

CASE REPORT

Cochlear implant in Kearns-Sayre syndrome: A case study of twin sisters

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ABSTRACT

Hearing loss may be related to several factors, including hearing loss resulting from certain genetic syndromes. Kearns-Sayre syndrome is characterized by mutations in mitochondrial DNA (Deoxyribonucleic Acid), responsible for the production of energy (adenosine triphosphate-ATP), which is extremely important for the development of structures that require it, such as the cochlea. The case was followed up at the hospital since 2000, due to the progressive characteristic of hearing loss found in audiological tests and findings in cases related to the syndrome. The intervention with individual sound amplification devices proved to be of little benefit for good oral communication of one of the patients, who was diagnosed with bilateral profound hearing loss. Thus, after discussions in clinical meetings, the team opted for the indication of the cochlear implant for the patient, according to the current criteria for indication of this surgery, and with which it obtained good results. His twin sister, who presented good results with hearing aids, will continue in audiological follow-up, to verify the evolution of the case and discuss a new approach, if necessary. Patients with suspected or diagnosed Kearns-Sayre syndrome should seek audiological diagnosis, because it is a possible progressive hearing loss, requiring rehabilitation with the use of hearing devices. Maintaining oral communication is extremely important because, in these cases, other functions will be impaired, such as muscle tone and vision.

Keywords: hearing loss; cochlear implant; syndrome; diseases in twins; audiology

1. Introduction

Several causes of hearing loss are reported in the literature and, regardless of the etiology, it is

important that the diagnosis and intervention are performed early. Approximately 30% of genetic hearing losses occur associated with a syndrome^[1,2].

Kearns-Sayre syndrome (KS) is related to ge-

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netic mutation in mitochondrial DNA. Mitochondria is an intracellular organelle that has its own genome (DNA)^[2], and multiple deletions of this genome are possible^[3]. The inheritance of the mitochondrial genome is maternal, because during fertilization the tail of the sperm, which contains the mitochondria, is displaced during penetration into the egg. In KS syndrome, part of the zygote DNA is not formed, but these mutations can also occur spontaneously^[4].

The main function of mitochondria is to provide energy to cells in the form of ATP (Adenosine Triphosphate) and some organs require higher energy and are most affected by cases of mutations in the DNA. Among these organs are nerve, muscle, optic, endocrine and auditory cells. The cochlea is an organ that requires a lot of energy, therefore mutations in the mDNA of hair cells can cause bilateral, symmetrical and progressive sensorineural hearing loss (SNHL)^[2,4,5].

KS syndrome was first described by Kearns and Sayre in 1959^[6], in a case report that presented with external ophthalmoplegia, pigmentary retinopathy and cardiac conduction disorder (CCD). It is a rare syndrome and it is estimated that the appearance of cases occurs in 1.6 for every 100,000 individuals^[7].

Diagnosis occurs through the observation of a triad: Progressive external ophthalmoplegia, pigmentary retinopathy and CCD. The first signs and characteristics of the syndrome usually appear before the age of 20, as observed in the literature^[3,6-10]. In addition, it is possible to perform genetic testing, mainly seeking information related to DNA, where multiple deletions or mutations are found in cases of KS syndrome^[11,12].

In the literature^[9], there are reports of the presence of KS syndrome in twin siblings: there was no presence of risk factors and, at 19 years of age, both began to present symptoms of the syndrome, such as eyelid ptosis and sensorineural hearing loss (SNHL).

Regarding progressive hearing loss, the literature recommended monitoring patients with this

suspicion at least every two months to check if there was progression. The authors also described that electrophysiological examinations in children help in the best conduct for the adaptation of individual sound amplification devices (ISADS)^[13,14]. It is believed that this monitoring is necessary to avoid loss of sensory and, consequently, cognitive auditory information, which can lead to delay in auditory and language development.

Few studies related to KS syndrome have focused on the diagnosis of hearing loss and do not correlate this finding in twin children. However, some authors argue that the most appropriate audiological intervention in cases of progressive hearing loss in patients with KS syndrome and others related to DNA mutations would be cochlear implant (CI)^[15].

