Case Series and Review

Auditory and language features in children with 18q deletion: Our experience and a brief review of the literature

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Abstract

18q deletion is a rare genetic condition that occurs approximately 1 in 40,000 live births. The aim of this study is to describe four cases of 18q deletion, analyzing their auditory and language skills. A secondary aim is to compare our findings with those reported in the literature in order to propose a standardized assessment protocol and guidelines for auditory treatment and rehabilitation. All children underwent a detailed audiological evaluation including otoscopy, pure-tone audiometry, and auditory brainstem responses. We also administered language and speech tests according to the children's age and skills. Comorbidities and disease severity varied depending on the genetic mutation. Data from the literature review are consistent with our findings. Therefore, the type of auditory rehabilitation changed among patients. Despite the heterogeneity of phenotypes and severity, hearing loss and stenotic external auditory canals were detected in all our patients with 18q deletion. Accurate diagnosis and follow-up are mandatory to improve auditory and language skills and quality of life. Due to the complexity of the cases, no standardized assessment protocols or treatment can be routinely proposed.

Keywords: 18q deletion, children, hearing loss, language delay

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INTRODUCTION

Terminal deletion of the long arm on chromosome 18 (18 q-) occurs approximately 1 in 40,000 live births.[1] These patients may exhibit different phenotypes, including developmental delay, facial dysmorphism, foot deformities, physical growth retardation, short stature, hypotonia, mental retardation, white matter abnormalities, endocrine and autoimmunity disorders, and hearing impairment.[2,3]

Hearing loss can be sensorineural hearing loss (SNHL), conductive hearing loss (CHL), or mixed hearing loss (MHL). A high percentage of affected patients may also have narrow or stenotic external auditory canals (EACs).[4] Since hearing loss is found in approximately 50%–60% of individuals with 18q deletion,[5] it could be considered a relevant diagnostic clue of the disease. Most women

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who carry babies with a deletion of 18q experience no problems during pregnancy. Therefore, suspicion of this genetic condition is generally raised by the presence of clear physical abnormalities at birth or later due to delays in the child's neurological development.[4] The great heterogeneity of the phenotypes is due to the high variability of the genetic disorder. Deletion can occur in different breakpoints on 18q with a range size of 0.5–30 Mb.[6] Under normal conditions, this DNA region includes the teashirt family zinc finger 1 (TSHZ1) and myelin basic protein (MBP) genes; it is reasonable to hypothesize that the auditory and otological phenotypes in individuals with 18q syndrome are secondary to the haploinsufficiency of these genes.[4] In particular, mutations in the TSHZ1 gene may be associated with congenital aural atresia syndrome. Because aural atresia is a very rare and highly penetrating finding, it represents one of the most distinctive clinical features of distal 18q deletion. Conversely, the MBP gene is associated with SNHL due to demyelination of the fibers.[3,4,7] The CHL component of the distal 18q deletion has been largely described through genetic analysis of TSHZ1; indeed, this gene is required for the embryogenesis of the craniofacial and axial skeleton.[8] CHL can be secondary to Eustachian tube dysfunction, serous otitis media, EACs stenosis/atresia, and/or tympanic membrane retraction. Moreover, the SNHL phenotype is not well characterized: SNHL may be found in different patterns, including high-frequency limited SNHL, flat SNHL, and "cookie bite" or "U-shaped" SNHL.[3] Otological and auditory conditions due to 18q deletions, as well as the presence of comorbidities, determine the need for a multidisciplinary evaluation of these patients. Indeed, all patients with 18q deletion should undergo a thorough assessment of the general health status, in particular of the neurological development, cognitive profile, hearing status, and language abilities, in order to provide them with specific medical therapies, surgical procedures, and rehabilitation programs. Timely and appropriate interventions should be combined with comprehensive family counseling, thus mitigating the impact of disabilities and maximizing each individual patient's potential. However, standardizing and suggesting clinically relevant prognoses and treatment for patients with 18q deletion is particularly challenging because each patient has a unique region of hemizygosity. As a matter of facts, because of the high heterogeneity of this genetic condition, the treatment of children with 18q deletion varies according to the different signs and symptoms.

