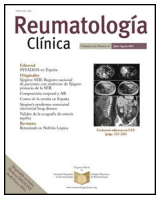
Reumatol Clin. 21 (2025) 501912

Sociedad Española de Reumatología - Colegio Mexicano de Reumatología

Reumatología Clínica

www.reumatologiaclinica.org



Case Report

Autoimmune inner ear disease and localized scleroderma in childhood: A case report

Pilar del Rosario Guarnizo Zuccardi,[a,*] Jacqueline de los Ángeles Piñeros Haiek,[b] Natalia Rodríguez Bonilla,[b] Sara Patricia Romero Orjuela,[c] Sara Juliana Guerrero León[c]

[a] *Servicio de Reumatología Pediátrica, Departamento de Pediatría, Fundación Cardioinfantil-Instituto de Cardiología, Bogotá, Colombia*
[b] *Departamento de Pediatría, Escuela de Medicina y Ciencias de la Salud, Universidad del Rosario, Bogotá, Colombia*
[c] *Escuela de Medicina y Ciencias de la Salud, Universidad del Rosario, Bogotá, Colombia*

ARTICLE INFO

Article history:
Received 24 April 2025
Accepted 29 May 2025
Available online 5 August 2025

Keywords:
Localized scleroderma
Hearing loss
Steroids
Labyrinth diseases
Sensorineural hearing loss
Autoimmune diseases

ABSTRACT

Autoimmune inner ear disease is frequently characterized by progressive bilateral hearing loss, which is not necessarily symmetrical. Vertigo, aural fullness, and tinnitus may also accompany it. There are 2 ways that the inner ear might be impacted: either as a primary disorder when the immune response directly attacks inner ear cells or as a secondary symptom of a systemic autoimmune disease.

We describe the case of an 11-year-old boy with morphea, who was diagnosed with autoimmune inner ear disease after he developed hearing loss. This relationship in children has not yet been documented in any prior reports. To improve diagnosis, management, and treatment and avoid long-term consequences, further research is required.

Enfermedad autoinmune del oído interno y esclerodermia localizada en la infancia: a propósito de un caso

Palabras clave:
Esclerodermia localizada
Pérdida auditiva
Esteroides
Enfermedad del laberinto
Pérdida auditiva sensorineural
Enfermedades autoinmunes

RESUMEN

La enfermedad autoinmune del oído interno se presenta como una pérdida auditiva bilateral progresiva, no siempre simétrica, con posible tinnitus, vértigo y plenitud aural. Puede ser primaria, cuando solo afecta a las células del oído interno, o secundaria, asociada a enfermedades autoinmunes sistémicas.

Presentamos el caso de un niño de 11 años con morfea y disminución auditiva, finalmente diagnosticado con enfermedad autoinmune del oído interno. No hay reportes previos de esta asociación en la infancia. La literatura sobre enfermedad autoinmune del oído interno en niños es limitada, lo que resalta la necesidad de más estudios para mejorar su diagnóstico y tratamiento, evitando secuelas a largo plazo.

Introduction

Autoimmune inner ear disease (AIED) is defined as a progressive, bilateral, and not always symmetrical sensorineural hearing loss that develops over 3–90 days. It is classified as primary when the inner ear is the only organ affected and antibodies are directed against specific antigens of the saccule, utricle, and endolymphatic duct, or secondary, when it occurs as a consequence of a systemic autoimmune disease and accounts for 15%–30% of cases. The estimated annual incidence is 5 cases per 100,000 people, with a prevalence of 45,000 affected individuals in the United States. AIED is considered to account for less than 1% of cases of bilateral sensorineural hearing loss, making it a diagnostic challenge, especially

* Corresponding author.
E-mail address: pilarguarnizo@gmail.com (P.d.R. Guarnizo Zuccardi).

in the paediatric population, where its prevalence has not been clearly established.[1]

Localised scleroderma or morphea is an inflammatory connective tissue disorder characterised by epidermal atrophy and thickening and induration of the dermis secondary to excessive collagen deposition. Morphea occurs most frequently in the paediatric population, characterised by inflammatory patches of thickened skin on the head, neck, and extremities, of varying shapes and sizes. This article reports the case of an 11-year-old patient with a history of morphea, who subsequently developed AIED. According to a literature search, this is the first case in a paediatric population in which these two diseases coexist.[2]

Case presentation

An 11-year-old male patient from Bogotá, Colombia, was diagnosed with linear morphea in the left hemisphere of the skull. The dermatologist initially treated him with topical steroids. In 2019, he was evaluated for the first time by our rheumatology service. Systemic management was initiated with steroids as bridging therapy and methotrexate, with improvement in the affected areas. After 48 months in remission, the methotrexate taper was initiated in July 2021, achieving remission without medication.

