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Case Report: Auditory Neuropathy and Challenges in Spoken and Sign Language in a Young Person with OTOF Mutation

Relato de Caso: Neuropatia Auditiva e Desafios na Linguagem Falada e Gestual em Jovem com Mutação OTOF

Informe de caso: Neuropatía auditiva y desafíos en el lenguaje hablado y de señas en una persona joven con mutación OTOF

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Abstract

Introduction: Auditory neuropathy spectrum disorder (ANSD) is a challenge due to the variability of clinical presentations and therapeutic responses. **Objectives**: This study aims to report the case of a young person with ANSD related to the OTOF gene mutation, highlighting the challenges faced in

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ISOP, MSG, VAGLF: article conception.
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the development of spoken and sign language. **Methods**: A clinical case of a patient with ANSD and improvement in tonal thresholds, despite very low discrimination, is reported. In the case under study, the young person presents, in addition to difficulties in oral language, problems in understanding and producing sign language in LIBRAS. This suggests that his difficulties are not related only to the lack of audibility, indicating the presence of other factors in linguistic development. **Results**: In the case under study, the young man presents, in addition to difficulties in oral language, problems understanding and producing sign language in LIBRAS, despite having attended a bilingual school in LIBRAS and living with the deaf community since early childhood. **Conclusion**: Individuals with hearing loss since birth have their language and learning difficulties often attributed to hearing loss. However, evaluating the functioning of these individuals through a broad clinical evaluation, such as phoniatrics since childhood, can contribute to the identification of more global difficulties, not always resulting from hearing loss. This will allow the indication of early and targeted therapies, minimizing the damage to their linguistic and learning development. Linguistic assessment and intervention in children with hearing impairment requires multidisciplinary skills and, ideally, should be carried out as early as possible to enhance therapeutic results.

Keywords: Hearing; Deafness; Communication; Language development

Resumo

Introdução: A desordem do espectro da neuropatia auditiva (DENA) é um desafio devido à variabilidade de apresentações clínicas e respostas terapêuticas. **Objetivos**: Este estudo tem como objetivo relatar o caso de um jovem com DENA relacionada à mutação do gene OTOF, destacando os desafios enfrentados no desenvolvimento da linguagem falada e gestual. **Métodos**: É relatado um caso clínico de um paciente que apresentava DENA com limiares auditivos flutuantes, mas sempre com discriminação muito baixa. No caso em estudo, o jovem apresenta, além das dificuldades na linguagem oral, problemas para compreender e produzir linguagem gestual em LIBRAS, sugerindo que suas dificuldades não estejam relacionadas apenas à falta de audibilidade, indicando a presença de outros fatores no desenvolvimento linguístico. **Resultados**: No caso em estudo, o jovem apresenta, além das dificuldades na linguagem oral, problemas para compreender e produzir linguagem gestual em LIBRAS, apesar de ter frequentado escola bilíngue em LIBRAS e convivido com a comunidade surda desde a primeira infância. **Conclusão**: Indivíduos com perda auditiva desde o nascimento têm suas dificuldades de linguagem e aprendizagem frequentemente atribuídas à perda de audição. No entanto, avaliar o funcionamento desses indivíduos por meio de uma avaliação clínica ampla, como a foniátrica desde a infância, pode contribuir para a identificação de dificuldades mais globais, nem sempre decorrentes da perda auditiva. Isto permitirá a indicação de terapias precoces e direcionadas, minimizando o prejuízo em seu desenvolvimento linguístico e de aprendizagem. A avaliação e intervenção linguística em crianças com deficiência auditiva requerem competências multidisciplinares e, idealmente, devem ser realizadas o mais precocemente possível para potencializar os resultados terapêuticos.

Palavras-chave: Audição; Surdez pré-lingual; Comunicação; Desenvolvimento da linguagem.

Resumen

Introducción: El trastorno del espectro de la neuropatía auditiva (ANSD) es un desafío debido a la variabilidad de las presentaciones clínicas y las respuestas terapéuticas. **Objetivos**: Este estudio tiene como objetivo informar el caso de un joven con ANSD relacionado con la mutación del gen OTOF, destacando los desafíos enfrentados en el desarrollo del lenguaje hablado y de señas. **Métodos**: Se reporta un caso clínico de un paciente que presentó ANSD y mejoró los umbrales tonales, a pesar de muy baja discriminación. En el caso objeto de estudio, el joven presenta, además de dificultades en el lenguaje oral, problemas para comprender y producir lengua de signos en LIBRAS. Sugiriendo que sus dificultades no están relacionadas únicamente con la falta de audibilidad, indicando la presencia de otros factores en el desarrollo lingüístico. **Resultados**: En el caso estudiado, el joven presenta, además de dificultades en el lenguaje oral, problemas para comprender y producir la lengua de signos en LIBRAS,