We report four cases of pediatric patients with 18q deletion syndrome who were admitted to the Audiology Department of Modena, Italy. The aim of this study is to describe the hearing characteristics and language outcomes of these patients, highlighting the different hearing rehabilitation strategies. A secondary aim is to provide a brief review of the literature in order to highlight the most common auditory features of 18q deletion disease and to identify, if possible, a specific assessment protocol for patients with this condition.

MATERIALS AND METHODS

This retrospective study was conducted at the Audiological Department of the Policlinic of Modena (Italy) between January 1, 2010, and December 31, 2022. The study included all patients under the age of 18 years diagnosed with 18q deletion who were referred to the Audiological Department of the Policlinic of Modena for a comprehensive audiological evaluation.

All patients underwent otoscopy, pure-tone audiometry, and auditory brainstem responses (ABRs). Language and perception levels were assessed through the AMBO and Ling tests[9] and then periodically re-evaluated with language and auditory tests, according to the age and level of communication skills.

These tests included the "LittlEARS" questionnaire,[10] the It-MAIS questionnaire,[11] the PRISE questionnaire (Italian Adaptation of Production Infant Scale Evaluation),[12] and the I-LIP test (Listening Profile, Italian version)[13] for the assessment of auditory skills; the McArthur questionnaire,[14] the intelligibility context scale (ICS),[15] the Rustioni and Lancaster morphosyntactic test,[16] and the L2MA2 test[17] for the evaluation of speech and language levels.

The LittlEARS is a standardized test assessing the development stage of auditory skills in children up to 24 months old or with a hearing age of 24 months.[10] The It-MAIS questionnaire investigates the changes in child's vocalization using the auditory devices; one section of the questionnaire focuses on the recognition of environmental sounds and voice.[11] PRISE is a questionnaire that investigates the evolution of the child's vocal production. It explores the stages of linguistic development from the prelexical stage (vocalizations and babbling) to the appearance of the first words.[12] The I-LIP test evaluates the development of listening skills in hearing impaired children; it is based on the observation and assessment of auditory behavior during spontaneous activity, play, and interaction with sound instruments.[13] The McArthur questionnaire assesses the child's linguistic and gestural communications in the early years of life, from nonverbal cues to vocabulary expansion and words combinations.[14]

The ICS is a 7-item parent-completed questionnaire to rate the degree to which children's speech is understood by different communication partners on a 5-point scale. It consists of a battery for the psycholinguistic examination of children's oral language, written language, memory, and attention of children.[15] The Rustioni and Lancaster test evaluates the child's morphosyntactic comprehension,[16] whereas the L2MA2 test assesses oral language, written language, memory, and attention.[17]

Parents were also administered structured questionnaires aimed at assessing their child's auditory and linguistic developments. The terms "18q deletion" AND "hearing loss" were searched in PubMed and Web of Science databases. We screened titles, abstracts, and full texts from relevant literature to evaluate the content of the articles and extract valuable information. Studies were included when the following criteria were met: (1) original reports; (2) cases of 18q deletion and hearing loss or 18q genetic disorders and hearing loss; (3) pediatric age of patients (0–18 years); (4) the study design was not editorial, letter to the editor, or review; and (5) the reports were published in English.

RESULTS

During the recruitment period, four patients with 18q deletion were referred to the Audiological Department of the Policlinic of Modena.

