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A Girl with Blue Eyes – A Case Report

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Abstract: A 20 years old girl with blue sclerae and history of multiple fractures in childhood with normal dentition and hearing, having a family history of repeated fractures with trivial trauma was clinically diagnosed as Osteogenesis imperfecta type I. She was treated with bisphosphonates and calcium.
Keywords: blue sclerae, multiple fractures

INTRODUCTION

Osteogenesis imperfecta is a heritable systemic disorder of connective tissue with many phenotypic presentations, manifesting as bone fragility and blue sclerae. It is often called "brittle bone disease."In 1835, Lobstein coined the term “Osteogenesis imperfecta”. In approximately 90% of individuals with osteogenesis imperfecta, mutations in either of the genes encoding the pro-_1 or pro-_2 chains of type I collagen (*COL1A1* or *COL1A2*) can be identified. Here we describe a case of osteogenesis imperfecta type 1 [1].

CASE REPORT

A 20 years old girl with blue eyes walked into our OPD with a history of multiple fractures with trivial trauma in the past, including a green stick fracture of tibia at 5 years and bilateral talus fractures at 12 and 14 years respectively with similar proneness to fractures seen in some first and second degree family members.

The analysis of family pedigree showed one case of OI. This genetic disease was present also in the grandmother of this patient as she had three fractures of the bones in her life after minor trauma, favouring autosomal dominant transmission.

On general examination she was 154 cms tall weighing 48kgs. The patient displayed normal development, and was well-proportioned with a normal gait and erects posture. She had blue sclerae (Figure 1).

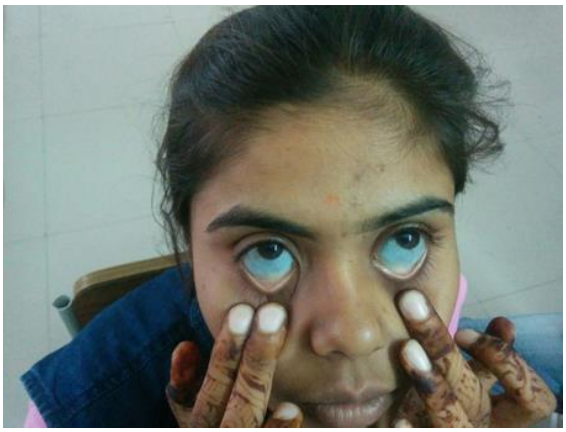

Fig-1: She had blue sclerae

Fig-2: She had normal dentition

There was no evidence of beading of the ribs, skeletal deformities, joint hyper mobility, hearing impairment, cardiac murmurs or respiratory difficulty and the neurological examination was unremarkable.

Investigations showed normal pure tone audiometry. X ray feet revealed healed fracture line over both talus (Figure 3).

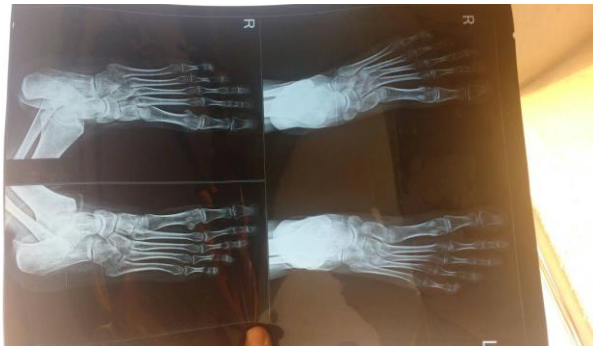

Fig-3: X ray feet revealed healed fracture line over both talus

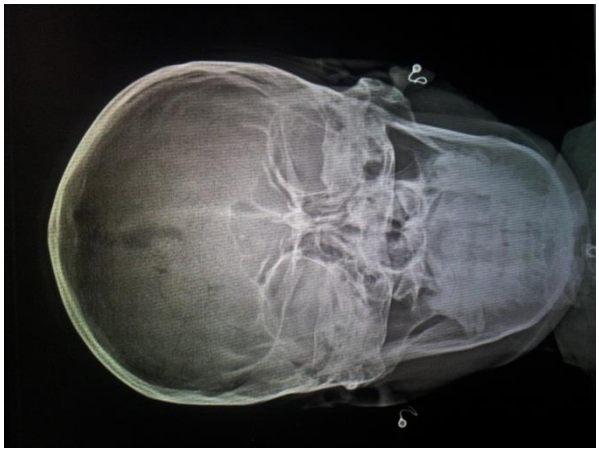

Fig-4: X ray skull did not show wormian bones normal ECG, normal serum calcium.