The present study aimed to report the case of twin sisters with KS syndrome, from their audiological diagnosis to the intervention.

1.1. Conducting the research

The study was initiated after approval by the Research Ethics Committee of the Hospital for Rehabilitation of Craniofacial Anomalies of the University of São Paulo, Campus Bauru: 090311/2015, CAE 42447215.8.0000.5441. This is a longitudinal descriptive study of twin sisters with KS syndrome and audiological diagnosis of sensorineural hearing loss, carried out by the interdisciplinary team of a hospital. Cases are described as Twin 1 (T1) and Twin 2 (T2).

The patients were registered at the hospital in June 2000 and have been followed up ever since. Therefore, in order to demonstrate more accurately the progression of hearing loss and the results of the intervention, we chose to describe two moments of the evaluation: Time of admission to the hospital: first audiological diagnosis, performed in June 2000, when they were 11 years old; the last attendance reported in the medical record, up to the time of the start of the research, performed in August 2014 and March 2015 for T1, and in August 2014 for T2, and

they were 25 years old then.

1.2. Patients

The mother of the patients, when registering them in the hospital in June 2000, signed the Free and Informed Consent Form, authorizing the consultation of the data from the medical records, for scientific subjects. In the year of this study, in 2015, patients and their families were informed that the research would be carried out through the analysis of documents attached to the hospital's medical records and thus obtained the existing permission for the development of the research.

2. Presentation of the clinical case

2.1. Medical evaluation

The first consultation at the hospital was performed by an otolaryngologist, who found complaints and characteristics typical of KS syndrome on clinical examination. During the anamnesis, the mother reported other evaluations and diagnoses made by doctors from her home city, such as astigmatism, hyperopia, visual fatigue, decreased muscle mass with preserved strength, myopathic face, slight restriction of eye motricity and alteration in muscle tone.

The patients (T1 and T2) were referred for the realization of the genetic test, to know the suspicion of the syndrome, already verified by another institution and informed by the mother, through document, to the multidisciplinary team, who reported all these data in the medical records, in the form of anamnesis and evolution of the case.

2.2. Audiological diagnosis

Twin 1

The following data were reported by the mother, in a speech-language pathology anamnesis, during the first consultation in June 2000, when the patient was 11 years old.

- There is no family history related to hearing loss and syndromes.
- There were no complications during pregnancy.
- Report of mumps and chickenpox, near 3 years of age.
- Neuropsychomotor and language development according to age, however, without previous specialized evaluations.
- Hearing complaints started at 10 years of age. Patient T1 began to respond to her own name when her voice was very strong and also reported bilateral tinnitus.

In relation to audiological tests, objective tests were analyzed, such as immittance testing, transient otoacoustic emissions and distortion product otoacoustic emissions (TEOAE and DPOAE) and auditory brainstem evoked potential (BAEP), and subjective tests, such as pure tone audiometry (PTA) and speech perception tests (SPT) (**Table 1**).

Table 1. Results of objective tests for the hearing of Twin 1 (2000 and 2014)

Examination performed	Right ear (RE)	Left ear (LE)
Imitanciometry	Type A curve Absent reflections in 2000 and 2014	Type A curve Absent reflections in 2000 and 2014
TEOAE and DPOAE	No record in the medical records in 2000 Absent in 2014	No record in the medical records in 2000 Absent in 2014
BAEP click	No record in medical records in 2000 Absent in 2014	No record in medical records in 2000 Absent in 2014

Legend: TEOAE = Transient Evoked Otoacoustic Emissions; DPOAE = Distortion Product Otoacoustic Emissions; BAEP = Brainstem Auditory Evoked Potential.

The results of the subjective tests were compatible with the electrophysiological tests, in both

evaluation moments, as shown in **Figure 1**.