Case 1

A 6-year-old boy with hearing loss and language delay was referred to our audiological department. He was diagnosed with a terminal mosaic deletion of 30.338 Mpb ± 0.100 Mpb on chromosome 18 (18q21.1q23) and a terminal mosaic duplication of 13.687 Mpb ± 0.100 Mpb on chromosome 18 (10p1132p11.21). Universal newborn hearing screening at birth, performed with transient-evoked otoacoustic emissions (TEOAEs), failed bilaterally. Air conduction (AC) ABRs showed the presence of wave V up to 75 dB nHL in the right ear and 80 dB nHL in the left one, whereas bone conduction (BC) ABRs revealed a hearing threshold of 45 dB nHL bilaterally. Therefore, a diagnosis of MHL was performed. Evaluation of perception skills with hearing aids (HAs) showed a positive response to drum, grater, and cowbell on the AMBO test. On the Ling test,[9] he recognized/m/,/a/and/i/. At our audiological assessments, pure-tone average (PTA) with HAs was 60 dB and the results were not satisfactory. Physical examination revealed stenotic EACs with a pinpoint opening, leading into the medial ear canal and a rudimentary tympanic membrane. The patient had no family history of childhood hearing loss or ear malformations.

He had been using HAs since he was 1½ years old due to severe bilateral hearing loss. The patient was also diagnosed with focal epilepsy, psychomotor retardation, myopia, convex right lumbar scoliosis with modest rotation of the metameres, and dorsal kyphosis with straightening of the lumbar spine. Moreover, the child was provided with percutaneous endoscopic gastrostomy tube carrier. We performed a further ABR evaluation that confirmed severe bilateral MHL: AC ABRs revealed the presence of wave V up to 70 dB nHL in the right ear and 80 dB nHL in the left one, whereas BC ABRs showed a hearing threshold of 45 dB nHL bilaterally. Perception tests showed detection of all sounds, except/s/and/sc/on the Ling test[9] and chick, castanet, grater, and drum on the AMBO test. Tympanographic morphology, compliance, and pressure peak were not detectable, and stapedial reflexes were not elicited bilaterally. Thus, we proposed hearing rehabilitation with the BAHA soft band. PTA with the BAHA soft band was found to be 45 dB; data logging analysis revealed that the patient used the BAHA soft band for at least 6 h per day. Parents were satisfied and reported positive reactions to environmental sounds (pots, music) and voices, even at nonsustained intensity, with the new hearing rehabilitation system, as well as the ability to identify familiar voices, and demonstrate interest and reactions to modulated voice; noise of dishes, pots, pans, and ditties; and sound of music box. Assessment of the communicative level revealed that the child expressed discomfort by crying or moving head. The LittlEARS questionnaire[10] score was 7/35 (expected value for 2–3 months), revealing that the child did not meet the auditory milestones for his age. Cochlear implantation was not considered a viable option due to severe comorbidities and high anesthesiology risks. Computed tomography (CT) scan of the head showed absence of the anterior wall of the EACs, whereas the mastoid and tympanic cavity were hypopneumatized, and the ossicular chain was malformed bilaterally. The diameter of the EACs was approximately 3.0 mm. The bony structures of the inner ear were nearly normal, whereas the inner ear canal was symmetrically enlarged on both sides. Magnetic resonance imaging (MRI) of the brain showed subtotal agenesis of the corpus callosum and hippocampal commissure, whereas the shape and volume of the lateral ventricles were altered (predominance of the right ventricle and bull's horn appearance of the lateral ventricles anteriorly).

Case 2

A 25-day-old female neonate was referred to our audiological department for an audiological evaluation. She was intubated for respiratory depression and her genetic analysis revealed deletion of 11 Mb at 18q22.2q23.

