

A Rare Case Report On Van Der Hoeve Syndrome

Utkarsh Rai¹, Leena Paul², Gariyashee Lahkar³, Arup Deuri⁴

^{1, 3, 4}Department of Ophthalmology, Assam Medical College, Dibrugarh; Assam, India

²Department of Ophthalmology, Assam Medical College, Dibrugarh; Assam, India (Corresponding author)

Abstract: A 15-year-old boy presented with diminution of vision and bluish discoloration of the sclera B/E for 1 month associated with progressive hearing loss for 6 months. There was history of frequent fractures in the past. Examination showed markedly blue sclera while examination of cornea, iris, lens, angle of anterior chamber, vitreous and retina were WNL. Vision was 6/18 OD, 6/12 OS and 6/6, N6 both eyes after correction. PTA detected moderately severe mixed hearing loss in left ear and CT Scan showed decreased mineralisation in left cochlea and vestibule. His BMD was diminished. The patient was managed conservatively with topical artificial tear substitute, NSAIDs along with oral bisphosphonates and Calcium supplements. Refractive glasses were prescribed. Primary Fenestration Stapedectomy L/E was done; the post-operative period was uneventful. During follow up, patient showed normal IOP, improved hearing levels and enhanced BMD.

Keywords: Blue sclera, hearing loss, mixed deafness, otosclerosis, multiple fractures, collagen disorder, connective tissue, osteogenesis imperfecta, audiogram, bisphosphonates

1. Introduction

Van der Hoeve-de Kleyn Syndrome comprises of a triad of blue sclera, otosclerosis and osteogenesis imperfecta which was first described by Van der Hoeve and de Kleyn in 1917. It is also known as Adair-Dighton Syndrome, Eddow's Syndrome, Ekman-Lobstein Syndrome or Brittle Bone Syndrome. Osteogenesis imperfecta (OI) is a rare connective tissue disorder of autosomal dominant inheritance that is caused by an error in collagen type I formation. Mutations in chromosome 17 or 7 result in a decreased synthesis of structurally normal type I collagen and/or synthesis of structurally abnormal type I collagen. The course is progressive, though patients may live up till an advanced age. Blue sclera occurs due to the blue hue of underlying choroidal vessels visible through the thin abnormal collagen tissue of sclera and is usually non-curable and persists through life. The objective of management is to treat hearing loss due to osteogenesis imperfecta of temporal bone and maintain bone mineral density of patients.¹

2. Case Report

A 15-year-old boy presented in the Out Patient Department of Assam Medical College and Hospital with diminution of vision in B/E and bluish discoloration of the sclera since 1 month as depicted in Figure 1. He had a visual acuity of 6/18, N6 in the right eye and 6/12, N6 in the left eye. Ocular examination showed markedly blue sclera on the right side and bluish discoloration of sclera on the left. Cornea was clear, transparent, normal in diameter and thickness while other external ocular findings in the anterior segment were within normal limits. The intra ocular pressure was recorded to be 12 mmHg in the right eye and 14 mmHg in the left eye. Gonioscopy showed open angles on both sides and funduscopy revealed normal fundus picture.

The patient also had gradually progressive hearing loss for last 6 months. Pure Tone Audiometry revealed moderately severe mixed hearing loss in left ear with air conduction hearing level of 63.6 dBHL, A-B gap of 20 dB and normal hearing sensitivity in right ear (18.3 dBHL). No stapedial

muscle reflex was seen. Rest of otoscopic examination was unremarkable.

Orthopedic evaluation showed no gait abnormality, no restriction of ambulation, no chest/spinal cord deformity. Hyper-extensibility of joints was noted. X-Ray both wrists didn't reveal non-union/malunion but wormian-like bones and features of osteoporosis were seen.

3. Investigations

The patient was subjected to a battery of investigations, as follows:

Routine Blood investigations was WNL

Ultrasound B scan of both eyes showed no abnormality (Figure 2).

S/ Calcium and Vitamin D levels (ELISA) – reduced.

Bone Mineral Densitometry - Diminished BMD (Z-Score - 2.1 SD)

Pure Tone Audiometry revealed moderately severe mixed hearing loss in left ear with air conduction hearing level of 63.6 dBHL, A-B gap of 20 dB (Figure 3); normal hearing sensitivity in right ear (18.3 dBHL).

CT scans of temporal bones through the level of the labyrinthine segment of the facial nerve (axial) and the cochlea (coronal) processed with a bone algorithm (2-mm section thickness; 512 × 512 matrix). The facial nerve canal showed mild irregularities along the labyrinthine segment; otherwise normal. Band-like progression of demineralization seen in pericochlear area & vestibule, with patchy fenestral involvement. (Figure 4).

