Case Report

Audiologic Consequences of Ototoxicity: Case Report with Deterioration of the Intelligibility of Speech

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Abstract

Hearing is a channel of extreme importance for life because it enables the development of oral language; acquiring the knowledge to communicate with the world. Hearing loss can occur due to innumerous factors and can be expressed in various forms, according to its type and degree, and any impediment in the transport of sound to the central auditory nervous system implies a loss of part or all of the message content. Cisplatin chemotherapy treatment has ototoxicity as one of its described side effects. For that reason, the monitoring of the hearing of individuals submitted to cisplatin chemotherapy treatment has been a growing concern, especially in children presenting retinoblastoma. This study had as objective to describe the consequences of a hearing loss due to ototoxicity in the speech intelligibility of a child diagnosed as having retinoblastoma diagnosed at 22 months of age. Audiological monitoring showed a progressive hearing loss as well as deterioration of speech intelligibility. We have verified that the use of accumulative doses of cisplatin can compromise neural components of the auditory system resulting in a deterioration of speech intelligibility. The early detection of hearing loss in these cases is fundamental to avoid deafness progression as well as to conduct an adequate orientation for the school and family of the patient.

Keywords: Hearing loss; Cisplatin; Central nervous system; Auditory pathways; Speech intelligibility.

Introduction

Hearing is a channel of extreme importance for life because it enables us to acquire the knowledge to communicate with the world and to be capable of developing language. Oral communication is the principal means by which we express our ideas.

To lose hearing means to lose an important form of contact with the world and with people. Although different degrees and types of hearing loss exist, any impediment in the transport of sound to the central auditory nervous system implies a loss of part or all of the message content in an oral communication situation. This damage provokes a still greater impact in children since they have yet to amass neither the knowledge nor the domination of the language, not even being able to interfere in its own acquisition.

Cisplatin has become part of various treatment protocols for different types of cancer by presenting significant therapeutic effect. [1-2] In spite of its effectiveness in the treatment of countless cancers, as much in adults as in children, cisplatin is ototoxic,[3-5] producing irreversible effects in the auditive system, such as *morphofunctional* alterations in the organ of Corti, lesions in the vascular stria and external hair cells of the basal turn, neuronal death and the degeneration of spiral ganglion cells [2,6] resulting in bilateral hearing loss in the high frequencies and tinnitus, which can also affect the low frequencies.[7] The ototoxicity of cisplatin is related to multiple mechanisms that include: breaks of DNA, alterations of the mechanism of cellular transport, mitochondrial DNA damage, interference in the enzymatic activities of the cells, among others.[8]

Hearing loss due to the use of cisplatin can occur

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after the first chemotherapy cycle, mainly in doses superior to 100 mg/m^2. [9]

The reports of incidence of hearing loss due to cisplatin use are abundantly variable, having descriptions from 9 to 91%.[10] This variability is related to factors as the age of the individual, evaluation method of the exposure to cisplatin, mode of drug administration, type of audiologic evaluation made and criteria of adopted ototoxicity.[1,7,11]

In an analysis of 451 cases treated for retinoblastoma in Hospital A.C. Camargo, the distribution of the cases of bilateral retinoblastoma is described as affecting children of even 12 months of life.[12] In these cases, the identification of hearing loss is crucial in order to avoid the consequences of sensory deprivation in the development of speech and of language.

Moreover, the most precise form of testing an individual's hearing sensitivity is through tonal audiometry, in which the minimum necessary sound intensity to provoke the hearing sensation is established, using pure tones between 250 and 8000 Hz as reference. [13]Although it is possible to quantify audition through conventional tonal audiometry, this measure does not show the hearing loss influenced by life-experiences and actions in interpersonal relationships of the individual.

The detection, recognition and interpretation of a speech sign involves more complex systems than the simple audibility of pure tone; a simple task for the hearing neural structures. In the Portuguese language, some phonemes are generated with little energy and formed by acute frequencies.[14,15] It is possible for adults who present hearing loss not to present difficulty in the perception of these phonemes because of the use of mental mechanisms that use files which are already acquired. On the other hand, with a child in the phase of acquisition and language development, a hearing loss in the acute frequencies can interfere significantly in the acquisition of such phonemes, evoking important social and education consequences.[7]Additionally, the literature refers to hearing losses in the acute frequencies represented as a crucial factor for lowered discrimination, mainly when the speech speed is fast or when the atmosphere is noisy.[16,17]

Vocal audiometry complements tonal audiometry with the results of speech intelligibility tasks, thus allowing the evaluation of more complex structures of the hearing system. The deterioration of the ability of speech intelligibility (not compatible with the hearing loss verified in tonal audiometry) is interpreted as a sign of retrocochlear compromise, or more recently as an alteration of the synapses or of the presence of ciliated cells in the depolarization of the nervous stimulus.[17-19]

This study had as objective to describe and discuss the consequences of ototoxicity due to the use of cumulative doses of cisplatin in a child with retinoblastoma.