Universal newborn hearing screening (performed with TEOAEs) had failed bilaterally; she also had narrow EACs and congenital nystagmus. AC ABRs recorded at 3 months of age revealed moderate bilateral hearing loss (wave V was detected up to 60 dB in the left ear and 70 dB in the right ear). Tympanometric parameters were undetectable, and stapedial reflexes were unelicitable bilaterally. The indication for HAs and speech therapy was given to rehabilitate auditory functions. During the audiological follow-up, it emerged that HAs were used for more than 10 h a day, without discomfort reactions. Speech and language assessments with HAs showed the presence of reactions to different sound intensities. The Ling sound test[9] was positive for the phoneme/ʃ/using the auditory channel and the normal speaking voice; sharp reactions were expressed to the sound of the drum and cowbell. At 6 months of age, on the It-MAIS questionnaire,[11] the patient obtained a score of 4/40 (low for the age), whereas on the "LittlEARS"[10] scored 5/35 (expected value for 1–2 months). The PRISE questionnaire (Italian Adaptation of Production Infant Scale Evaluation)[12] score was 20/44 (50th percentile for 3–4 months) and the I-LIP (Listening Profile, Italian version) questionnaire score was 3/16 (low for the age).[13] The diameter of the EACs was approximately 2.5 mm, whereas no other abnormalities were detected by brain CT; conversely, brain MRI revealed a weakly hyperintense appearance of the lobar white matter of both cerebral hemispheres and the splenium, with a poorly recognizable capsular system on T2. The size of the supratentorial ventricular system was increased, whereas the peripheral liquor spaces were slightly enlarged bilaterally. Acoustic and facial nerves and the membranous labyrinth were normal bilaterally. At 9 months of age, AC ABRs revealed the presence of wave V up to 60 dB nHL bilaterally, whereas BC ABRs showed a hearing threshold of 35 dB nHL bilaterally; PTA with HAs was approximately 30 dB. At 1 year of age, she gained the ability to turn her head towards the speaker and to look for sound sources. The hearing threshold with HAs was improved up to 20 dB. On the expressive level, the patient achieved the ability to vocalize with the sound/a/and to produce babbling with the occlusive phonemes/p/,/b/,/t/and the bilabial phoneme/m/. At 1 year and 6 months of age, she produced the words/mom/and/dad/, was interested in toys, and reacted to voices. The Ling test[9] was positive for the sounds/m/,/u/,/a/,/i/,/ʃ/and occasionally for the fricative/s/using the auditory channel and the normal speaking voice. The "LittlEARS" questionnaire score[10] was 13/35 (expected value for 5–6 months) and the PRISE questionnaire (Italian Adaptation of Production Infant Scale Evaluation) score[12] was 28/44 (50th percentile for 7–8 months). The McArthur questionnaire[14] revealed that the patient had the skills to recognize 66% of the first signs and 3 out of 28 of sentences; imitation and repeat skills were absent. She was detected at the 25th–50th percentile for 8–9 months for word comprehension, 50th percentile for 10–11 months for word production, and 25th–50th percentile for 8–9 months for gesture production.

Case 3

A 12-year-old boy with deletion of 18q was referred to our audiological department. At birth, TEOAEs were PASS bilaterally. AC ABRs revealed the presence of wave V up to 30 dB nHL bilaterally, whereas BC ABRs showed a hearing threshold of 15 dB nHL bilaterally (mild CHL). Stapedial reflexes were present bilaterally. The EACs were bilaterally stenotic, and the tympanic membranes were only partially visible (CT scan documented that the diameter of the EACs was about 3.8 mm), whereas no other abnormities were detected; nasal air leakage, labial rhyme not fully competent, occasional sialorrhea, and nasal regurgitation were also detected. MRI of the brain showed reduced length of the corpus callosum and incomplete development of the rostrum, knee, and lower third of the cerebellar vermis. Pontocerebellar angles were normal bilaterally. Due to the presence of difficulties in performing simple praxis (lateralization of the tongue, difficulty in inflating the cheeks), the patient was referred to receive speech therapy and use augmentative alternative tools for communication since he was 1 year old. No indication for HAs was given as the child's hearing threshold was considered acceptable. He also took valproic acid for epilepsy. During the communication skills assessment, the patient was able to pronounce single words in succession. He sometimes reversed words using simple phrases and expressions, with poorly intelligible speech, altered prosody, and nasal gasps. The phonetic–phonological level (PFLI test) was not complete as the velar phonemes/k/,/g/ were absent; simplifications of the phonological system, distortion of the alveolar/r/, and instability of the affricate phonemes/tʃ/,/dʒ/and/dz were also detected. On the in-context intelligibility scale (ICS),[15] the child scored 17/35 (frequency of child functional speech intelligibility: Sometimes-rarely). On the Rustioni and Lancaster morphosyntactic test,[16] more than acceptable mistakes were found; gestures were used to aid comprehension.