Final Diagnosis: Blue sclera + Otosclerosis grade 2 + Osteogenesis imperfecta tarda.

Management

A multidisciplinary team approach was mandated including the Department of Ophthalmology, Otorhinolaryngology and Department of Orthopaedics to provide treatment. The patient was managed conservatively with topical artificial tear substitute, NSAIDS from the Department of Ophthalmology. Refractive error was corrected with BCVA 6/6, N6 in both eyes. He was started on age and height matched dose of oral bisphosphonates along with Calcium and Vitamin D supplements. Primary Fenestration Stapedectomy was done in the left ear, the post-operative period was uneventful.

Follow – Up

Vision corrected to 6/6, N₆ with the help of corrective glasses. The patient was regularly followed up with monitoring of IOP. He was showing average improvement in hearing levels up to 31.7 Db. Air-Bone gap was 10 Db in the post-operative period. 1-year follow-up BMD improved to normalcy with supplements (Z-score within 2 SD).

4. Discussion

Early evolution of the nomenclature of this syndrome is under Ekman-Lobstein Syndrome. In 1900, Alfred Eddowes addressed the cause of scleral blueness to be defect of mesenchyme. In 1912, Charles Adair-Dighton discovered the dominant mode of transmission of blue sclerae and the association with early adult-onset deafness. The triad of blue sclerae, fragile bone, and progressive hearing impairment was first described by Van der Hoeve and de Kleyn in 1917 and was thus named Van der Hoeve-de Kleyn syndrome.

Osteogenesis imperfecta (OI) is a rare genetic disorder of connective tissue that is caused by an error in collagen type I formation⁽²⁻⁵⁾. Mutations on chromosome 17 or chromosome 7 result in a decreased synthesis of structurally normal type I collagen, the synthesis of structurally abnormal type I collagen, or both⁽²⁻⁵⁾. The disease is characterized by abnormal bone fragility, osteopenia, blue color of the sclerae, defective dentition, presenile hearing loss, and ligamentous laxity.⁶ The triad of fragile bone, blue sclerae, and progressive hearing impairment was first described by van der Hoeve and de Kleyn in 1917 and was thus named Van der Hoeve-de Kleyn syndrome.

The density of scleral blueness appears to decrease with age. The course is progressive, though patients may live until an advanced age, hence management is aimed at

improving the quality of life of the patient with a combination of multidisciplinary medical and surgical modalities.

5. Declarations

Funding: Nil

Conflict of interest: There are no conflicts of Interest

Ethical approval: The case study was conducted as per the guidelines of the Declaration of Helsinki and the institutional ethics committee.

6. Consent

Written informed consent was obtained from the patient parents for publication and/or presentation of his medical data, including this case report and any accompanying images.

References

- [1] Alkadhi H, Rissmann D, Kollias SS. Osteogenesis imperfecta of the temporal bone: CT and MR imaging in Van der Hoeve-de Kleyn syndrome. *American journal of neuroradiology*. 2004 Jun 1;25(6):1106-
- [2] Van der Hoeve J, de Kleyn A. Blaue Scleren, Knochenbrüchigkeit und Schwerhörigkeit. *Arch Ophthalmol* 1918;95:81–93
- [3] Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. *J Med Genet* 1979;16:101–116
- [4] Ablin DS. Osteogenesis imperfecta: a review. *Can Assoc Radiol J* 1998;49:110–123
- [5] Ross UH, Laszig R, Bornemann H, Ulrich C. Osteogenesis imperfecta: clinical symptoms and update findings in computed tomography and tympano-cochlear scintigraphy. *Acta Otolaryngol (Stockh)* 1993;113:620–624
- [6] Shea JJ, Postma DS. Findings and long-term surgical results in the hearing loss of osteogenesis imperfecta. *Arch Otolaryngol* 1982;108:467–470
- [7] Huygen PLM, Cremers CWRJ, Verhagen WIM, Joosten FBM. Camurati-Engelmann disease presenting as “juvenile otosclerosis.” *Int J Pediatr Otorhinolaryngol* 1996;37:129–141