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A.R., female, nine years of age, diagnosed with presence of retinoblastoma intraocular bilateral in 1990. Patient was submitted to chemotherapeutic and radiotherapeutic treatment in the Treatment and Research Center of Hospital A.C. Camargo, receiving a cumulative cisplatin dose of 662 mg/m^2 for retinoblastoma treatment between March and May of 1991 and 480 mg/m^2 between January and May of 1992.

In radiotherapeutic treatment, the cumulative dose was 4600 cGy (between July and August of 1991). In a simulation carried out in the Radiotherapy Service of this institution, it was verified that only 20% of the dosage used in the irradiation of the eye reaches the internal contralateral ear.

In 1998, the presence of an osteosarcoma of the left femur was diagnosed. Surgical treatment was undergone in March of 1999 completed by one cycle of chemotherapy of 116 mg/m2 of cisplatin in six hours.

The audiologic evaluations performed consisted of tonal audiometry, vocal audiometry, measures of acoustic immittance, *transient otoacoustic emissions* (TOAEs) and brainstem auditory evoked potential (BAEP). The following equipment was used to perform these procedures: (1) Audiometer Madsen Orbiter 922, for obtaining the audibility thresholds in the frequencies of 250, 500, 1000, 2000, 4000, 6000 and 8000 Hz bilaterally; (2) Imitanciômetro Zodiac 901- ANSI Standard 1969, for obtaining the measures of acoustic immittance (tympanometry and research of the acoustic reflex); (3) Otodynamics ILO 92, analyzer of *otoacoustic emissions*; (4) Amplaid MK 12 acoustic equipment.

Formal audiologic assessment through tonal and vocal audiometry began in 1995, after the end of retinoblastoma treatment, because, before this period, the patient did not present consistent responses in function to the age group.

Figure 1 shows the audiometric tests carried out after the end of retinoblastoma treatment. It can be verified that the thresholds obtained in the first evaluation were within normal limits, although the child had responded in an inconsistent manner according to the evaluator.

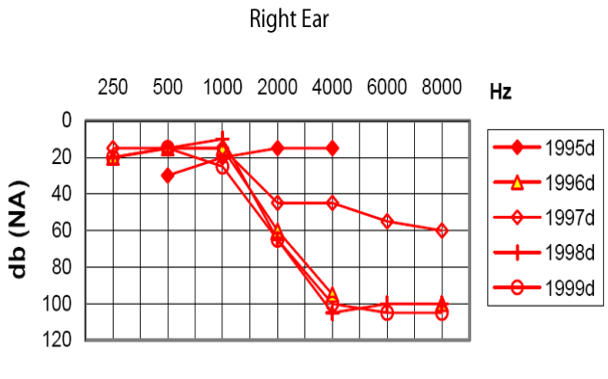

Figure 1A - Audiometric tonal threshold series (from 1995 to 1999) for the right ear

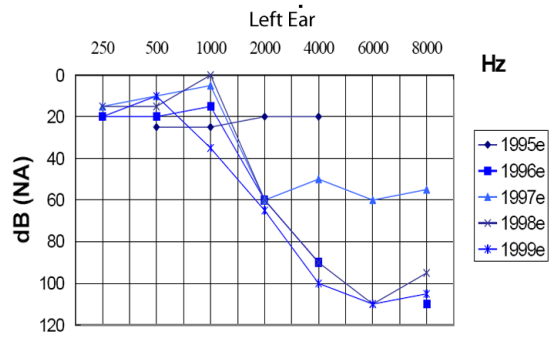

Figure 1B - Audiometric tonal threshold series (from 1995 to 1999) for the left ear

Table 1 displays the results of the averages of the tonal thresholds (500 to 4000 Hz) and the speech reception thresholds (SRTs) in dB NA, of both ears, obtained in all evaluations.

Table 1 -Result of the averages of the tonal thresholds and SRTs in dB NA, obtained in both ears, from all audiologic evaluations.

	Tonal average (in dB NA)		SRT (in dB NA)	
	RE	LE	RE	LE
1995	20	25	25	25
1996	46	46	20	20
1997	30	31	25	30
1998	48	41	20	10
1999	51	52	15	15

Table 2 displays the percentage of successes of the Speech Recognition Index (SRI), obtained in all of the audiologic evaluations made.

