ELSEVIER

Canadian Association of Radiologists Journal 62 (2011) 296–298

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Canadian Residents' Corner / Coin canadien des résidents en radiologie

Case of the Month #171: Osteogenesis Imperfecta of the Temporal Bone

Elisa Fuller, BSc[a], Vincent Lin, MD, FRCSC[b], Mary Bell, MD, FRCPC[c], Aditya Bharatha, MD[a], Robert Yeung, MD, FRCPC[a], Richard I. Aviv, MBChB, FRCR[a], Sean P. Symons, MPH, MD, FRCPC[a,b,*]

[a]*Division of Neuroradiology, Department of Medical Imaging, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada*
[b]*Department of Otolaryngology–Head and Neck Surgery, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada*
[c]*Division of Rheumatology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada*

Clinical Presentation

A 35-year-old man presented to the Department of Otolaryngology with progressive bilateral hearing loss, worse on the right, over the past 12 years. Audiometry determined the hearing loss to be mixed, both conductive and sensorineural. He had no otalgia, vertigo, or otorrhea. There was no history of otologic surgery, noise exposure, or familial hearing loss. He described remote minor head injury at age 4 years that required stitches, and prior fractures, which generally occurred during hockey matches, of his clavicle, fingers, a toe, and the left tibia and fibula. He was not taking any regular medications. Results of a general physical examination were normal. Results of an otologic examination revealed tortuous external auditory canals bilaterally but normal tympanic membranes. High-resolution computed tomography of the temporal bones was performed (Figures 1 and 2).

Diagnosis

Osteogenesis imperfecta (OI), type I.

Findings

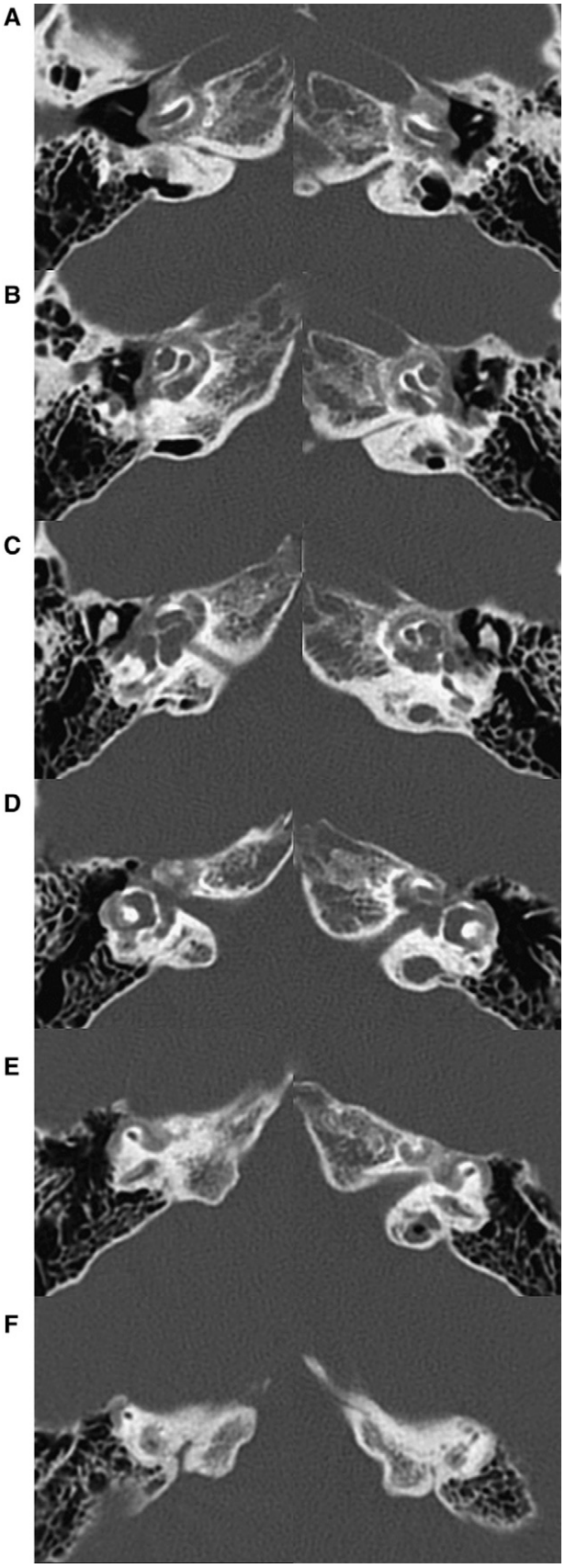
High-resolution computed tomography of the temporal bones (Figures 1 and 2) demonstrated extensive lucency of the bony otic capsule around the cochlea, vestibule, and semicircular canals bilaterally. There was no ossification of the membranous labyrinth. The middle ears and ossicles appeared normal, in particular, the stapes did not demonstrate any footplate thickening. The external auditory canals, mastoids, internal auditory canals, and vestibular aqueducts were unremarkable.