In 2000, after the exams, professionals were able to diagnose hearing loss as severe bilateral sensorineural hearing loss (SNHL) and thus adapt the individual sound amplification device (ISAD) and perform the respective validation and verification tests. However, in 2014, there was a significant

progression of the degree of hearing loss, which became of deep bilateral degree, requiring replacing the hearing aid with another, higher and more recent technology, as well as redoing the verification tests (**Figure 2**).

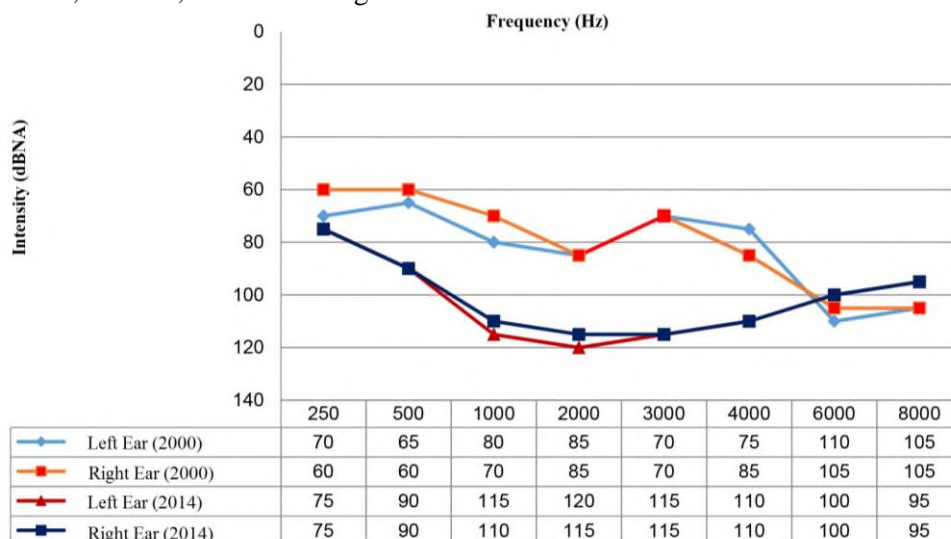


Figure 1. Threshold tonal audiometry-Twin 1.

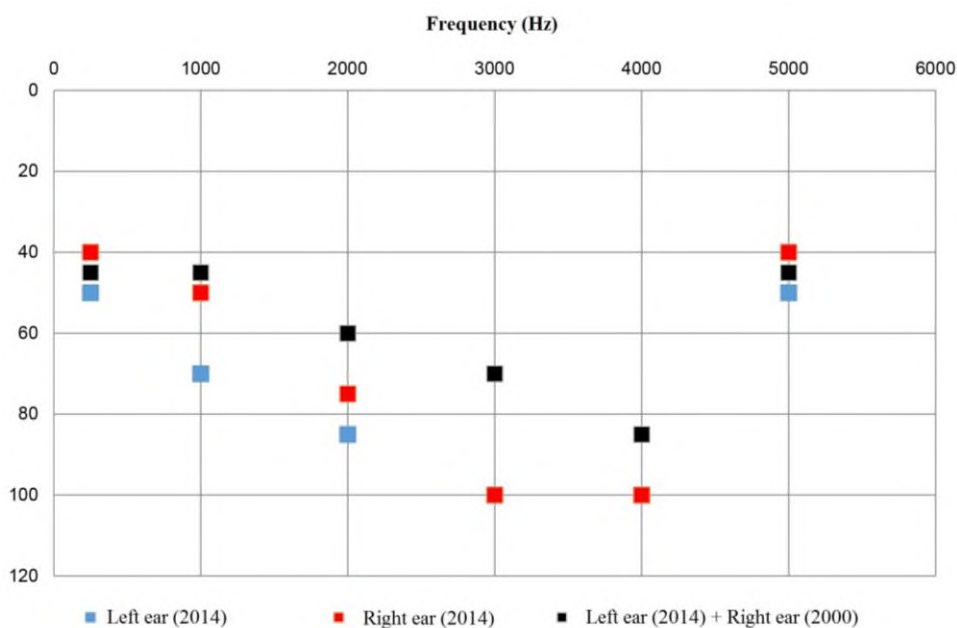


Figure 2. Research of the amplified threshold with individual sound amplification apparatus-Twin 1.

