Holt-oram syndrome ad conductive hearing loss: treatment with bilateral bone conduction implant (OSIA)

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Abstract
Holt-Oram Syndrome is a rare genetic disorder characterized by congenital malformations of the upper limbs and cardiac anomalies, with possible involvement of the auditory system. We present the case of a 6-year-old girl diagnosed with Holt-Oram Syndrome in 2019, who also presented bilateral conductive hearing loss that did not respond to previous surgical interventions. In May 2020, a bilateral BAHA 6 with soft band was applied; however, in February 2025, following adequate temporal bone development, a bilateral bone conduction implant (OSIA) was performed, leading to significant improvement in auditory thresholds. This case highlights the importance of early monitoring and treatment of auditory anomalies in patients with Holt-Oram Syndrome and confirms the effectiveness of bone conduction implants as a therapeutic solution.

Keywords: Holt-Oram Syndrome, hearing loss, bone conduction

Introduction

Holt-Oram Syndrome (HOS) is a rare genetic condition first described by Holt and Oram in 1960, primarily affecting the upper limbs and the cardiovascular system. It is caused by mutations in the TBX5 gene, which is involved in the embryonic development of the limbs and heart. Clinical manifestations include skeletal anomalies (such as agenesis or hypoplasia of the radius, digital malformations, and syndactyly) and congenital heart defects, including atrial septal defects (ASD) and valve abnormalities. Although hearing loss is not considered a primary manifestation of the syndrome, it has been reported in a significant proportion of patients, particularly in its conductive form (Jones et al., 2021). Early identification of auditory deficits and appropriate treatment are crucial to ensure optimal communicative and cognitive development. In our patient, Holt-Oram Syndrome was genetically diagnosed in 2019, and the patient initially presented bilateral conductive hearing loss. In May 2020, a bilateral BAHA 6 with soft band was applied, and significant improvement was observed. In February 2025, after the appropriated temporal bone development, a bilateral bone conduction implant (OSIA) was performed, leading to significant improvements in auditory thresholds. This case emphasizes the importance of timely and adaptive treatment based on the progression of skeletal conditions in patients with congenital anomalies.

Materials and Methods

This study is structured as a case report, with informed consent obtained from the patient prior to participation. A comprehensive audiological evaluation was performed, including pure-tone audiometry, speech audiometry, tympanometry, and auditory brainstem response (ABR) testing to assess the degree and type of hearing loss. Additionally, imaging studies were conducted, comprising computed tomography (CT) scans and magnetic resonance imaging (MRI) of the temporal bones, to evaluate anatomical malformations of the middle and external ear structures. All procedures were carried out in accordance with relevant clinical guidelines and ethical standards. This study was conducted in accordance with the tenets of the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee (Territorial Ethics Committee Lombardy 6, IRCCS Policlinico San Matteo, Pavia).

Results

Patient information

The patient was a 6-year-old girl, the first-born child, diagnosed with Holt-Oram Syndrome in 2019. Despite associated skeletal malformations and cardiac abnormalities, her neuropsychomotor development was normal until the identification of hearing impairment. In May 2020, a bilateral BAHA 6 with soft band was applied, but due to skeletal progression, the definitive bone conduction implant was only possible in 2025.

Reason for hospitalization and initial symptoms

The patient was referred to our center for audiological evaluation following suspected bilateral hearing loss, as reported by her family due to difficulty perceiving sounds. Audiological screening confirmed bilateral conductive hearing loss (Figure 1). In May 2020, a bilateral BAHA 6 with soft band was applied, which temporarily improved the condition, confirming its effectiveness in improving auditory deficit.

Bilateral myringotomy with transtympanic tube insertion was performed in December 2024, leading to the tympanogram changing from type B to type A (Figure 2). Therefore, the effusive conductive component of hearing loss was eliminated, although the conductive component associated with the malformative condition was still present. Consequently, due to the lack of further progress and in light of the adequate bone development, in February 2025, bilateral bone conduction implant (OSIA) was performed.

