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IMMUNE-MEDIATED SENSORINEURAL HEARING LOSS: A CASE REPORT

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Introduction: Immune-mediated sensorineural hearing loss is a rare condition characterized by bilateral and asymmetrical hearing loss, with rapid onset and variable progression, caused by an autoimmune reaction against inner ear proteins. Its pathophysiological mechanisms are still uncertain and there are no well-defined diagnostic criteria, with antibody testing against HSP70 being the test most associated with these hearing losses. Treatment is based on corticosteroid and immunosuppressant therapy. **Aims: To** describe a case of a patient with right-sided immune-mediated sensorineural hearing loss. **Methods:** This is a descriptive, narrative and reflective case report. The participant was chosen because of the rarity of his disease and the data was obtained from an analysis of the patient's medical records. **Case description:** 54-year-old man complaining of reduced hearing acuity on the right and bilateral tinnitus. He also reported arthralgia and swelling in the joints of the fingers, elbows and knees, as well as a positive family history of autoimmune diseases. Audiometry and impedanciometry were suggestive of right-sided sensorineural hearing loss and rheumatology screening was positive for anti-HSP70 antibodies. The patient was referred to a rheumatologist to start immunosuppressive therapy. **Discussion:** Systematic studies and meta-analyses have established a strong association between autoimmune diseases and sensorineural hearing loss. The patient's clinical condition together with his family history and positivity for anti-HSP70 antibodies corroborate the suspicion that the patient's hearing loss is due to an autoimmune process. The patient was therefore correctly referred for treatment, with the aim of stabilizing the hearing loss and treating the underlying autoimmune condition. **Conclusion:** It is clear that the association between sensorineural hearing loss and autoimmune diseases highlights the need for a multidisciplinary approach in the management of patients with progressive hearing loss and systemic symptoms, with a view to preventing possible major functional losses resulting from the disease and significantly improving quality of life.

Keywords: sensorineural hearing loss; autoimmune diseases; inner ear.

ZIP CODE	Research Ethics Committee
CNS	National Health Council
DIMOI	Immune-mediated Inner Ear Disease
FAN	Antinuclear Factor
FR	Rheumatoid Factor
HSP70	Heat Shock Protein 70
LES	Systemic Lupus Erythematosus
PANS	Sensorineural Hearing Loss
PCR	C Reactive Protein
TCLE	Informed Consent Form
VHS	Sedimentation rate

INTRODUCTION

Autoimmune sensorineural hearing loss (ASHL) is a rare clinical condition that accounts for less than 1% of hearing loss cases (MANCINI et al., 2018). It was first addressed by Lehnhardt in 1958, who hypothesized that a direct autoimmune reaction against inner ear proteins could lead to sensorineural deafness. In 1979, McCabe carried out studies on a population with SSNHL who underwent treatment with immunosuppressants and obtained a good response to therapy, suggesting the autoimmune origin of deafness. There are cases in which this immune response is restricted to the ear, but in 25% to 30% of cases, hearing loss is the result of a systemic autoimmune disease, including rheumatoid arthritis, systemic lupus erythematosus, scleroderma, Behcet's disease, fibromyalgia, among others (LOURENÇO; NINA, 2020). This condition is classified as Immune-Mediated Inner Ear Disease (IMIOD) and affects more middle-aged women, with an estimated prevalence of 15 cases per 100,000 individuals (CIORBA et al., 2018).

The clinical manifestations of DIMOI can be heterogeneous, but most of them are characterized by bilateral and asymmetrical SCA, with rapid onset and progression in weeks to months, and there may be fluctuations in the hearing deficit threshold. Tinnitus, ear fullness and vestibular symptoms may be present in up to 50% of cases (CIORBA et al., 2018).

The pathophysiological mechanisms of IMPOI are still uncertain and there are no well-defined diagnostic criteria. However, the theory of immune-mediated SHL is supported by evidence that the inner ear is immunocompetent and can therefore be affected by autoimmune diseases. The presence of circulating autoantibodies against specific and non-specific inner ear antigens is commonly detected in patients with DIMOI and is the main basis for diagnostic investigation. Testing for anticochlear antibodies or anti-HSP70 is the test most commonly associated with progressive hearing loss. These are antibodies against Heat Shock Protein 70 (HSP70), which has a molecular weight of 68 kilodaltons (kD). The Western blot is the test to be carried out using gel immunoelectrophoresis, which determines the exclusive reactivity of the antibodies in the patient's serum against this protein, and is the only diagnostic marker available to identify DIMOI disease activity and a positive response to corticosteroid therapy. This test has a sensitivity of 42% and a specificity of 90%. Therefore, a diagnosis should be considered if the clinical history is suggestive of DIMOI, if there is an associated systemic immune disease and altered non-specific tests. Early and accurate diagnosis is therefore extremely important in order to achieve successful treatment, even though there are no universally validated tests (LOURENÇO; NINA, 2020).