a pesar de haber asistido a una escuela bilingüe en LIBRAS y convivir con la comunidad de sordos desde la más tierna infancia **Conclusión**: Las personas con pérdida auditiva desde el nacimiento tienen dificultades de lenguaje y aprendizaje atribuidas a menudo a la pérdida auditiva. Sin embargo, evaluar el funcionamiento de estos individuos a través de una evaluación clínica amplia, como la foniatría desde la infancia, puede contribuir a la identificación de dificultades más globales, no siempre resultantes de la pérdida auditiva. La evaluación e intervención lingüística en niños con discapacidad auditiva requieren habilidades multidisciplinarias e, idealmente, deben realizarse lo más temprano posible para mejorar los resultados terapéuticos.

Palabras clave: Audición; Sordera; Comunicación; Desarrollo del Lenguaje

Introduction

Auditory neuropathy spectrum disorder (ANSD) is a diagnosis that requires attention and monitoring of babies and children because it often impairs their communication and speech and can cause developmental problems [1]. One of the best-known genetic etiologies of ANSD is related to the mutation of the OTOF (Otoferlin) gene, associated with autosomal recessive non-syndromic hearing loss (DFNB9) [2,3].

Moderate, severe or profound hearing loss of various etiologies may be associated with difficulties in oral language and school learning. However, children with hearing impairment, children of deaf parents, exposed to sign language at an early age, usually demonstrate normal sign language skills [4].

Some children with auditory neuropathy have disproportionately lower linguistic, spoken and/or gestural abilities than their peers with hearing impairment, and their language difficulties cannot be attributed to their hearing loss, which is characterized in these cases as a language disorder. [5,6]

This study aims to report the case of a young man with ANSD related to the OTOF gene mutation, highlighting the challenges faced in the development of spoken and sign language. The article seeks to examine the implications of the mutation in the OTOF gene on auditory perception and linguistic development, as well as discuss the difficulties encountered in auditory rehabilitation and language acquisition, despite the interventions carried out.

Case report

DRG, 23 years old, male, hearing loss (HL) due to Auditory Neuropathy Spectrum Disorder (ANSD) due to a mutation in the OTOF gene (exon sequencing showed a deletion of 6 base pairs between nucleotides 1552-1567 of chromosome 16). The patient sought phoniatric care, accompanied by his mother, because he had great difficulty communicating, including in Brazilian Sign Language (LIBRAS) **,** which negatively impacted his academic and professional life and his autonomy.

The mother reported that the young man was never able to acquire proficiency in LIBRAS, unlike his sister, who has the same auditory etiological diagnosis. Despite having received the same education, he is unable to communicate in LIBRAS, in addition to having difficulties reading, writing and manipulating numbers mentally.

The patient presented fluctuation in tonal auditory thresholds since birth, with a tendency to improve, but without progress in auditory discrimination. Adaptation to a hearing aid (HA) was unsuccessful since childhood and the use of a cochlear implant was not considered due to the fluctuation of tonal auditory thresholds in the audiometry.

The patient uses LIBRAS and orofacial reading for communication. DRG studied from kindergarten to the 3rd year of high school in a bilingual school in LIBRAS. He currently works in the service industry (butcher shop), but has great difficulty in keeping a job, remaining dependent on his mother.

Phoniatric assessment, carried out with the help of a LIBRAS interpreter, in addition to the difficulties in communicating in oral language, significant difficulties were observed in the lexicon and syntactic structure of sign language, which was not expected after years of immersion in LIBRAS both at school, at home and in other environments.

His spontaneous writing was poor, disorganized and had spelling errors. The significant alteration in visuospatial working memory and spatial organization in the graphic plane that could not be justified by hearing loss was noteworthy. Therefore,

the diagnosis of Language Disorder (TL) associated with ANSD was concluded and not justified solely by the auditory condition.

No cognitive or functional aspects that indicated intellectual deficit were observed in clinical history or in the phoniatric evaluation, despite the academic and professional impairment resulting from the delay in spoken sign language.

Discussion

Auditory neuropathy spectrum disorder is generally characterized by the recording of otoacoustic emissions and the presence of cochlear microphonics, combined with the absence or alteration of short-latency auditory potentials [2,3,7,8]. It presents high genetic heterogeneity, being considered one of the most challenging hearing disorders for diagnosis and rehabilitation. The most common genetic cause of ANSD is the mutation of the OTOF gene (human [2,3,7]otoferlin).

