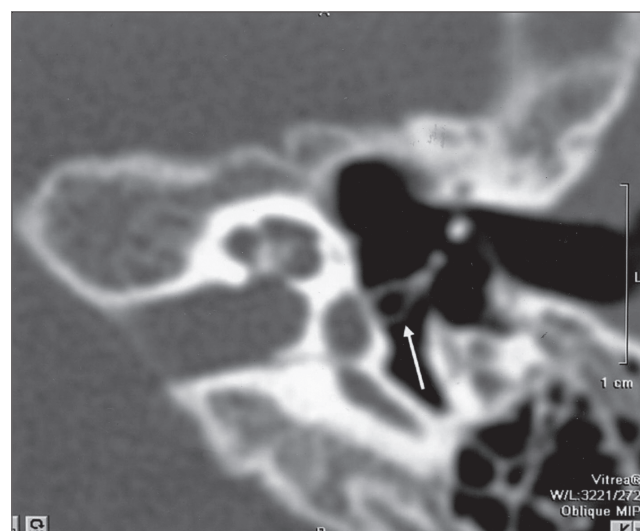
Picture 4. Patient 2: Mild pericochlear radiolucent foci (arrows) in CT coronal view.

side. Tympanometry curve type A and absence of acoustical reflex bilaterally.

CT of temporal bones shows a bilateral displasia of the lateral semicircular canals, which are shorter in comparison with the posterior and superior semicircular canals, globosity of vestibules (Picture 2 and 3) and mild pericochlear radiolucent foci (Picture 4). Deformity of the stapes was found at the left side, characterized as a kinking of the posterior crus (Picture 5). This finding was only detected after an oblique reformation parallel to the stapes (about 30° to 45°).

DISCUSSION AND CONCLUSIONS

Hearing loss is a very frequent symptom in VCFS and in most instances is related to chronic or recurrent middle ear infections. Our findings, which have already been described by others, shows that there can be also middle and inner ear malformations, along with malformations of vestibule and



Picture 5. Patient 2: Oblique CT reformation with evidence of deformity of the posterior crus of the left stapes (arrow).

semicircular canal. On the other hand these primary middle and inner ear malformations in VCFS leads to the studies about the role of the genes TBX1, in the morphogenesis of middle and inner ear (11). From the clinical point of view, we consider it to be highly important to carry out a thorough evaluation and the monitoring of the hearing evolution, as well as the occurrence of symptoms related to the vestibular function, already described in children with the VCFS (12). Further studies are necessary to establish whether this is a consistent morphological trait in VCFS. From the radiological point of view, oblique reformations with zoom parallel to the stapes are very helpful in detecting mild deformities or incomplete crus. Sometimes the routine axial images do not show completely the stapes and reformations based on multislice acquisitions are of high quality. Regarding the labyrinth, a three-dimensional reconstruction is an interesting tool for a global analysis.

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