BRIEF COMMUNICATION

Osteogenesis Imperfecta and Hearing Loss—Description of Three Case Reports∗

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Received 25 November 2012; accepted 12 February 2013

KEYWORDS
Osteogenesis imperfecta;
Hearing loss;
Bony alterations

Abstract Osteogenesis imperfecta is the commonest connective tissue hereditary disease. Its clinical presentation has a wide spectrum of characteristics, which includes skeletal deformities and hearing loss. We describe three case reports of individuals carriers of this disease presenting with different patterns of hearing loss.

Hearing loss prevalence and patterns are variable and have no clear relation with genotype. Its assessment at initial evaluation and posterior monitoring is essential to provide the best therapeutic alternatives.

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PALABRAS CLAVE
Osteogénesis imperfecta e hipoacusia. Descripción de 3 casos

Resumen La osteogénesis imperfecta es la enfermedad hereditaria del tejido conectivo más frecuente. Su presentación clínica tiene un amplio espectro de características, que incluyen deformidades esqueléticas e hipoacusia. Se describen 3 casos clínicos de pacientes portadores de esta enfermedad, que se presentan con diferentes patrones de hipoacusia.

La prevalencia y los patrones de la hipoacusia son variables y no tienen una relación clara con el genotipo. Su evaluación en la exploración inicial y posterior seguimiento es esencial para ofrecer las mejores alternativas terapéuticas.

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Background

Osteogenesis imperfecta (OI) is one of the most common inherited bone diseases, with an estimated prevalence of 1 in 10,000 to 20,000 births. It is characterized by a generalized connective tissue dysfunction and has a variable clinical presentation, including features such as increased susceptibility to bone fractures, skeletal deformities, joint

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laxity, blue sclera, dentinogenesis imperfecta and hearing loss.1

Sillence et al. initially distinguished four types of OI depending on whether the disease phenotype was mild, lethal, severe or moderate. Later there were defined another four types of moderate to severe disease (types V–VIII).2

OI results from mutations involving the genes responsible for type I collagen synthesis or intracellular processing, seven genes being known to date.3,4

Almost 90% of individuals with clinical diagnosis of OI have an autosomal dominant transmitted mutation identifiable in the COL1A1 or COL1A2 genes, encoding the collagen type I α1 and α2 chains, respectively.1

Approximately 3%–5% of OI cases are transmitted as an autosomal recessive trait and are associated with severe/lethal disease forms (types VII and VIII). There are involved mutations in genes encoding CRTAP (cartilage-related protein), P3H1/LEPRE1 (prolyl 3-hydroxylation 1), PPIB (citrin) and HSP-47 (chaperone protein) responsible for intracellular processing of type I collagen.4

Currently, the treatment is primarily based on bisphosphonates intake, effective on decreasing the fractures and pain crisis and improving mobility. Physiatric rehabilitation and orthopedic surgery are reserved for the moderate/severe OI types.5

The prevalence of OI associated hearing loss in family studies ranges from 37% to 64% and in international population studies the prevalence reported was 45% to 58%.7

Patients and Methods

Discussion of three case reports and review of the existing literature on OI auditory involvement.

Results

The first two case reports describe two brothers with type I OI caused by an autosomal dominant transmitted mutation of COL1A1 gene.

The sister, aged 34, presented with a history of multiple fractures in pre-adolescence, lumbar spine osteoporosis, dentinogenesis imperfecta and blue sclera. She had a progressive bilateral hearing loss and carried a left hearing aid for the past 15 years. There was no history of previous infectious ear disease, use of ototoxic drugs or acoustic trauma. At otoscopic observation there were no significant changes, Rinne test was negative bilaterally and Weber test had no lateralization.

The vocal and tonal audiogram showed a severe mixed hearing loss bilaterally with 98% of discrimination bilaterally. There was an air-bone gap of about 40 dB bilaterally. The tympanogram was type Ad and the acoustic reflexes were only present with a stimulus of 2000 Hz or higher frequency (Fig. 1).

Cranial computed tomography (CT) scan showed signs of translucency in the otic capsules, especially in areas adjacent to the semicircular canals and cochlea (Fig. 2).

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Figure 1 Audigram and impedanciometry showing bilateral mixed hearing loss, type Ad tympanogram and absence of acoustic reflexes with a stimulus of 1000 Hz bilaterally. Acoustic reflexes can be found with a stimulus of 2000 Hz.
Osteogenesis imperfecta and hearing loss

We proceeded to exploratory tympanotomy on the right ear as the hearing was symmetrical and the left ear was already rehabilitated. In surgery we found evidence of an ossicular chain excessive mobility with preserved incudo-malleolar mobility despite the shortness of the incus long process. The stapes footplate was fixed in position and had an abnormally increased thickness. A stapedotomy was performed with placing of a Causse prosthesis (0.4 mm × 4.25 mm).

At 4 weeks post surgery, we observed a significant reduction of the air-bone gap in the audiogram and we expect the complete closure of the gap in the coming months.