Family condition and medical history

The patient comes from a Pakistani family with non-consanguineous parents. Significant familial medical conditions were detected, including maternal hypertension, paternal type 2 diabetes mellitus, and a history of cerebral palsy on the maternal side. Regarding her medical history, the mother's pregnancy was complicated by intrauterine growth restriction. The patient was born at 41 weeks with a weight of 2.625 kg, a length of 45.5 cm, and a head circumference of 32 cm. During the neonatal period, the patient was admitted to the Neonatal Intensive Care Unit (NICU) due to complex malformations, including desaturation episodes.

Diagnostic examination

On February 2025, a CT scan was performed, revealing several anomalies in the auditory structures. On the right side, an abnormal ossicular chain was observed, with the malleus adhering to the tegmen tympani and the stapes inserted abnormally, anterior to the oval window. The external auditory canal was narrow, with an abnormal course, and poor mastoid pneumatization. On the left side, the external auditory canal and tympanic membrane were normal, but tympanic drainage was visible. The ossicular chain on the left was correctly positioned. Audiometric tests confirmed bilateral conductive hearing loss. Additionally, ABR (Auditory Brainstem Response) test detected mild hearing loss on the left side and moderate hearing loss on the right, probably also due to upper respiratory tract inflammation (Figure 1).

Finally, Holt-Oram Syndrome was diagnosed, in association with bilateral conductive hearing loss, linked ossicular chain malformations.

AccuScreen PRO TDA
2389 18

Operatore:

Risultati TEOAE

Orecchio sx

08.11.18 12:09

REFER
Durata:
TEOAE:
A:18% S: 96%

Note:

AccuScreen PRO TDA
2389 18

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REFER
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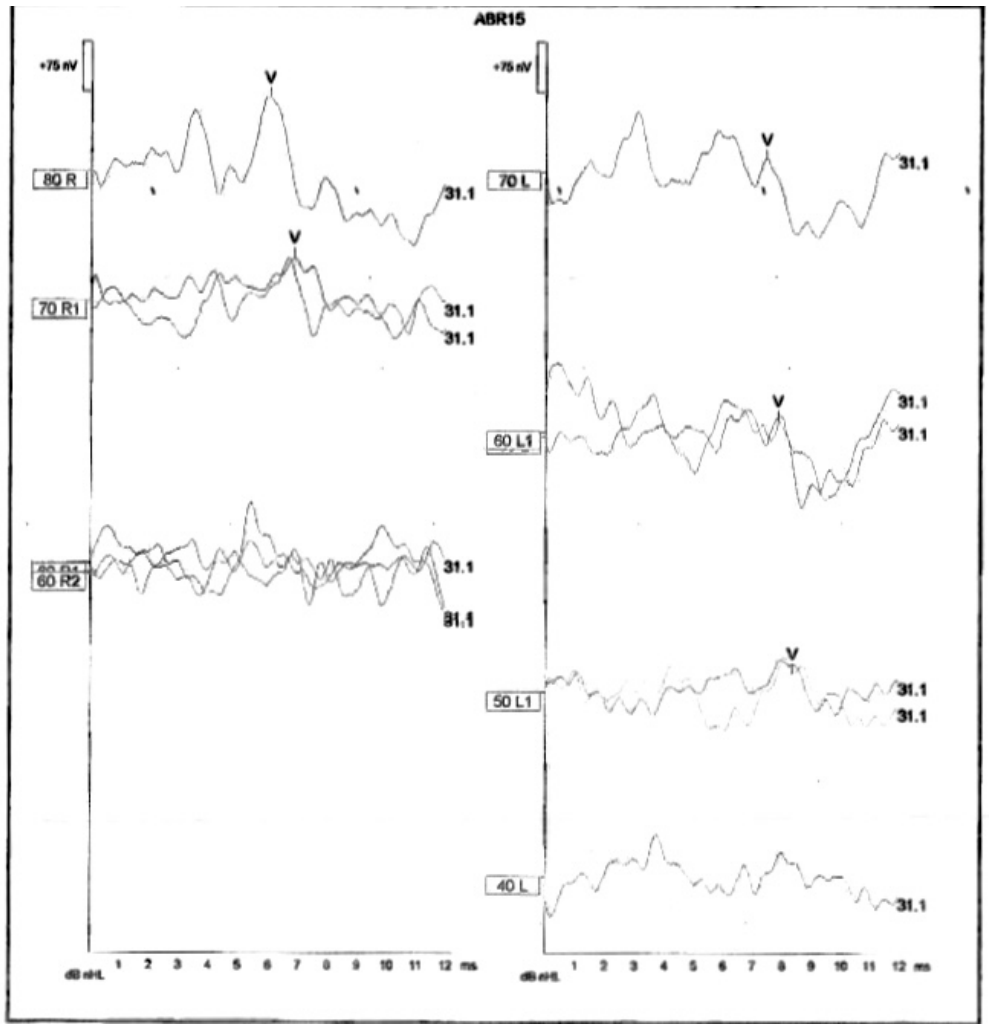