Although some OTOF mutations are located mainly on chromosome 2 (2p23.3), there are currently several identified variants of this gene, which makes this condition highly heterogeneous [1,9,10]. The otoferlin protein**,** expressed mainly in the inner hair cells (IHCs) of the cochlea, is responsible for the transduction of acoustic signals into nerve impulses at the synapses between the inner hair cells (IHCs) and the neurons of the cochlear nerve [11].

otoferlin is a multivalent calcium-binding protein that mediates vesicle fusion for the release of the neurotransmitter glutamate, which acts at synapses between these cells and ganglion cells. Mutations in the OTOF gene result in impaired synaptic transmission of the ICCs, which causes sensorineural hearing loss [1]. This hearing loss can range from moderate to profound, be progressive or regressive, and is usually present from birth. [1,12,13]Studies using gene therapy are underway, one of them with an adeno-associated virus (AAV) serotype 1 carrying a human OTOF transgene (AAV1-hOTOF) as a treatment for children with autosomal recessive deafness 9 [3,7]. The results appear promising and should change the clinical history of these patients.

Although many patients with OTOF mutations have preserved pure tone detection thresholds, communication and language processing may remain compromised, even with improved auditory functions after cochlear implantation [1,9,10,12].

In the case under study, the young man presents, in addition to difficulties in oral language, problems in understanding and producing sign language in LIBRAS, despite having attended a bilingual school in LIBRAS and having lived with the deaf community since early childhood. This suggests that his difficulties are not related only to the lack of audibility, indicating the presence of other factors in linguistic development.

Language involves complex interactions between different brain regions. The first years of life are fundamental for its development. Hearing is part of the language system, and the processing of acoustic stimuli is essential for the acquisition of oral skills [14–16].

A child with sensorineural hearing loss acquires oral language through the use of electronic devices that promote the audibility of speech sounds (cochlear implant or hearing aid), visual support (orofacial reading and context of linguistic information) associated with speech therapy. Since the acoustic signal is only partially compensated by hearing aids or implantable devices [4], even in mild or moderate hearing losses, there may be a delay in the acquisition of spoken or written language.

Most children with hearing loss demonstrate normal language skills in the visual modality if exposed to sign language early in life. However, some children have disproportionately lower language skills, both spoken and gestural, than their peers with hearing loss, which cannot be explained by their hearing loss alone [5,6].

The recognition of sign languages as natural languages has led to advances in understanding the mechanisms involved in language processing by deaf signers. Studies suggest that the superior and posterior temporal regions are highly sensitive to language processing, regardless of the stimulus modality [17]. Thus, theoretically, when a deaf person is exposed to LIBRAS at an appropriate time, the brain regions involved in language will be activated in a similar way to those of a hearing person [4].

During the phoniatric evaluation of the case reported here, many of the changes observed could not be explained by the patient's hearing loss, such as the difficulties in understanding LIBRAS and the changes in visual perception skills, which were far below what was expected for his age. The phoniatric evaluation was performed with a LIBRAS interpreter, and the patient had difficulty understanding the suggestions, needing the

information to be repeated several times in sign language for him to understand it. He presented poor spontaneous writing, disorganized and with spelling errors. These changes could be related to the hearing difficulty, however, the difficulties in understanding LIBRAS and the changes in visual perception could not be explained solely by this deficiency. We believe that phoniatric evaluation should be considered in children with hearing loss related to ANSD, even when the cause is genetic and well known, due to the wide spectrum of associated clinical presentations [18,19].

Individuals with hearing loss since birth often have their language and learning difficulties attributed to this loss. However, assessing the functioning of these individuals through a comprehensive clinical evaluation, such as phoniatrics, early on can help identify more global difficulties that are not always due to hearing loss. This will allow for the indication of early and targeted therapies, minimizing the harm to their linguistic and learning development.

Final comments

Understanding the molecular mechanisms underlying the function of otoferlin altered by the OTOF gene mutation, the characteristics of speech development and the development of therapeutic approaches in these cases are frequent and active research in the field of hearing. In the case of the patient, phoniatric evaluation was essential to identify changes in skills compatible with a language disorder, which could not be explained solely by hearing loss.

Phoniatric assessment carried out in early childhood or during the school phase can contribute with additional information about impaired skills, relevant for therapeutic planning, minimizing the impact of ANSD on language acquisition and contributing to the patient's independence, quality of life and overall development.

This study, as it is a case report, does not intend to generalize about ANSD, but to contribute to the knowledge of this condition with such diverse manifestations.

Therefore, linguistic assessment and intervention in children with hearing impairment requires multidisciplinary skills and, ideally, should be carried out as early as possible to enhance therapeutic results.

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