Case 4

A 12-year-old Belgian boy was referred to our department for an audiological evaluation. He was born prematurely (30 weeks of gestational age), and genetic analysis showed an 18q21 deletion (no more information about his mutation were given). Universal newborn hearing

screening (performed with TEOAEs) failed bilaterally. At the AC ABRs assessments, wave V was identifiable up to 50 dB nHL in the left ear and 45 dB nHL in the right one, whereas BC ABRs revealed a hearing threshold of 35 dB nHL bilaterally. He had been using HAs since he was 3 years old. The medical objective examination revealed congenital right nystagmus, as well as facial and body abnormalities such as a high-arched palate and short fingers. External ear malformations were also noted, including preauricular pits and narrow external auditory canals. Brain MRI showed partial agenesis of the corpus callosum and nonspecific abnormalities of the white matter. CT of the ear had already been performed in Belgium: The parents reported that the imaging confirmed a lower diameter of the EACs and the presence of malformations of the ossicular chain bilaterally.

The phonological evaluation revealed numerous simplification processes and sporadic impairment of speech intelligibility. On the L2MA2 test, the phonological level was lower than the age-predicted average, with values below 6 σ and 2 σ for simple and complex syllables, respectively; lexical skills, especially expressive ones, were impaired (−1.1 σ).[17] The patient also had developmental delay, cardiac abnormalities, snoring and eosinophil esophagitis; he underwent adenoidectomy, cholecystectomy, umbilical and inguinal hernia repair.

Brief literature review

Overall, 35 manuscripts were retrieved from PubMed and Web of Science databases. Nine articles met the inclusion criteria and were included in the present study.[3,5,7,18-23] Table 1 summarizes the results of the review. A total of 125 patients (49 males and 76 females) were analyzed, ranging from 8 months to 18 years old. The size of the deletion on 18q was different; moreover, duplication, inversion, and mosaicism of 18q were also found.[21,23,24] Patients generally developed SNHL, CHL, or MHL and often had stenotic EACs. In one case, enlarged EACs were detected; two subjects had low-set ears, whereas one had periauricular pits. Most patients also presented with facial, neck, heart, and body dysmorphia; neuro-motor development delay; intellectual disability; abdominal obesity; endocrinal disease; and/or autoimmune disease. Language and speech skills were delayed, and sometimes behavior and self-care abilities were impaired.[3] Regarding the treatment of hearing loss, HAs were the preferred solution,[5,19] whereas bone-anchored HA was proposed only in one case.[7] Early external ear surgery was occasionally performed in order to improve hearing level.[3,5]

DISCUSSION

The present study describes the auditory and language features of four young patients diagnosed with 18q syndrome. Interestingly, although similar genetic alterations can occur, patients generally do not develop the same conditions. Indeed, the size and site of the deleted region result in broad phenotypes, such as short stature, cognitive impairment, hypotonia, abnormal genitalia, growth hormone deficiency, flattened midface, aural atresia, renal abnormalities, and neurologic manifestations (including delayed myelination). Patients can develop CHL or SNHL, even with a sudden onset; these conditions may coexist.[3] At the same time, aural atresia/EACs stenosis have been suggested as warning signs for distal 18q deletion due to their high prevalence. Moreover, other rare genetic mutations involving 18q (e.g. inversion or mosaicism) may be responsible for hearing loss and/or narrow EACs.[21,23] An early and accurate diagnosis is of paramount importance to ensure the most appropriate rehabilitation treatment and to improve patients' quality of life. Auditory screening tests through pure-tone or behavioral audiometry (depending on age), Otoacoustic Emissions (OEAs) and ABRs, and brain CT/MRI imaging should be performed to better evaluate the severity of the disease. Consistent with the literature, when appropriate, both HAs and BC HAs may be successful auditory solutions for the patients. Early surgery could help achieve better anatomic conditions and outcomes.