Figure 1: TEOAE and ABR Trace (December 2018)
TEOAE: refer bilateral; ABR: Mild hearing loss on the left side and moderate hearing loss on the right, influenced by upper respiratory tract inflammation.

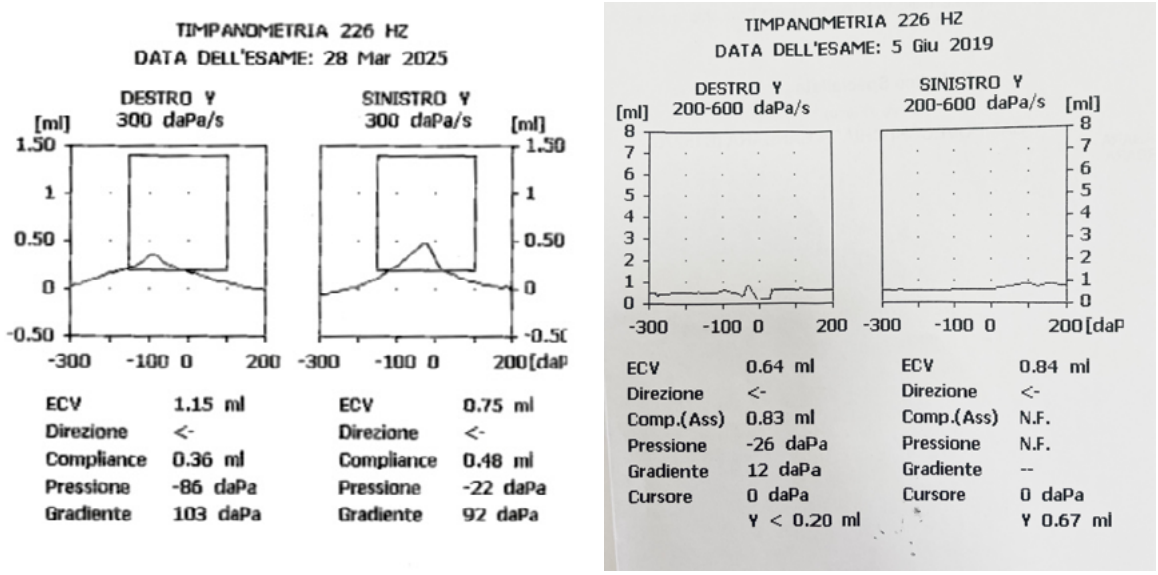

Figure 2: Tympanogram
2.1 Pre-operative tympanogram (before myringotomy): The tympanogram shows type B, indicative of the presence of a conductive effusive component in the middle ear.
2.2 Post-operative tympanogram (after bilateral myringotomy with transtympanic tubes): The tympanogram shows type A, indicating the resolution of the effusive conductive component, while the malformative conductive component persists.

Treatment provided

The patient underwent a bilateral bone conduction implant (OSIA), an effective surgical solution to bypass ossicular chain anomalies and improve sound conduction through the temporal bone. This treatment resulted in a significant improvement in auditory thresholds, overcoming the limitations of previous treatments such as myringotomy and transtympanic drainage, which addressed the conductive component related to the inflammatory condition but not the malformative one.

Bone conduction implant indications according to guidelines

According to international guidelines for the treatment of conductive hearing loss, such as those established by the European Society of Otology and Neurotology (ESPO), bone conduction implants (OSIA) are recommended for patients with conductive hearing loss caused by congenital anomalies of the ossicular chain or external auditory canal. They are also indicated for patients with middle and inner ear malformations, as well as for patients who do not benefit from other solutions such as traditional hearing aids or ossicular surgery (Sennaroglu & Aslan, 2014). Bone conduction implants are also a solution in case of unilateral or bilateral hearing loss, if other options are not effective.