Discussion

OI is a genetic disease that affects collagen type I (COL1), which leads to a range of manifestations dependent on the mutation. The classic syndrome is progressive hearing loss, blue sclera, and bone fragility. COL1 is composed of 2 alpha-1 chains and 1 alpha-2 chain, in which each third residue is a glycine amino acid, and elucidates the formation of the triple helical structure [1]. OI results from mutations in the COL1A1 or COL1A2 genes responsible for encoding the alpha chains. Dependent on the mutation, different phenotypes result and create subtypes I-IV [2–4]. Recently, additional mutations were discovered in proteins associated with the structural formation of COL1, which led to identification of subtypes V-VII [5]. OI type I is most common and is the least-severe subtype [5,6]. It results from a frame shift mutation, premature stop codon, or splice site mutation in COL1A1 or COL1A2, which leads to decreased production of normal COL1 [3]. OI type I is autosomal dominant and results in blue sclera, increased risk of bone fractures, and progressive hearing loss in the second or third decade of life. There may be dentinogenesis imperfecta. Patients are of normal height, with no bone deformities [5]. OI type II is the most severe form and usually leads to perinatal death. It results from mutations in the glycine residue of the alpha chains, greatly disrupting the structural stability of COL1. It is autosomal recessive and presents with multiple bone fractures and deformities at birth, particularly

Key Words: Osteogenesis imperfecta; Temporal bone; Hearing loss.
* Address for correspondence: Sean P. Symons, MPH, MD, FRCPC, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, AG31D, Toronto, Ontario M4N 3M5, Canada.
E-mail address: sean.symons@sunnybrook.ca (S. P. Symons).

0846-5371/$ - see front matter
doi:10.1016/j.carj.2010.04.002



rib fractures that can have respiratory effects. Babies may or may not present with blue sclera [5,6]. OI type III is the most-severe subtype in those babies who survive the neonatal period. It also is caused by a glycine residue mutation, which leads to severe bone deformities, short stature, high bone fragility, and possibly blue sclera, although this fades with age. These patients are often wheelchair bound and may have respiratory difficulties [6]. OI type IV is of intermediate severity and usually represents the cohort of patients that do not fit into subtypes I-III [6]. OI type V is autosomal dominant, seen in 4%–5% of patients with OI. It shows no dentinogenesis imperfecta or blue sclera but is characterized by bone fragility and hypertrophic callous formation [5–7]. Type VI also shows no blue sclera or dentinogenesis imperfecta but presents with bone fragility and deformity. It is autosomal recessive, with negative screening results in assays for COL1 mutations and does not respond to bisphosphonate therapy [5,6]. Type VII is only observed in an Aboriginal community in northern Québec and presents with coxa vara and rhizomelia [5,6,8]. It is associated with a mutation that leads to a change in expression of cartilage-associated protein. In all subtypes of OI, DNA and fibroblast screening can confirm a diagnosis, but a negative result does not rule out the possibility of OI [5]. In our case, type I was confirmed by genetic testing that demonstrated a COL1A1 mutation, a single nucleotide substitution that resulted in a premature chain termination codon. There was no family history of OI, so the patient's mutation was likely sporadic, although type I can have variable penetrance. The patient presented with blue sclera, progressive hearing loss, and a history of bone fractures but did not show any bone deformities, short stature, or respiratory difficulties.