Figure 1: Patient at presentation

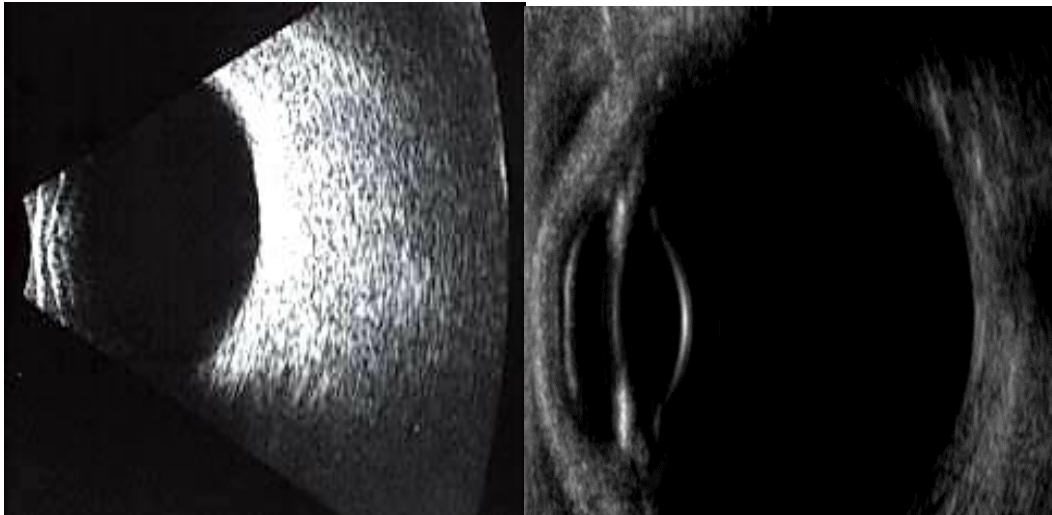


Figure 2: USG B Scan B/E

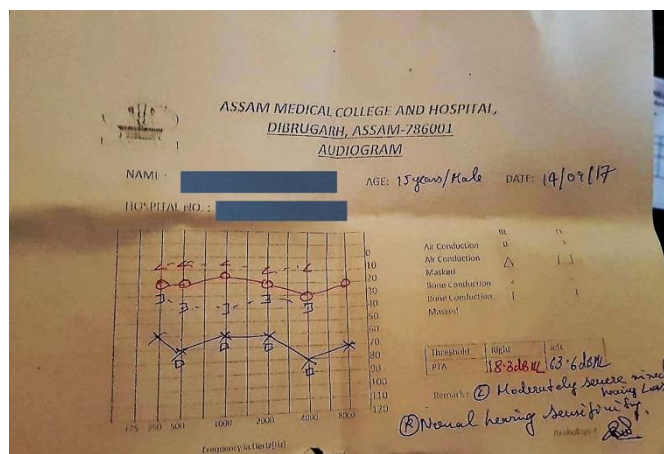


Figure 3: Audiogram

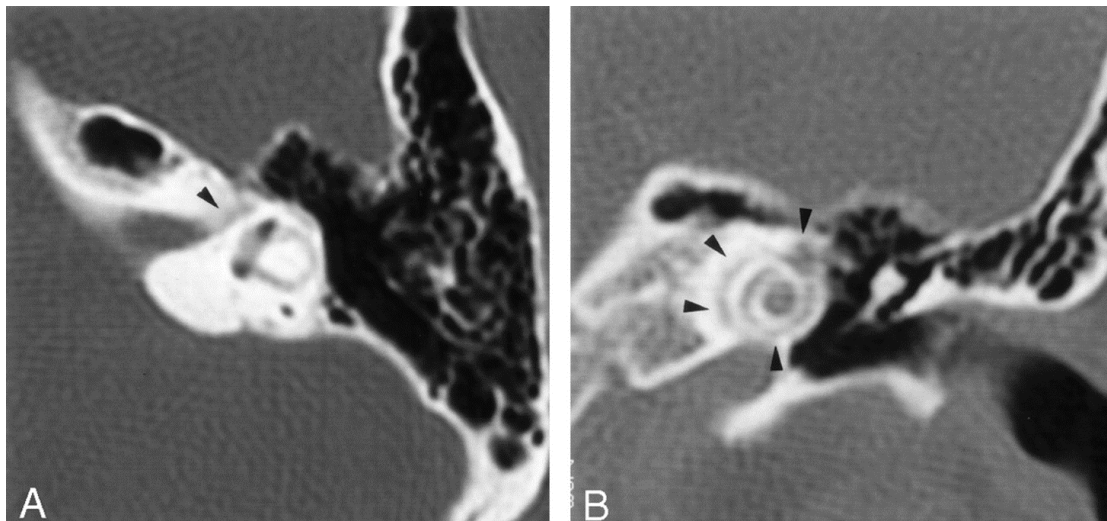


Figure 4: CT Scan Left temporal bone