CONCLUSIONS

The 18q deletion is a rare and complex genetic condition. As it may involve different genes on the chromosome 18, it results in a wide range of phenotypes, requiring different pathways of care and management. The main audiological features include SNHL, CHL, and stenosis of the EACs. Language and speech skills vary according to the severity of the otological and hearing impairments, as well as the initiation and type of auditory rehabilitation programs. General health status and comorbidities should be considered when evaluating children's improvements as they can negatively impact long-term outcomes. Due to the great heterogeneity of the condition, no assessment protocols can be standardized, although a comprehensive medical evaluation including ABR, OEA, CT/MRI imaging, language tests, and accurate follow-up should be performed. The therapeutic indications should be personalized on the basis of the patient's clinical conditions. In the presence of the same hearing impairments, different rehabilitation strategies may also be proposed to achieve the best outcomes. Correct diagnosis and early rehabilitation may help improve patient's quality of life.

Table 1: Literature review and description of our patients

Reference	*n*, sex and mean age	Deletion	HL	Aural structure	Language and communication skills	Auditory treatment	Imaging	Comorbidities
Strathdee *et al*., 1997[18]	2 females (2.7 years)	46, XX del (18) (pter-+ q22::q23-+qter)	Moderate bilateral HL	Stenotic EACs, middle–external ear dysmorphia (50%), periauricular pits (50%)	Expressive language delay (50%)	NR	NR	Facial, neck, and body dysmorphia; developmental delay; gross-motor delay; psychiatric disease
Keppler-Noreuil *et al*., 1998[19]	1 female, 8 males	46, XX Inv (18) (q21.1q23)	Bilateral HL	Low-set ears, stenotic EACs	Low language and speech skills	NR	MRI: Increased signal intensity areas in the deep white matter of the cerebral hemispheres, with abnormal myelination	Facial, neck, heart, and body dysmorphia; mild generalized hypotonia; developmental delay
Jayarajan *et al*., 2000[5]	2 (1 female, 1 male) (7 years)	18q. 22-qter	Bilateral mild SNHL; bilateral MHL	Stenotic EACs (50%), enlarged EACs (50%), no tympanic membranes, ossicular chain deformities	NR	HA (50%), external ear surgery	MRI and CT: Normal	Facial, neck, and body dysmorphia
Gunn *et al*., 2003[20]	1 male (12 years)	46, XY del (18) (q23)	Mixed bilateral HL	Stenotic EACs	Delayed and very low language and speech skills	HA	CT: Normal MRI: Diffusely hyperintensity of deep white matter of the cerebral hemispheres	Facial, neck, and body dysmorphia; hypotonia; brachycephaly; developmental delay; cognitive impairment, motor delay
Dostal *et al*., 2006[7]	1 male (2.5 years)	46, XY del (18q22.2Yqter)	Bilateral asymmetric (RE > LE) CHL	Low-set ears, total right atresia, stenotic L-EAC	NR	Bone-anchored HA	CT: Normal	Facial, neck, heart, and body dysmorphia; hypotonia; brachycephaly; developmental delay
Özsu *et al*., 2014[21]	2 females (12.8 years)	18(q21.31-q23); 18q21.32	Bilateral HL	Auricular anomaly (50%)	NR	NR	NR	Facial, neck, heart, and body dysmorphia; neuromotor development delay; intellectual disability; abdominal obesity; endocrinal disease; scoliosis of the lumbar vertebrae; right nystagmus; allergic disease short stature; moderately high TSH level; renal disease
Perry and Cody, 2014[3]	113 (45 males, 68 females) (8 years)	18q deletion	CHL: 66% (improving over time) SNHL: 28% (HFSNHL 75%, flat SNHL 19%, cookie bite pattern or low frequency loss 6%)	Aural atresia/ stenosis (66%), ETD (78%)	Delayed language and speech skills, low home living, daily self-care, managing social and leisure activities, impulse control, adapting to unexpected changes, planning and organizational skills	Previous reconstructive surgery (22%)	NR	Facial, neck, heart, and body dysmorphia; delayed myelination of the brain; cognitive impairment; autoimmune disease
Choi *et al*., 2016[23]	1 male (1.8 years)	mosaic der (18) t (1; 18) (q32.1;q21.3)	Moderate bilateral asymmetric (RE > LE) HL	NR	Delayed language and speech skills	NR	MRI: Mild increased T2 signal in bilateral periventricular white matter	Facial, neck, heart, and body dysmorphia; developmental delay
Gunes *et al*., 2008[24]	1 female (18 years)	46, XX del (18) (q21.2→qter)	NR	NR	NR	NR	NR	Facial, neck, heart, and body dysmorphia; mental and growth developmental delay; endocrinal disease