The second case report refers to the brother, a 43 years old man with a history identical to his sister’s and rehabilitated with a hearing aid for the past 20 years.

The audiogram showed an almost exclusively sensorineural bilateral hearing loss with an average hearing threshold of 50 dB in the right ear and 65 dB in left ear. The discrimination was of 98% bilaterally.

The tympanogram was type A and there were no acoustic reflexes bilaterally.

The CT scan showed translucency areas in the otic capsules, with pericochlear predominance.

The third case report refers to a female patient followed in Otorhinolaryngology consultation since age 41. She has type I OI and presents with blue sclera and lower limbs malformations due to multiple fractures in childhood. She also suffers from type I Chiari malformation with consequent dysphagia, dysphonia and nistagmo.

At the initial assessment there were no relevant alterations in the otoscopy, the Rinne test was negative bilaterally and the Weber test lateralized to the left side.

The tonal and vocal audiogram revealed a moderate mixed hearing loss in the right ear and severe mixed hearing loss in the left ear. The tympanogram was type A with absence of acoustic reflexes bilaterally.

She was submitted to a left ear exploratory tympanotomy, which revealed a fractured stapes crura and a fixed stapes footplate. It was performed a stapedotomy by placing a Causse prosthesis (0.4 mm × 4.25 mm) and 4 months after surgery the air-bone gap was completely closed.

Currently, LMM has 57 years old and the audiogram shows a mild sensorineural hearing loss in the left ear and severe mixed hearing loss in the right ear and she uses a hearing aid on the left side (Fig. 3).

Figure 2  CT scan with axial cuts images showing areas of translucency in the otic capsules, particularly in pericochlear areas and adjacent to the CSC. The ossicular chains do not show visible changes. Images (a)–(c) relate to the right ear and images (d)–(f) to the left ear.
Discussion

OI associated hearing loss is generally bilateral and develops through the second to fourth decades of life. It usually begins as a conductive hearing loss with later development of a sensorineural component. Isolated sensorineural hearing loss is observed only in a minority of patients. As other disease characteristics, hearing loss phenotype is heterogeneous in occurrence, type, severity and progression. Although most often reported in association with COL1A1 mutations and milder types of OI it has not been scientifically demonstrated an association between hearing loss characteristics and the mutation or gene involved in OI. In fact, identical mutations lead to considerable inter and intra-familiar variability in hearing loss pattern, as noted in the first two clinical cases described.

Type I collagen deficit, either qualitatively or quantitatively, involves both the bony structures and soft tissues of the ear, causing an early onset of hearing loss.

Imaging evaluation by CT scan or magnetic resonance shows a demineralization of the otic capsule. The etiology of hearing loss in OI is not fully understood, but may be due to cochlear hair cells and stria vascularis atrophy as well as from abnormal bone formation in the cochlea and surrounding structures.

Moreover the conductive hearing loss can be associated either to footplate fixation, deficient ossification of the ossicles with atrophy or fractures of stapedic crura or malleus, mucosal hypervascularization or otospongiotic-like lesions in the stapes footplate causing fixation or discontinuity of the ossicular chain. Some characteristics of OI associated hearing loss, as their progression and ossicular involvement, mimics deafness associated with otosclerosis. However in OI there is a generalized disorder of the connective tissue and bone, while in otosclerosis the disease is limited to the temporal bone. Additionally, it was found that the sensorineural hearing loss is reported most frequently and at earlier ages in OI. The treatment of hearing impairment associated with OI varies according to its type and severity.

The conductive hearing loss caused by ossicular deformities can often be surgically corrected however, outcomes are worse than in patients without OI possibly due to diminished stability of the supporting bones and possible thickening and hypervascularization of the footplate. Published results from stapedectomies in type I OI showed a decrease of the air-bone gap to 10 dB in 75–85% of patients, compared to 90–95% of patients without OI.

The use of active middle ear implants is currently being developed to allow the conduction of sound directly to the ossicular chain. Theoretically, since bone deformity in OI may reach the temporal bone and ossicles, these techniques could not be successful. However, in the study recently presented by Kontorinis et al, the placement of three Vibrant Soundbridge implants in the oval window in combination with stapedectomy obtained an average improvement of 36.8 dB in average hearing thresholds postoperatively. Thus, this technique can be considered as an alternative to isolated stapedectomy/stapedotomy.

The bone-anchored hearing aid, an osteointegrated implant that sends sound directly to the cochlea by bone conduction, has not yet been evaluated in patients with OI. However it may not be the best option because it requires a functioning inner ear and patients with OI often develop a sensorineural hearing loss.

The treatment of sensorineural hearing loss associated with OI is identical to that of sensorineural hearing loss from other etiologies. Hearing aids such as those employed in the case reports presented allow the amplification of sounds arriving at the ear and are important instruments widely available.

Some patients with OI (2%–11%) develop a sensorineural hearing loss that no longer benefits from the use of hearing aids. In these cases, the cochlear implant is an available option, with results similar to that of individuals free of disease.
Conflicts of Interest

The authors have no conflicts of interest to declare.

References