In our case the patient has a few fractures with minimal trauma in childhood with blue sclera since birth, with no hearing loss or dentinogenesis Imperfecta (DI) or cardiac rhythm abnormality. She thus is diagnosed as osteogenesis imperfecta type 1.

DISCUSSION

OI is an orphan disease with estimated incidence being approximately 1 per 20,000 births. The clinicopathogenetic classification of OI classifies it into 15 subgroups namely type I to XV (Table 1) [2]. As per the International Society of Skeletal Dysplasias, it has been grouped as per severity into 5 types (Table 2) [1]. Mutaions in the genes *COL1A1* or *COL1A2* encoding the alpha-1 and alpha-2 chains of type I collagen cause OI, resulting from two molecular mechanisms, namely, chain exclusion and chain nonexclusion[2]. In type I OI, due to chain exclusion, there is no incorporation of the mutant chain into the collagen triple helix, as the abnormal collagen microfibril is unable to be incorporated into the triple helix and is thus degraded leaving the remaining allele to produce less structurally intact collagen triple helix, thereby causing milder disease. Chain nonexclusion leads to moderate to severe disease [2].

OI type I is characterized by bone fragility and blue sclerae. First fractures occur in infancy and with a decrease in frequency post puberty. These fractures heal normally with occasional deformities. Joint hypermobility may be present. These patients usually have normal stature. Individuals with OI type I have distinctly blue sclerae which remain intensely blue throughout the life. In OI type IIIand IV the sclerae may also be blue at birth and during infancy, but the intensity fades with time as the child grows, such that these individuals have normal hued sclerae by adolescence and adult life[3]. DI is uncommon but patients may have opalascent teeth and premature wearing down. Conductive deafness is seen in about 50% of the patients [2].

Lanting *et al*. described the biophysical mechanism of blueness of sclera. It is due to the differential path scattering of light of different wavelengths by the molecular grating of the sclera. The shorter wavelengths colours yellow, orange and red are effectively backscattered more than the longer wavelengths colours like blue [4]. Decreased scattering coefficient and decreased thickness of sclera secondary to decreased thickness of collagen fibrils, decreased packing of collagen fibrils, and increased amount of water between collagen fibrils form the pathlogical basis of blue sclerae [3].

Clinically OI is diagnosed on the basis of clinical featutres, the etiological diagnosis requires collagen analysis and genetic studies. Skin biopsy combined with DNA sequencing has high yield. In some cases bone biopsy is helpful. Perinatal screening in patients with positive family history with the help of transvaginal and transabdominal ultrasound with chorionic biopsy with DNA sequencing is done. Genetic studies using multiplex ligation depdendent probe amplification (MLPA) is considered superior than the collagen electrophoresis or gene sequence test [1].

Biochemical markers like serum calcium, serum vitamin D levels and bone turnover markers like alkaline phosphate, osteocalcin are usually normal.

Current treatment status

The mainstays for therapy are physiotherapy, orthopaedic surgery & rehabilitation. Medical management comprises of bisphosphonates. They are potent antiresorptive drugs acting by inactivating osteoclasts and thereby an increase in bone mineral density. They have no effect upon collagen. Hence, biphosphonates are an adjunctive therapy. They are pamidronate, zolendronate, neridronate, olpadronate [1,2,5,6]. Teriparatide an anabolic agent, Denosumab, a monoclonal nuclear kappa B ligand activator are the newer drugs being used. Bone marrow transplantation, gene therapy to prevent mutant allele's expression and stem cell transplantation are being tried [1].

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