In May 2022, during a rheumatology check-up, asymmetry was detected in the right side of the face, leading to a brain MRI, which showed no acute changes. The paediatric neurology department determined that, despite the facial asymmetry, there were no findings indicating systemic involvement. Almost a year later, in March 2023, the mother reported hearing impairment.

Having been lost to follow-up care, the patient returned to the clinic in January 2024, with hearing impairment and the use of an external device. At that time, the patient had an established lesion in the left parieto-occipital region and an area of hyperpigmentation in the frontoparietal region. No evidence of morphea activity had been reported, and he had been in remission since February 2019. A review of the patient's medical history and auditory potentials from March 2023 revealed a wave V at 55 dB NHL in the right ear and a wave V at 60 dB NHL in the left ear, demonstrating moderate bilateral electrophysiological impairment. Based on these findings, the otolaryngology department determined the patient to be suffering from hearing loss secondary to methotrexate ototoxicity.

Rheumatology departments diagnosed autoimmune hearing loss, and methotrexate toxicity was ruled out. Studies were requested with positive anticochlear antibodies (anti-P68) using the immunoblot technique, and methotrexate levels were almost undetectable (.01 nmol/L), unrelated to toxicity, confirming the diagnosis of AIED. Treatment was initiated with oral steroids plus azathioprine.

The patient provided a pre-treatment audiometry from December 2023, showing sensorineural hearing loss presenting mildly at 500 Hz and moderately at 1000 to 8000 Hz, affecting both ears, with 100% discrimination at 80 dB bilaterally. The patient currently reports improved hearing and is undergoing multidisciplinary management by otorhinolaryngology and rheumatology with oral steroids combined with azathioprine. Intratympanic steroid injection is scheduled.

Discussion

In this article, we present the first reported case, based on an exhaustive literature search, of a paediatric patient with morphea and AIED. Autoimmune diseases that have been associated with AIED include vasculitis, rheumatoid arthritis, Cogan's syndrome, systemic lupus erythematosus, vitiligo, and even Kawasaki disease. However, an association between localised scleroderma and AIED has not been described. In a patient who already has an autoimmune disease, an association therefore cannot be avoided.[3]

Our patient presented with limited facial morphea ("en coup de sabre"), and although the manifestations of this disease are predominantly cutaneous, systemic involvement, such as musculoskeletal disorders, has also been documented as being the most common. Additionally, it has been reported that patients with head injuries are at increased risk of developing neurological disorders such as seizures, headaches, encephalitis, and cognitive impairment. Other manifestations include neuropsychiatric problems and cranial nerve palsies.[4]

Although both diseases present an exaggerated immune response, their pathophysiology is different. Morphologically, certain stimuli trigger vascular and immune dysregulation in patients with a genetic predisposition. Particularly evident is the activation of T cells and the release of cytokines associated with interferon gamma, triggering profibrotic and inflammatory pathways that result in excess collagen production.[2] In contrast, in AIED, there is a cross-reaction in which antibodies or "rogue T cells" cause accidental damage to the inner ear, which shares antigens with viruses and bacteria.[1]

In this case, during the patient's follow-up, an audiometry test was performed that revealed hearing impairment. This was subsequently studied with an evoked potential test, the result of which was abnormal and revealed bilateral sensorineural hearing loss. After ruling out other causes of hearing loss, such as methotrexate toxicity, the diagnosis of AIED was reached. This is consistent with the literature review, which describes that diagnosis should be based on the patient's clinical presentation, the exclusion of other causes of sensorineural hearing loss, and a positive response to immunosuppressive therapy.[5] Regarding diagnostic serological tests, associations have been observed between AIED and HSP70, a potential diagnostic serological marker under study.[1,5] Other potential biomarkers include the P0 protein and anti-endothelial cell antibodies. However, these have high sensitivity but low specificity, so the diagnosis of AIED remains challenging and relies on the ruling out of other aetiologies.[1] Although the aforementioned biomarkers were not found in the patient, positive anticochlear antibodies were found.

According to the treatment, during the initial phase, a good clinical response to corticosteroids was observed, due to their anti-inflammatory properties and their role in the reparative process at the blood-labyrinth barrier. Other therapeutic options include transtympanic infusion or nonsteroidal immunosuppressants.[1] Most authors describe a variation of the Rauch treatment regimen, which consists of an initial course of high-dose steroids (prednisone 1 mg/kg/day) for 4 weeks, followed by a slow taper over 9 weeks to a maintenance dose of 10–20 mg/day.[1,6] In our patient's case, he was managed with the aforementioned Rauch regimen, with adequate modulation of the clinical picture.

