ORIGINAL RESEARCH PAPER

Paediatrics

KEY WORDS:

A CASE REPORT OF OSTEOGENESIS IMPERFECTA

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INTRODUCTION

Osteogenesis imperfect also known as brittle bone disease, is a group of genetic disorder that result in bones that break easily. Osteogenesis imperfecta affects bones as well as other organs. Symptoms seen in different types of Osteogenesis Imperfecta include bluish discolouration of the eye (sclerae), short stature, loose joints, hearing loss, breathing problems and problems with the dentition. In severe cases it may affect major arteries e.g. Aorta (aortic dissection), may cause basilar invagination, or failure of heart valves leading to life threatening complications. The mechanism of Osteogenesis Imperfecta is absence or defective collagen type-1 synthesis due to mutation in COL1A1 / COL1A2 genes. The mutation may occur spontaneously (de novo) but mostly it is autosomal dominant (hereditary). Diagnosis is based on symptoms and confirmed by collagen biopsy or DNA analysis. Although there is no cure, most cases of Osteogenesis Imperfecta do not have a major effect on life expectancy, maintaining a healthy lifestyle by exercising, eating a balanced diet sufficient in vitamin D and calcium can help prevent fractures. Treatment includes acute care of broken bones, pain medication, physical therapy, vitamin D supplementation and especially in childhood, rodding surgery. Rodding is an implantation of metal intramedullary rods along the long bones (such as the femur). Bisphosphonates e.g. Pamidronate can be used to increase bone density (specially in children). Role of Romosozumab , a monoclonal antibody is unclear and is under research.

ETIOLOGY

Osteogenesis imperfecta is a rare genetic disease. In the majority of cases, it occurs secondary to mutations in the *COL1A1* and *COL1A2* genes. More recently, diverse mutations related to OI have been identified.

The following is the OI classification according to the International Society of Skeletal Dysplasia's based on the mode of inheritance and genes involved.

Osteogenesis Imperfecta / Type / Inheritance / Genes

- Nondeforming OI (Type I) / AD / *COL1A1, COL1A2* / X-linked / *PLS3*
- Perinatal (type II) / AD, AR / *COL1A1, COL1A2, CRTAP, LEPRE1, PPIB, BMP1*
- Progressively deforming (type III) / AD, AR / *COL1A1, COL1A2, CRTAP, LEPRE1, PPIB, FKBP10, SERPINH1, SERINF1, WNT1*
- Moderate (type IV) / AD, AR / *COL1A1, COL1A2, CRTAP, FKBP10, SP7, SERPINF1, WNT1, TMEM38B*
- Calcification of interosseous membrane or hypertrophic callus (type V) / AD / *IFITM5*

CASE PRESENTATION

A 1-year-old female child came with complaints of excessive cry and not moving her right lower limb for 1 day. Mother said that baby was apparently well 1 day back before she fell down in the lap of mother when mother was playing with baby. Mother also complains of similar history 1 month back. On examination eyes of the child was bluish, x-ray of right thigh shows fracture in femur. On suspicion of brittle bone disease, genetic study was done, which was positive for COL1A1 gene mutation (Autosomal dominant). Paediatric orthopaedics' opinion was taken and disease was explained to the parents. Regular follow was advised to parents and possibly future complications were described to them.


RESULTS

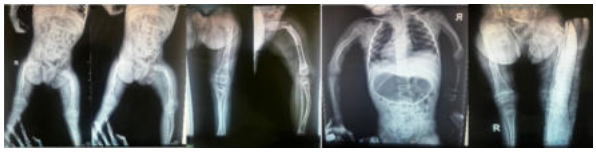
LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

SNV(s)/INDELS

Gene# (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification$
COL1A1 (-) (ENST00000225964.10)	Exon 36	c.2461G>A (p.Gly821Ser)	Heterozygous	Osteogenesis imperfecta type III (OMIM#259420); Osteogenesis imperfecta type IV (OMIM#166220)	Autosomal dominant	Likely Pathogenic (PS4, PP3, PP5)

Parental testing is recommended, and classification of the variant(s) may change based on segregation analysis.

On genetic analysis COL1A1 gene mutation was detected



X-rays showing multiple fractures of upper and lower limbs.

TREATMENT

There is no cure for osteogenesis imperfecta.Maintaining a healthy lifestyle by exercising and avoiding smoking can help prevent fractures. Treatment may include care of broken bones, pain medication, physical therapy, mobility aids such as braces or wheelchairs, and surgery.

- *Acute bone fracture care- e.g. using cast , hip spica, orthosis*
- *Medications- BISPHOSPHONATES e.g. pamidronate, alendronate, zolendronate.*
- *Nutritional Supplements*
- *Surgery- Rodding surgery*

CONCLUSION

A child presenting with complaints of repeated episodes of limb pain following trivial trauma, leading to fracture of long bones, Osteogenesis imperfecta is to be considered as an important differential diagnosis.

Osteogenesis Imperfecta is a genetic bone disorder charecterised byfragile bomnes that breaks easily.it is also known as brittle bone disease. Osteogenesis imperfecta literally means bones that is made imperfectly madefrom the beginning of life.