Treatment is based on immunosuppressive therapy with corticosteroids. The drug of choice is prednisone, initially at 60 mg/day for 4 weeks until the condition stabilizes, followed by a maintenance dose of 10 mg/day for 6 months (MANCINI et al., 2018). During the stabilization period, around 70% of patients show a good response to treatment, with improved vocal discrimination and/or an increase of more than 10 dB in tonal thresholds in two consecutive frequencies. This reinforces the need for monthly tonal audiometry. Other possible criteria for improvement are: an increase of 15 dB or more in the average for pure tones, an improvement of 20% or more in vocal discrimination and stabilization of hearing with complete regression of vertigo (LOURENÇO; NINA, 2020). On the other hand, it is very important to be aware of some complications related to the use of corticosteroids, such as suppression of the hypothalamic-pituitary-adrenal axis (hypotension, lethargy, hypoglycemia, hyponatremia, seizures and coma), hypertension, hyperglycemia, bone fragility and cataracts (VAMBUTAS; DAVIA, 2021). Such side effects can occur in up to 15% of patients during the first month. The alternative in these cases is to administer intratympanic corticosteroids, increasing the intralabyrinthine concentration and reducing the systemic effects. If conventional treatment fails or the use corticosteroids is contraindicated, there are other options such as methotrexate, cyclophosphamide, azathioprine, among others (MANCINI et al., 2018).

Finally, given that this condition can lead to significant functional losses and limitations that considerably impact patients' quality of life, it has become a topic of great interest in the medical community, given the possibility of reducing sequelae and morbidity (LOURENÇO; NINA, 2020). Therefore, it is extremely important to explore the clinical history, pathogenesis, as well as delving into the diagnosis and treatment of this disease.

OBJECTIVES

PRIMARY OBJECTIVE

To describe a case of an adult patient with right-sided immune-mediated SHL.

METHOD

This is a descriptive, narrative and reflective case report. The participant was chosen because of the rarity of his disease and the data was obtained from a private clinic in Linhares - Espírito Santo, by analyzing the medical records of a patient with immune-mediated SHL, with information on the tests carried out, the treatment established and the referrals indicated.

The case report involves risks related to the possible exposure or leakage of patient information. Therefore, all data collection and storage was carried out in accordance with the ethical principles of Resolution 466 of 2012 of the National Health Council (CNS).

In order to carry out the report, the patient's Informed Consent Form (ICF) was requested to be waived by the Human Research Ethics Committee of the Escola Superior de Ciências da Santa Casa de Misericórdia de Vitória (CEP - EMESCAM). Attempts were made to contact the patient by telephone, all of which were unsuccessful because the patient did not answer the calls made at different times and dates. In addition, he was no longer under the direct care of the clinic due to a referral to another specialist. It was therefore necessary to waive the ICF in order to publish this report, which was approved by the CEP - EMESCAM on August 27, 2024, under number 7.035.506, as shown in ANNEX A.

The study was therefore prepared in such a way as to preserve the patient's privacy and confidentiality, avoiding undue exposure, using only the information necessary to illustrate the clinical case. The data was stored in its own password-protected file, guaranteeing the secrecy and confidentiality of the data obtained.

For the patient in the case described, there were no benefits since the treatment had already been established. However, for the scientific community there will be the elucidation of a rare case, which may help in future diagnoses and interventions, acting as a source of information and enrichment of the medical literature.

CASE DESCRIPTION

This is a 54-year-old man who had his first consultation with an otorhinolaryngologist in August 2020, complaining of reduced hearing acuity on the right, as reported in a recent occupational examination. He also reported hearing loss on the left after an episode of meningitis in childhood, and tinnitus for many years, bilaterally, evolving with significant impairment to communication, which progressively worsened over time. When asked about his working environment, the patient reported that he sometimes worked in noisy places, without wearing personal protective equipment. On physical examination, there were no alterations on otoscopy, and audiometry and impedanciometry were requested as the first step in assessing the condition.

On his return visit, these tests were suggestive of left-sided cofosis, as the patient had mentioned, as a result of the meningitis, and mild to severe descending PANS on the right, with a speech recognition index of 80% and 0%, type A tympanometric curves and stapedial reflexes present ipsi to the right. At this appointment, the patient reported joint pain and swelling in the joints, especially in the fingers, elbows and knees. He also reported having family members with autoimmune diseases, such as a sister diagnosed with rheumatoid arthritis. With this in mind, a series of laboratory tests were ordered to screen for rheumatological diseases.