In 2000, it was not yet common in the hospital to apply the speech perception test (SPT) with hearing aids in all patients. They were performed only in those whose cases would be presented in a meeting, for discussion about cochlear implant surgery (CI). For this reason, in the medical records of

patient T1, SPT evaluation was found only in 2014. The right ear score (RE) was: Detection of Ling test sounds for /a/, /u/, /i/ and /m/=100% and for /s/ and /ʃ/=0%; name recognition=100%; question/statement breakdown=0%; identification of vocabulary extension=44%; identification of the

length of sentences=60% and identification of sentences=0%.

In the left ear (LE), the score found was: Detection of Ling test sounds for /a/, /i/, /u/ and /m/=100% and for /s/ and /f/=0%; name discrimination=90%; question/statement breakdown=0%; identification of vocabulary extension = 28%; identification of the length of sentences=30% and identification of sentences=0%.

Despite the progression of hearing loss, Twin 1 had good vocabulary and oral language, since the hearing loss was post-lingual. Specific language tests were not included in the medical records. It is believed that the reason is the fact that the patient was already in adolescence in 2000 and later in adulthood in 2014, and there are no specific language protocols in the hospital sector to evaluate these age groups.

After the exams, the case was selected to be discussed by the multidisciplinary team, regarding

the need for surgery for cochlear implant (CI). Several criteria were addressed, from the analysis of other professionals, such as social worker, psychologist, otolaryngologist and speech therapist, and from the SUS and hospital criteria at the time.

Regarding the speech therapy analysis, the main criterion for the indication of surgery was the low result in the speech perception tests in closed set and difficulty in open set. In addition, professionals were concerned about not having other hearing aid replacement options in the future if the hearing loss progressed. In addition, the team physicians emphasized that the patient was losing other functions, including vision. Therefore, it was necessary to maintain good oral communication in order to preserve their quality of life, despite the other difficulties caused by the syndrome.

Therefore, we chose to perform CI surgery on the left side, which decided by surgeons, and the activation occurred in February 2015 (**Figure 3**).

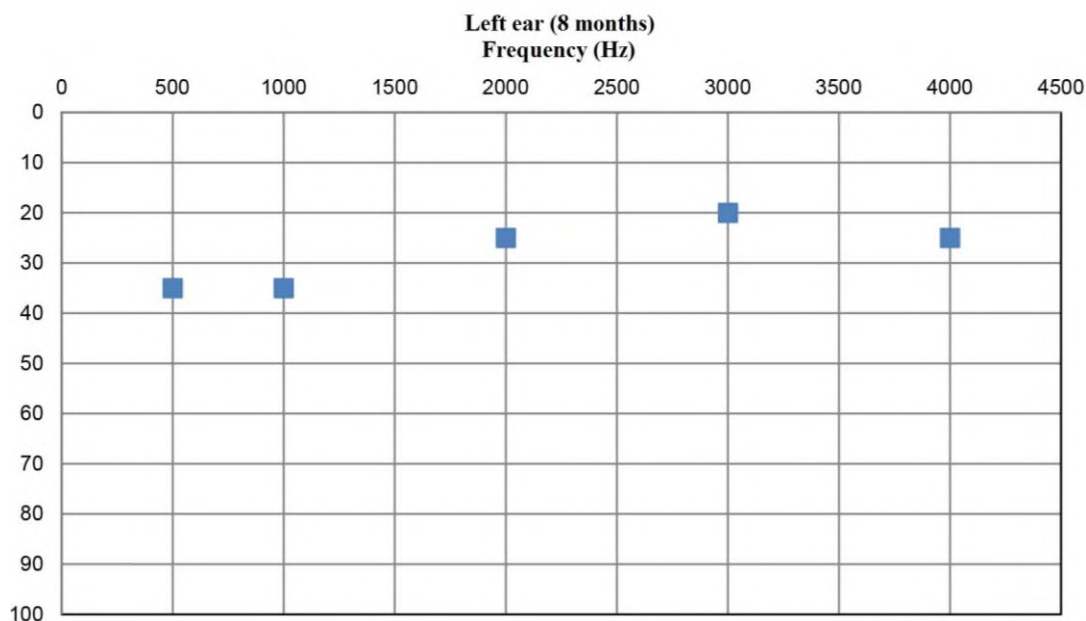


Figure 3. Research of the amplified threshold with cochlear implant—Twin 1.