Bone fragility results from decreased bone mass and deficient bone tissue. Demineralization of the temporal bone can lead to hearing loss [9–11]. Differential diagnosis of this appearance of the temporal bones includes otosyphilis, otosclerosis, Paget disease, and rheumatoid arthritis [12]. Otosyphilis is only seen in advanced cases, and it manifests as labyrinthitis, internal auditory canal gummatous lesions, or inflammatory resorptive osteitis [13]. Paget disease is unlikely in our patient, because this condition is expected at an older age, and symptoms would be expected to manifest in the axial skeleton before presentation of hearing loss. Otosclerosis is the condition that most closely resembles OI on computed tomography, but the extensiveness of demineralization makes it less likely in this case [14]. The otic capsule lucency in otosclerosis is usually only around the cochlea and at the cochlear promontory (fissula ante fenestram), with relative sparing of the semicircular canals [14]. Rheumatoid arthritis can occasionally show temporal bone erosions.

Figure 1. Axial computed tomography images of the temporal bones at the level of the cochlea (A–C), lateral semicircular canals and vestibule (D), posterior semicircular canals (E), and superior semicircular canal (F). There is extensive bony lucency in the otic capsule that surrounds the cochlea, vestibule, and semicircular canals.

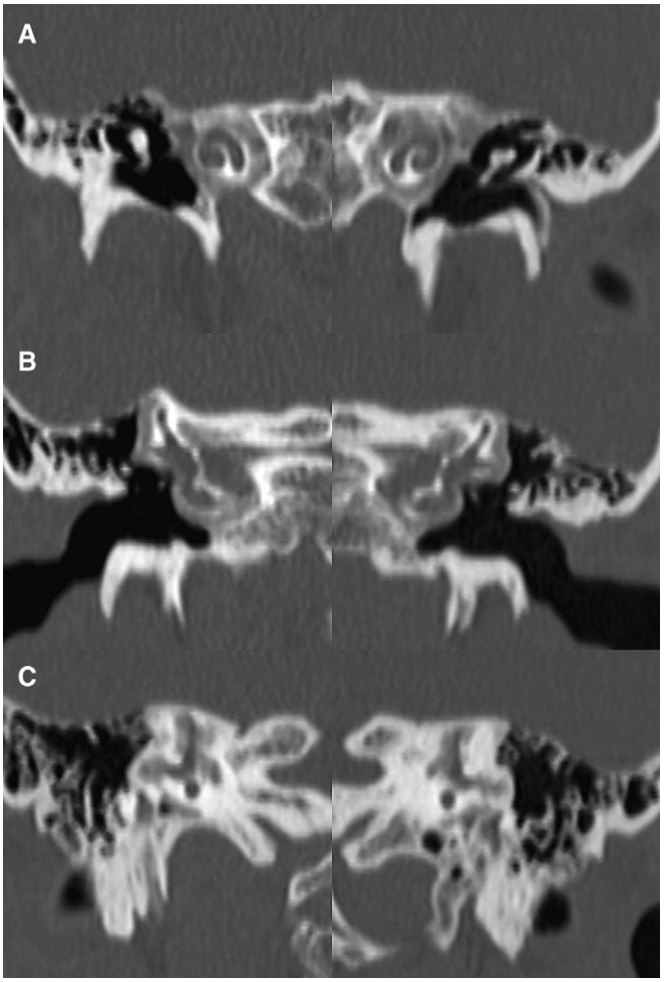


Figure 2. Coronal computed tomography re-formations of the temporal bones at the level of the cochlea (A), vestibule and oval window (B), and semicircular canals (C). There is extensive bony lucency in the otic capsule that surrounds the cochlea, vestibule, and semicircular canals.