Additionally, to reduce the risk of relapse and improve the prognosis of the disease, immunosuppressive therapy with azathioprine was initiated, and a right tympanostomy was proposed along with the application of intratympanic steroids. Saraçaydin et al. conducted a study of 12 patients with AIED, who were treated with 1 mg/kg of azathioprine once daily, adding 30 mg of prednisolone every 48 h for 4 weeks. The results indicate a significant increase in the ability to hear pure tones and in sound discrimination, as evidenced by audiometry.[7]

Other therapeutic agents that have been studied in small cohorts are TNF-gamma inhibitor monoclonal antibodies (golimumab, infliximab, and etanercept), which have demonstrated improvement in hearing.[3] Likewise, there are case reports of the use of abatacept in localised scleroderma.[8] In turn, due to the relationship between interleukin 1B and AIED, anakinra has been

studied, which may be a therapeutic measure in patients who do not respond to steroids.[1,9] However, there is currently insufficient evidence to recommend the aforementioned biologic agents.

This underscores the importance of continuing and expanding studies in this setting to provide alternatives to steroids for patients with AIED, who have high non-response rates to this first-line treatment. Although our therapeutic approach has shown good results so far, further studies are needed to broaden our understanding of this disease and develop new, timely therapeutic strategies for these patients. Emotional management is the greatest challenge parents face with this type of diagnosis.[10]

Conclusion

In this case, the intrinsic relationship between systemic or localised autoimmune diseases and AIED can be seen. The relationship between morphea and AIED has not been described in the literature, but it remains an important field of research in the paediatric population. Although AIED does not have a clear prevalence in children, morphea does occur at a higher rate in this age group. As a result studying the relationship that triggers hearing loss and its treatment is of utmost importance to prevent irreversible sequelae in a population that has been understudied to date.

CRediT authorship contribution statement

- Pilar del Rosario Guarnizo Zuccardi, paediatric rheumatologist: participated in the patient's care.
- All authors participated in the literature review and the writing of the manuscript. All approved the final version of the document.

Ethical considerations

Informed consent was obtained from the patient's legal representative for the publication of this clinical case, guaranteeing the confidentiality of the information. This study complies with current regulations on bioethical research and has been authorised by the Clinical Research Ethics Committee of the Cardioinfantil Foundation-Institute of Cardiology.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this study, the authors used Chat GPT to perform grammar correction. After using this tool, the authors reviewed and edited the content as needed, assuming full responsibility for the content of the publication.

Funding

Not applicable.

Declaration of competing interest

None.

References

1. Das S, Bakshi SS, Seepana R. Demystifying autoimmune inner ear disease. Eur Arch Otorhinolaryngol. 2019;276:3267–74, http://dx.doi.org/10.1007/s00405-019-05681-5.
2. Papara C, De Luca DA, Bieber K, Vorobyev A, Ludwig RJ. Morphea: the 2023 update. Front Med. 2023;10:1108623, http://dx.doi.org/10.3389/fmed.2023.1108623.
3. Balouch B, Meehan R, Suresh A, Zaheer HA, Jabir AR, Qatanani AM, et al. Use of biologics for treatment of autoimmune inner ear disease. Am J Otolaryngol. 2022;43:103576, http://dx.doi.org/10.1016/j.amjoto.2022.103576.
4. Li SC, Zheng RJ. Overview of juvenile localized scleroderma and its management. World J Pediatr. 2020;16:5–18, http://dx.doi.org/10.1007/s12519-019-00320-9.
5. Penêda JF, Lima NB, Monteiro F, Silva JV, Gama R, Condé A. Immune-mediated inner ear disease: diagnostic and therapeutic approaches. Acta Otorrinolaringológica Esp (Engl Ed). 2019;70:97–104, http://dx.doi.org/10.1016/j.otorri.2017.08.008.
6. Ciorba A, Corazzi V, Bianchini C, Aimoni C, Pelucchi S, Skarżyński PH, et al. Autoimmune inner ear disease (AIED): a diagnostic challenge. Int J Immunopathol Pharmacol. 2018;32, http://dx.doi.org/10.1177/2058738418808680, 2058738418808680.
7. Saraçaydin A, Katircioğlu S, Katircioğlu S, Karatay MC. Azathioprine in combination with steroids in the treatment of autoimmune inner-ear disease. J Int Med Res. 1993;21:192–6, http://dx.doi.org/10.1177/030006059302100 40.
8. Kalampokis I, Yi BY, Smidt AC. Abatacept in the treatment of localized scleroderma: a pediatric case series and systematic literature review. Semin Arthritis Rheum. 2020;50:645–56, http://dx.doi.org/10.1016/j.semarthrit.2020.03.020.
9. Huang KH, Lin HC, Lin CD, Wu PC. Relapsing autoimmune inner ear disease with significant response to methotrexate and azathioprine combination therapy: a case report and mini literature review. Medicine (Baltimore). 2023;102:e33889, http://dx.doi.org/10.1097/MD.0000000000033889.
10. Hamzah NFA, Umat C, Harithasan D, Goh BS. Challenges faced by parents when seeking diagnosis for children with sensorineural hearing loss. Int J Pediatr Otorhinolaryngol. 2021;143:110656, http://dx.doi.org/10.1016/j.ijporl.2021.110656.