Regarding the SPT with CI, performed one month after activation, in March 2015, the patient detected all the sounds of the Ling test, but could not perform other speech tests, complaining that she had not yet gotten used to all the sounds, because the CI was very different from the hearing aid, which she

used for 15 years. The best results appeared eight months after activation, when, then, the patient performed the SPT in an open set, with a result of 45% for the list of sentences. However, regular follow-ups are still made for new approaches and guidelines.

Twin 2

The data presented below, as well as for Twin 1, were reported by the mother in a speech-language pathology anamnesis during the first visit in June 2000, and the patient was 11 years old then.

- There is no family history related to hearing loss and syndromes.
- There were no complications during pregnancy and childbirth.
- She contracted mumps and chickenpox near 3 years old.
- Neuropsychomotor and language development, according to age, however, without previous spe-

cialized evaluations.

—Hearing complaints started at 10 years old. Patient T2 started to respond to her own name only when her voice was very strong and also reported bilateral tinnitus.

In relation to audiological tests, objective tests were analyzed, such as immittance, transient otoacoustic emissions and distortion product (TEOAE and DPOAE) and brainstem auditory evoked potential (BAEP), and subjective tests, such as pure tone audiometry (PTA) and speech perception tests (SPT) (**Table 2**).

Table 2. Results of objective tests for the hearing of Twin 2 (2000 and 2014)

Examination performed	Right ear (RE)	Left ear (LE)
Imitiatometry	Type A curve Absent reflections in 2000 and 2014	Type A curve Absent reflections in 2000 and 2014
TEOAE and DPOAE	No record in the medical records in 2000 Absent in 2014	No record in the medical records in 2000 Absent in 2014
BAEP click	Absent in 2000 Absent in 2014	Absent in 2000 Absent in 2014

Legend: TEOAE = Transient Evoked Otoacoustic Emissions; DPOAE = Distortion Product Otoacoustic Emissions; BAEP = Brainstem Auditory Evoked Potential.

The results of the subjective tests were compatible with the electrophysiological tests, in both evaluation moments, as shown in **Figure 4**.

After all evaluations, in 2000, when Twin 2 was 11 years old, the professionals diagnosed the patient with mild sensorineural hearing loss (SNHL) in the left ear and moderate in the right ear. Therefore, the fitting of hearing aids compatible with this type of hearing loss was performed, as well as validation and verification tests.

In 2014, when the patient was 25 years old, progression of hearing loss was observed, as shown in **Figure 4**. Thus, the diagnosis became severe bilateral SNHL, which made it necessary to replace the hearing aid and perform new tests to verify its benefits (**Figure 5**).

Regarding the SPT with hearing aids, performed in 2014, the patient was able to perform all tests in a closed set and obtained a result of 80% in

RE and 97% in LE, for the tests in an open set (list of sentences).

Despite Patient T1 was experiencing hearing loss, Patient T2 had good vocabulary and oral language, since hearing loss was post-lingual. Specific language tests were not included in the medical records.

The reason was thought to be that the patient was already in adolescence in 2000 and later became an adult in 2014, and the hospital department did not have specific language protocols to assess these age groups.

The case was also selected for a multi-disciplinary meeting to discuss the CI, including to compare the results with those of Twin 1. All professionals, such as social worker, psychologist, otolaryngologist and speech therapist informed the results of their evaluations and, based on this information and the criteria established by SUS and

the hospital in 2014, Twin 2 were not indicated for CI surgery.