Current treatment options do not offer a cure but can provide some symptom relief and potentially improve mobility and outcome. For mobility problems, rehabilitation, physiotherapy, and orthopaedic surgery are important treatments. Bisphosphonates, specifically pamidronate, have been used with success. These act as antiresorptive agents, disrupting the mevalonate pathway in cholesterol biosynthesis in osteoclasts, thus inhibiting their function [5]. There have been reports of improved lower back pain, increased performance on muscle-strength grip tests, and improved metacarpal and iliac bone cortical thickness. Adverse effects include flu-like symptoms after the first dosage, unexplained weight gain, and interference with bone remodelling after surgery. Other pharmacologic agents that have been investigated include growth hormone and parathyroid hormone. Growth hormone actually increases bone turnover, which is already accelerated in OI. This is not desirable as a therapy by itself but may be useful in combination with bisphosphonate therapy [5,6]. Parathyroid hormone has been shown to cause osteosarcoma in young patients and thus has not been used as a viable treatment option, especially in young children [5,6]. Bone marrow stromal cells have been transplanted into patients with OI, but, unfortunately, the clinical benefits were minimal. Current research is focusing on gene therapy ideally to turn off the mutant allele and find a way to express the desired wild type allele [5,6].

References

[1] Kadler KE, Holmes DF, Trotter JA, et al. Collagen fibril formation. Biochem J 1996;316:1–11.
[2] Byers PH. Osteogenesis imperfecta: perspectives and opportunities. Curr Opin Pediatr 2000;12:603–9.
[3] Willing MC, Deschenes SP, Slayton RL, et al. Premature chain termination is a unifying mechanism for COL1A1 null alleles in osteogenesis imperfecta type I cell strains. Am J Hum Genet 1995;59:799–809.
[4] Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. J Med Genet 1979;16:101–6.
[5] Rauch F, Glorieux FH. Osteogenesis imperfecta. Lancet 2004;363:1377–85.
[6] Cheung MS, Glorieux FH. Osteogenesis imperfecta: update on presentation and management. Rev Endocr Metab Disord 2008;9:153–60.
[7] Glorieux FH, Rauch F, Plotkin H, et al. Type V osteogenesis imperfecta: a new form of brittle bone disease. J Bone Miner Res 2000;15:1650–8.
[8] Ward LM, Rauch F, Travers R, et al. Osteogenesis imperfecta type VII: an autosomal recessive form of brittle bone disease. Bone 2002;31:12–8.
[9] Alkadhi H, Rissmann D, Kollias SS. Ostegenesis imperfecta of the temporal bone: CT and MR imaging in Van der Hoeve-de Kleyn syndrome. Am J Neuroradiol 2004;25:1106–9.
[10] Ross UH, Laszig R, Bornemann H, et al. Osteogenesis imperfecta: clinical symptoms and update findings in computed tomography and tympano-cochlear scintography. Acta Otolaryngol 1993;113:620–4.
[11] Tabor EK, Curtin HD, Hirsch BE, et al. Osteogenesis imperfecta tarda: appearance of the temporal bones at CT. Radiology 1990;175:181–3.
[12] d'Archambeau O, Parizel PM, Koekelkoren E, et al. CT diagnosis and differential diagnosis of otodystrophic lesions of the temporal bone. Eur J Radiol 1990;11:22–30.
[13] Fayad JN, Linthicum Jr FH. Temporal bone histopathology case of the month: otosyphilis. Am J Otol 1999;20:259–60.
[14] Lee TC, Aviv RI, Chen JM, et al. CT grading of otosclerosis. Am J Neuroradiol 2009;30:1435–9.