In October 2020, the patient returned with a blood count, C-reactive protein (CRP), ery-

throcyte sedimentation rate (ESR), anti-DNA double helix, anti-SSA, anti-SSB, antinuclear factor (ANF) and rheumatoid factor (RF), all negative. However, he tested positive for anticochlear antibodies, the 68kD HSP70. Without any further action on the part of the ENT department, he was referred to a rheumatologist who recommended starting immunosuppressive therapy and, depending on the rheumatological assessment, investigating the presence of underlying diseases.

DISCUSSION

The aim of this study was to describe a case of right-sided immunomediated SHL in an adult patient, highlighting the particularities of the clinical picture. The patient in question had a previous history of left-sided hearing loss since childhood after a bout of meningitis. In addition, he currently reports tinnitus and arthralgia and works in a noisy environment, which may have contributed to the new hearing loss on the right. These factors raise the hypothesis of a multifactorial etiology, involving both environmental factors, such as exposure to noise, and a possible autoimmune component. According to Pawlak-Osińska et al. (2018), SNHL is often classified as idiopathic due to its unknown pathogenesis and etiologies, but viral infections and vascular and autoimmune diseases stand out as the main primary causes, in addition to a complex multifactorial network involving even genetic factors.

After analyzing systematic studies and meta-analyses, a strong association was established between autoimmune diseases and SHL. The study by Li et al. (2023) showed a significant prevalence of SHL in patients with autoimmune diseases, 21.26% in systemic lupus erythematosus (SLE) and 16.14% in rheumatoid arthritis. These data corroborate the suspicion that the patient's hearing loss may be related to an autoimmune process, especially considering the family history of rheumatoid arthritis and the laboratory findings of anticochlear antibodies.

According to Ciorba et al. (2018), DIMOI is characterized by progressive, bilateral SHL, which can be associated with tinnitus and vestibular symptoms. The patient in question has left-sided scoliosis and right-sided SHLP, associated with bilateral tinnitus, findings that align with the clinical picture of DIMOI, a hypothesis reinforced by the positivity for anticochlear antibodies. On the other hand, the literature shows that immune-mediated SHLP is more common in middle-aged women, whereas the patient studied is a 54-year-old male.

there are no validated tests for diagnosis, and the literature still lacks studies on the role of HSP70 in SHL, the finding of anti-HSP70 associated with the patient's clinical condition is highly suggestive of an autoimmune component associated with the disease. Pawlak-Osińska et al. (2018) observed that of the 64 patients with sudden SCA in their study, 48% had the presence of HSP70 in the blood. Ianuale et al. (2013), in their meta-analysis, showed a high specificity of tests for detecting anti-HSP70 antibodies in the diagnosis of immune-mediated hearing loss.

In addition, the literature reviewed emphasizes the importance of early immunosuppressive treatment in cases of SNHL associated with autoimmune diseases. Ciorba et al. (2018) as well as Li et al. (2023) emphasize the use of corticosteroids as first-line treatment, highlighting non-steroidal immunosuppressive agents as additional options in cases of insufficient response. Another study by Nishimura et al. (2021) shows the results obtained with immunosuppressive therapy in a retrospective cohort of 16 to 26 years of follow-up. It was observed that in the long-term follow-up of these patients there were many fluctuations in the intensity of hearing loss, based on audiometry results, culminating in multiple needs for escala-

tion and de-escalation of the prednisolone dose to maintain hearing, with an average of approximately 10 mg/day, in addition to sometimes requiring the use of other corticosteroids, such as betamethasone and hydrocortisone. In addition, it was concluded that treatment should be individualized, since the effects of the doses and the gradual de-escalation schedule to maintain hearing differed for each patient. At the end of the study, it was found that all 4 patients evaluated progressed without hearing loss when compared to the start of therapy, suggesting that proper drug management can control the activity of the disease, despite the limitation due to the small sample size addition, according to Vambutas and Davia (2021) approximatelyof patients respond well to corticotherapy initially, with a subsequent drop in responsiveness after 3 years of follow-up, reaching only 14%. As a result, the approach to treating ILMD in those resistant to corticosteroid therapy could be carried out with some immunobiologicals, since it has been shown that these patients respond well, especially to interleukin-1 inhibition.

In this study, the patient was correctly referred for rheumatological assessment and immunosuppressive therapy was started, following current recommendations, in an attempt to stabilize the hearing loss and treat the underlying autoimmune condition. However, the patient's loss of follow-up demonstrates a limitation of this study, as it does not show the response obtained with the treatment instituted in this case.