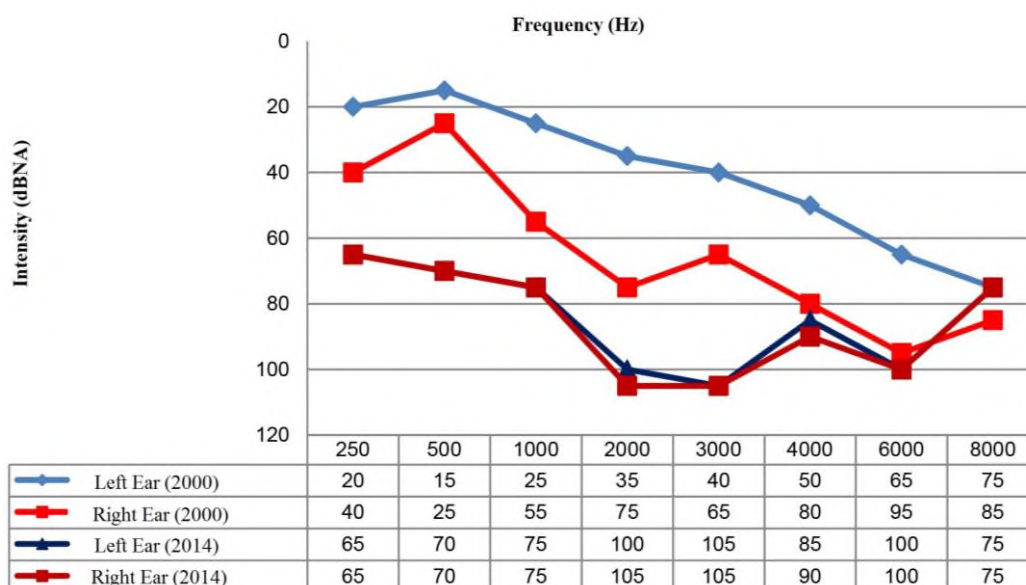


Figure 4. Threshold tonal audiometry-Twin 2.

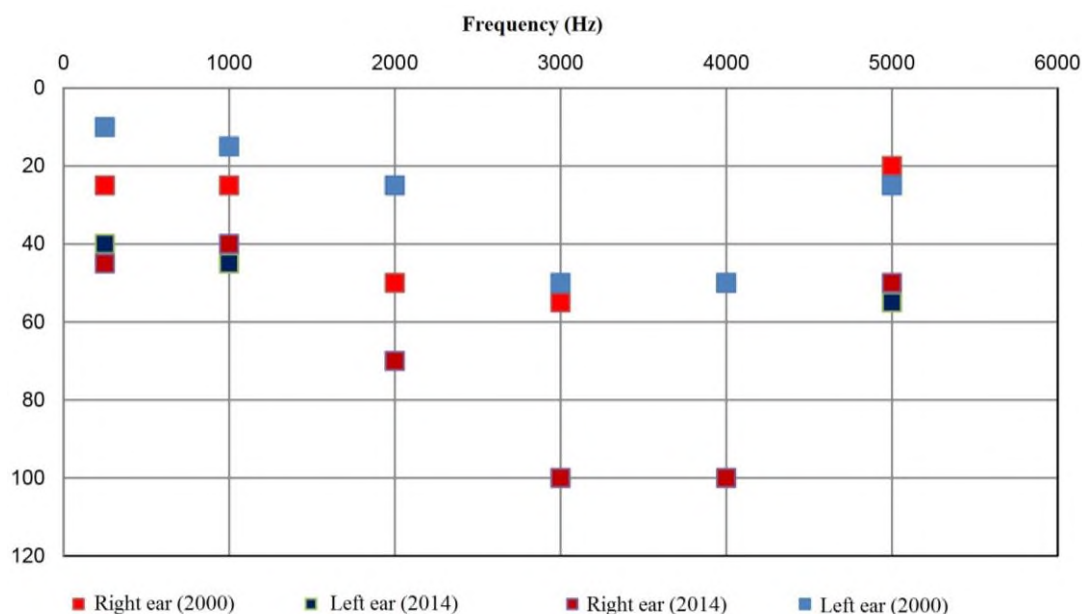


Figure 5. Research of the amplified threshold with individual sound amplification apparatus-Twin 2.