Contd...

Table 1: Contd...

Reference	*n*, sex and mean age	Deletion	HL	Aural structure	Language and communication skills	Auditory treatment	Imaging	Comorbidities
Anlaş *et al.*, 2023[25]	1 female (3.11 years)	Dup18p11.32p11.21 18q11.1q11.2, del18q21.33q23	Bilateral SNHL (LE > RE)	Stenotic EACs	Delayed language and speech skills	NR	MRI: Thinning of posterior areas of the corpus callosum	Facial, neck, heart, and body dysmorphia; severe intellectual disability; and motor retardation
Our patients	4 (3 males, 1 female) (7.75 years)	18q21.1q23 18q22.2q23 18q21	Severe bilateral MHL; moderate bilateral MHL; mild CHL; moderate bilateral MHL	Narrow EACs, pinpoint opening of the medial ear canal, rudimentary tympanic membranes, preauricular pits	Delayed language and speech skills; phonetic impairments	BAHA soft band; HAs	CT: Absence of the anterior wall of the EACs, bilaterally malformed ossicular chain and inner ear canals. MRI: Agenesis of the corpus callosum and hippocampal commissure agenesis, lateral ventricle abnormality; CT: Normal. MRI: Weakly bilateral hyperintensity of lobar white matter, poor representation of capsule system, supratentorial ventricle, and peripheral liquor spaces alterations; MRI: Reduced length of the corpus callosum, incomplete development of the rostrum, knee and lower third of the cerebellar vermis; MRI: Partial agenesis of the corpus callosum, nonspecific white matter abnormalities	Facial and body abnormalities, epilepsy, psychomotor delay, developmental delay, myopia, congenital nystagmus, PEG, nasal air leakage, not entirely competent labial rhyme, sialorrhea, cardiac abnormalities, snoring and eosinophil esophagitis

HL: Hearing loss, CHL: Conductive HL, CT: Computed tomography, EACs: External auditory canals, ETD: Eustachian tube dysfunction, HA: Hearing aids, LE: Left ear, MRI: Magnetic resonance imaging, NR: Not reported, RE: Right ear, SNHL: Sensorineural HL, MHL: Mixed HL, PEG: Percutaneous endoscopic gastrostomy, TSH: Thyroid stimulating hormone, HFSNHL: High-frequency limited sensorineural HL

Limitations

The rarity of the 18q syndromes influenced the number of patients involved in this study. The tests used to evaluate the language and communication skills of the patients were chosen according to age and learning levels, therefore the same battery of tests was not always administered to the patients. Similar restrictions are also reported in the literature. Therefore, data should be evaluated and compared considering these limitations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the forms, the legal guardians have given their consents for the patients' images and other clinical information to be reported in the journal. The guardians understand that the patients' names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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