CONCLUSION

It is clear that the association between SHL and autoimmune diseases highlights the need for a multidisciplinary approach in the management of patients with progressive hearing loss and systemic symptoms. This case underlines the importance of investigating autoimmune causes in patients with SHL, especially in the presence of a family history and joint symptoms. In addition, early intervention and appropriate treatment are crucial to optimizing the hearing and systemic prognosis of these patients. Finally, as this is an extremely rare condition, the literature lacks studies that fully cover the subject, and it is extremely important that discussions take place on the subject in order to clarify and offer the best approach for these patients, with a view to preventing possible major functional losses resulting from the disease and significantly improving quality of life.

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PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: PERDA AUDITIVA NEUROSSENSORIAL IMUNOMEDIADA: UM RELATO DE CASO
Pesquisador: JOAO DANIEL CALIMAN E GURGEL
Área Temática:
Versão: 1
CAAE: 81885924.4.0000.5065
Instituição Proponente: Escola Superior de Ciências da Santa Casa de Misericórdia de Vitória -
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 7.035.506

Apresentação do Projeto:
Trata-se de relato de caso de condição clínica rara denominada Perda Auditiva Neurossensorial (PANS) autoimune que acomete menos de 1% dos casos de perda auditiva.

A escolha do participante se deu em razão da raridade de sua doença, cujos dados serão obtidos a partir da análise do prontuário do paciente de uma clínica particular de Linhares - Espírito Santo. Serão coletadas informações referentes aos exames realizados, o tratamento estabelecido e os encaminhamentos indicados.

Objetivo da Pesquisa:
OBJETIVO GERAL:
Descrever um caso de um paciente adulto com Perda Auditiva Neurossensorial (PANS) imunomediada à direita.

Avaliação dos Riscos e Benefícios:
RISCOS:
O pesquisador reconhece a existência de riscos relacionados à possível exposição ou vazamento de informações do participante da pesquisa e se compromete em evitar a exposição indevida. Para tanto, garante que os dados serão armazenados em arquivo próprio,

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protegido por senha evitando, assim, a exposição das informações individuais, sendo garantido o sigilo e confidencialidade dos dados obtidos.

BENEFÍCIOS:
Não há benefícios diretos para o participante da pesquisa, uma vez que o tratamento já foi estabelecido. Entretanto, para a comunidade científica haverá a elucidação de um caso raro, podendo auxiliar em diagnósticos e intervenções futuras, funcionando como uma fonte de informação e enriquecimento da literatura médica.

Comentários e Considerações sobre a Pesquisa:
Pesquisa viável e relevante tendo em vista a raridade da condição clínica descrita.
Pesquisador solicita dispensa de TCLE considerando que o paciente não está mais sob os cuidados diretos da clínica e que todas as tentativas de contato foram sem sucesso. O pesquisador reafirma o compromisso com a privacidade e confidencialidade dos dados, utilizando-se apenas de informações necessárias para ilustrar o caso clínico.

Considerações sobre os Termos de apresentação obrigatória:
Foram apresentados:
- Carta de anuência assinada pelo próprio pesquisador.
- Folha de rosto assinada pela Coordenadora de Pesquisa e iniciação científica da Emescam.
- Projeto de pesquisa e PB ¿ Informações Básicas do Projeto adequados.
- Cronograma e orçamento adequados.

Recomendações:
Sem recomendação.

Conclusões ou Pendências e Lista de Inadequações:
Sugere-se aprovação.

Considerações Finais a critério do CEP:
Projeto aprovado por decisão do CEP. Conforme a norma operacional 001/2013:
- riscos ao participante da pesquisa deverão ser comunicados ao CEP por meio de notificação via Plataforma Brasil;
- ao final de cada semestre e ao término do projeto deverá ser enviado relatório ao CEP por

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meio de notificação via Plataforma Brasil;

- mudanças metodológicas durante o desenvolvimento do projeto deverão ser comunicadas ao CEP por meio de emenda via Plataforma Brasil.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_2375869.pdf	27/07/2024 11:55:51		Aceito
Outros	CARTA_DE_ANUENCIA.pdf	27/07/2024 11:48:42	VICTOR STAUFFER DUARTE	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_de_Pesquisa.pdf	27/07/2024 11:41:02	VICTOR STAUFFER DUARTE	Aceito
Folha de Rosto	Folha_de_Rosto_assinada.pdf	27/07/2024 11:40:20	VICTOR STAUFFER DUARTE	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

VITORIA, 27 de Agosto de 2024

Assinado por:
rubens josé loureiro
(Coordenador(a))

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