In our patient's case, non-conservative treatments (such as myringotomy) did not result in significant improvements, making the bone conduction implant the appropriate therapeutic choice (Balkany & Thompson, 2014). Bone conduction implants have proven particularly beneficial in pediatric patients, as in the case of our patient, where the intervention significantly improved quality of life and linguistic development (Loske & Dempsey, 2015).

Clinical evaluation and follow-up

Post-implantation, the patient was regularly monitored through audiometric exams, showing significant improvement in auditory thresholds after the procedure (Figure 3). The patient's quality of life greatly improved, with notable progress in verbal communication and social and linguistic development.

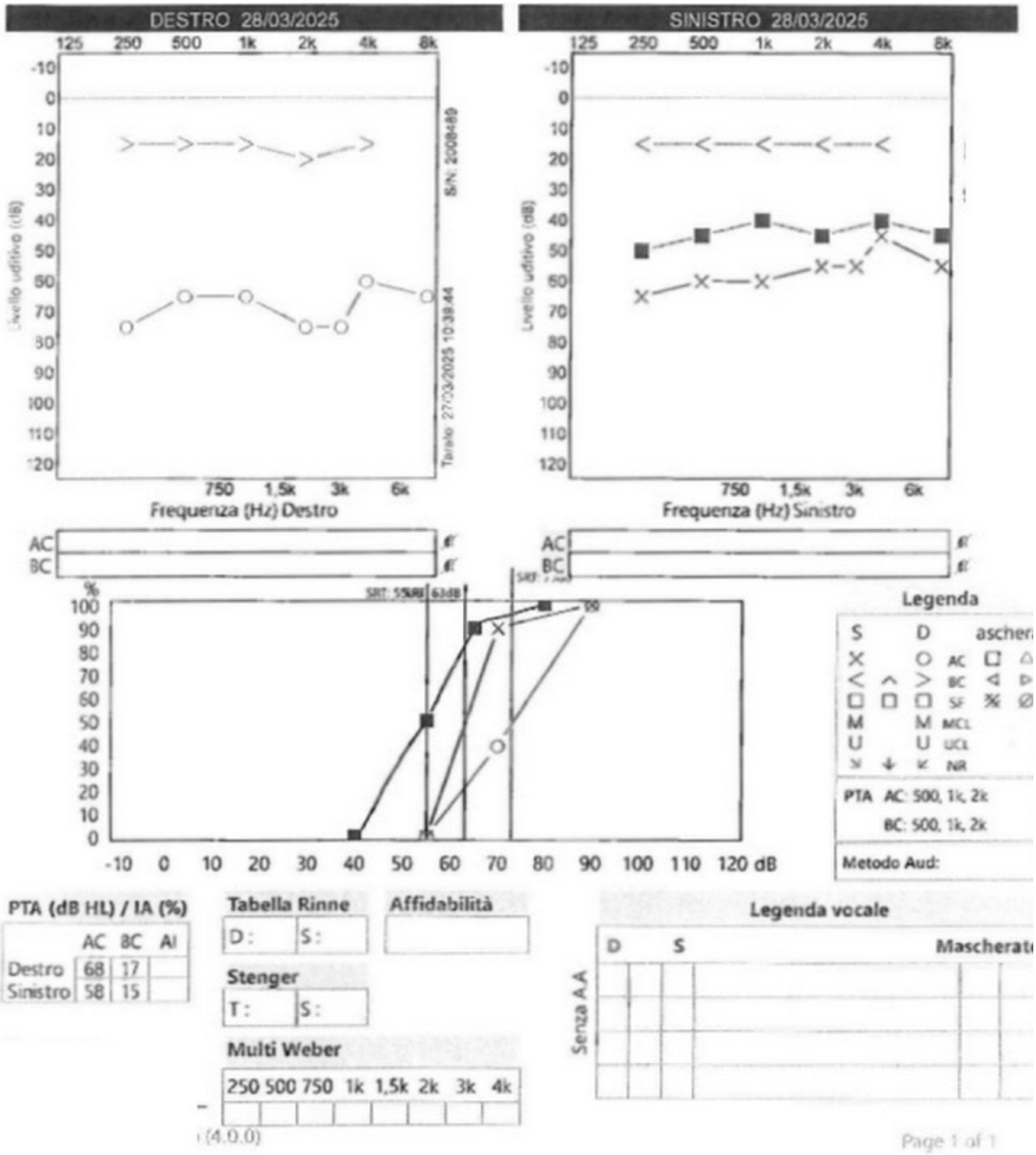

Figure 3: Post-operative Audiogram (after OSIA implant)
The post-operative audiogram shows a significant improvement in bilateral hearing thresholds, with an enhancement in conductive hearing following the bone conduction implant.