Table 2 -Right Ear; Left Ear

	RE	LE
	Monosyllables	Monosyllables
1995	100	100
1996	84	80
1997	92	92
1998	80	68
1999	60	64

During the fifth evaluation, in 1999, after the end of osteosarcoma treatment, besides conventional tests, research of *transient otoacoustic emissions were made*, verifying the absence of response in all of the bilateral frequency bands. In addition to this, BAEP was made, observing a latency value of Wave V (RE: 6.16 ms; LE: 6.28 ms), with morphology very defined to the right and poor to the left (Figure 2).

Discussion

Word recognition tests are of great importance in the audiologic diagnosis. The audiologic battery is considered incomplete without the measures of speech recognition. The tests used to measure the hearing performance of the individuals in speech recognition tasks use isolated stimuli, as monosyllabic words are more commonly used in the Portuguese language.[15]

Observing the evolution of the results presented in the evaluations during the audiologic attendance, it can be noted that although the hearing thresholds had maintained stable after the last dose of cisplatin after the treatment of osteosarcoma in 1999, there was a significant reduction in the percentage of successes in the SRI, the test that involves the ability of speech recognition. Such a reduction can be interpreted as a gradual deterioration of the auditive system, responsible for the decoding of the sounds, which could have occurred due to peripheral hearing loss, with the total loss of ciliated cells in specific regions of the cochlea [17,19] or to the cumulative impregnation of cisplatin in the cells of the spiral ganglion.[2]

In adults, the loss of hearing when limited to the acute frequencies can occur without generating social limitations.[20] However, in children, a hearing loss can bring irreversible consequences for the development of speech and language,[21] because the perception of the sounds of the speech depends on a complete peripheral hearing system.[16]

In general, the hearing loss in the high frequencies has been considered a crucial factor for poor

discrimination. The focal complaint of individuals with hearing loss in the high frequencies is usually related to audition difficulty in noisy environments.[17] The compromise in speech perception, in many cases, however, cannot totally be explained by the audiogram of pure tone, principally in the cases of retrocochlear alterations.[18]In fact, individual bearers of sensorineural hearing loss can present different types of cochlea defects, where lesions on external ciliated cells (ECC) and/or internal ciliated cells (ICC) can occur with direct influence on the perception of sound stimuli.[19]

According to Gordo,[17] the relation between the absence of benefit with the use of hearing aids and the functional reduction or complete loss of the internal ciliated cells and/or neurons in certain regions of the cochlea represents a very ancient concept. Nevertheless, no clinical test was carried out for the identification of "cochlea dead-zones". In these regions, the information produced by the vibration of the basilar membrane cannot be transmitted to the central auditory nervous system; however, if sufficiently strong, the frequency tone corresponding to the dead-zone can be detected by the spread of the vibration in other functional regions of the cochlea.[17,22]

Even though,[19]mention that the diagnosis of the dead-zones in the cochlea cannot be made on the basis of an audiogram, emphasizing that the information produced by ICC to the auditive nerve are important for a better recognition of the sounds, principally the sounds of speech.

Histopathologic studies made after the use of cisplatin[2,23-25] have shown that not just the external ciliated cells of the cochlea are committed, but also sustentacular cells, the vascular groove, the spiral ganglion and sometimes the fibers of the cochlear nerve. In this way, the difficulties in the tasks of speech intelligibility of the child in question can be explained not only for the affliction of sensorial structures, but for the involvement of the neural auditive structures, as can be evidenced by the tracing obtained in BAEP (Figure 2), that showed a bilateral increase in the latency values of Wave V (RE: 6.16 ms; LE: 6.28 ms), as well as poor morphology to the left. In fact,[26] suggest latency values superior to 6.0ms as abnormal.

The radiotherapy dose described in the literature as a risk for hearing alterations varies between 4500 and 6000 cGy. Thus, it is considered that the final dose of the radiotherapeutic treatment employed in this case (4600 cGy) was not a risk for hearing, though it is possible to have been a factor of the ototoxic effect of cisplatin.[27] Considering the results presented in this case report, they show that the hearing alterations due to the cumulative-dose use of cisplatin can affect as much the sensory as the neural components of the hearing system.

Principally in respect to the abilities of speech intelligibility, the importance of early detection of hearing loss should stand out, as well as the audiologic attendance of children submitted to chemotherapeutic treatment with cisplatin, seeking not only to avoid the progression of deafness but also carrying out adequate orientation to those that work with a hearing deficient child in the attempt of minimizing the effects in the education, social and psychological levels, provoked by hearing loss.

We verified in this case study that cumulative doses of this drug can compromise not only the peripheral portion of the auditive system but also its neural components, indispensable in the recognition of the speech signal, and consequently, in the acquisition and development of speech and language.

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