Regarding the speech therapy evaluation, the main factor that did not indicate CI was a good percentage of correct answers in the SPT with hearing aids, demonstrating that the device still provided a benefit. Thus, it was decided to keep Twin 2 in audiological follow-up and verify if the hearing loss will progress. Even if this may happen, professionals believe that there are still other options

for hearing aid replacement to maintain good oral communication of the patient, which makes it unnecessary, at the moment, to undergo surgery, since the benefits of CI are very similar to those that the hearing aid still provides. However, as soon as the hearing aid does not provide the same benefits, the case of Twin 2 will be discussed again by a multi-disciplinary team, regarding the need for CI, to

prevent progressive loss from aggravating the patient's current good communication.

All data related to the discussion of Case T1 and Case T2 by the multidisciplinary team were collected from the medical records and from interviews with the professionals responsible for the cases.

3. Discussion

The literature^[7] described the case of twin siblings with KS syndrome, showing the absence of risk factors associated with preconception and early childhood, as both developed normally until years old, when the first symptoms of visual changes and hearing impairment began to appear. These findings were consistent with those of the present study, as the sisters also did not have any complaints or symptoms until the age of 10 years. Other studies^[2,4,5] also mentioned the onset of symptoms and diagnosis before 20 years old.

In terms of audiometric testing, a diagnosis of SNHL was obtained, as well as a progression of hearing thresholds, one of the typical features of patients with hearing loss due to KS syndrome, which in most cases is sensorineural, symmetrical and progressive^[1,2]. Therefore, audiological diagnosis and early intervention, as well as follow-up every two or three months, were considered extremely important to verify the progression of hearing loss and determine the optimal behavior related to hearing aid adaptation^[13,14]. Thus, delay in auditory and language development can be avoided.

The etiology of the syndrome remained controversial in the literature. In the cases studied (T1 and T2), the only early complications in children were a diagnosis of mumps and chickenpox. However, these viral infections usually did not leave serious sequelae after treatment. Therefore, it was believed that the syndrome may have occurred due to genetic mutations.

Another factor that indicated the presence of genetic mutation, in the case of this study, was bi-

lateral, symmetrical and progressive hearing loss, because it demonstrated alteration in the cochlea, in agreement with the literature, regarding the genetic mutation of the mDNA, which impairs the supply of energy (ATP), especially to the organs that need it most, such as the cochlea^[1,2].

According to the authors^[15,16], in cases of hearing loss due to mitochondrial disease, the best intervention option was CI, because of the progressive nature of these losses. In the present study, this was also the case in Patient T1, where the auditory benefit verified in the test was not obtained after the diagnosis of profound SNHL, even after the replacement of the hearing aid, which was the main reason for the CI indication. In the case of T2, despite the progression of the hearing loss, even with the use of hearing aids, from 2000 to 2014, the patient presented a good speech perception condition, that was, there was still an auditory benefit only with the use of hearing aids, but due to the characteristics of this case, the patient would continue to be monitored.

Authors^[15] reported the case of patients with KS syndrome who underwent CI. The responses regarding speech recognition and electrophysiological tests with CI were very similar to those of CI patients who did not have the syndrome.

It was believed that the patient who already uses CI (Twin 1), together with contralateral hearing aid, added to speech rehabilitation, could present even more satisfactory results in relation to speech recognition, and maintain good oral communication.

4. Conclusions

Subjects with suspected KS syndrome should be evaluated to confirm the syndrome and have an early hearing evaluation, as if necessary rehabilitation with hearing aids and/or cochlear implants, coupled with speech therapy, can bring beneficial outcomes.

Conflict of interest

The authors declare no conflict of interest.

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