Discussion and case relevance

Holt-Oram Syndrome is a rare genetic disorder with an estimated prevalence of approximately 1:100,000–1:200,000 live births (Holt & Oram, 1960; Jones et al., 2021). While it is primarily characterized by upper limb malformations and cardiac anomalies, conductive hearing loss is one of the most common manifestations of the syndrome. The prevalence of hearing loss in patients with HOS is estimated to be between 25% and 50%, often related to malformations of the ossicular chain and external auditory canal (Jones et al., 2021). The management of conductive hearing loss in HOS patients requires a multidisciplinary

approach, as congenital anomalies can vary significantly. In our case, the bilateral bone conduction implant resulted in significant improvement in auditory abilities, confirming the effectiveness of this technology in patients with refractory bilateral conductive hearing loss.

Common Approaches for Managing Hearing Loss in Patients with Holt-Oram Syndrome

Management of hearing loss in patients with Holt-Oram Syndrome (HOS) requires a tailored, multidisciplinary approach due to the complexity of associated congenital anomalies affecting the skeletal, cardiac, and auditory systems.

1. Comprehensive Audiological and Diagnostic Assessment

A thorough audiological evaluation is essential, including pure-tone and speech audiometry, tympanometry, and when indicated, radiological imaging (CT or MRI) to assess middle ear and external auditory canal malformations. This diagnostic work-up is critical to determine the type and severity of hearing loss and to guide appropriate intervention (Jones et al., 2021; Smith et al., 2018).

2. Conventional Hearing Aids

For mild to moderate hearing loss, conventional air conduction hearing aids are often the first line of treatment. However, structural abnormalities of the external auditory canal or chronic otitis media frequently limit their effectiveness in HOS patients (Brown et al., 2019).

3. Bone Conduction Hearing Devices

Bone conduction implants, including bone-anchored hearing aids (BAHA) and active bone conduction implants, are widely reported as effective interventions for refractory conductive hearing loss in this population. These devices bypass the malformed middle ear by transmitting sound vibrations directly to the cochlea via bone conduction. Several studies have demonstrated significant improvements in auditory thresholds and patient-reported outcomes following implantation (Jones et al., 2021; Lee et al., 2020; Smith et al., 2018).

4. Surgical Interventions

In select cases where anatomical conditions permit, reconstructive surgery aimed at correcting ossicular chain anomalies or canalplasty may be attempted. However, the success of these procedures is variable due to the complexity of congenital malformations in HOS (Anderson et al., 2017). Surgical management requires careful risk-benefit analysis and is less commonly pursued than prosthetic solutions.

5. Multidisciplinary Approach

Given the multisystem involvement in HOS, an integrated team including otolaryngologists, audiologists, cardiologists, geneticists, and maxillofacial surgeons is crucial for comprehensive patient care. This collaborative model enhances both auditory and systemic outcomes (Jones et al., 2021).

Reported Outcomes

Literature consistently supports bone conduction devices as an effective treatment modality, with substantial improvements in hearing function and quality of life in patients with HOS-related conductive hearing loss (Jones et al., 2021; Lee et al., 2020). While surgical correction may offer benefits in select patients, its role remains limited.

Overall, individualized assessment combined with advanced hearing technologies and multidisciplinary management constitutes the current standard of care for HOS patients with hearing impairment, resulting in favorable auditory rehabilitation and enhanced patient well-being.

Conclusion

The treatment of Holt-Oram Syndrome requires a multidisciplinary approach that considers orthopedic, cardiologic, and auditory implications. In the presented case, the bilateral bone conduction implant resulted in a significant improvement in auditory abilities, contributing to the enhancement of linguistic development and the quality of life of the patient.

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