Case Report

Osteogenesis imperfecta type 111

Rugmini Kamalammal*, Venkatamurthy M, Aditya Kumar Bandari

Department of Pediatrics, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Nagamangala Taluq, Mandya District, Karnataka, India

Received: 20 October 2015

Accepted: 05 December 2015

***Correspondence:**

Dr. Rugmini Kamalammal,

E-mail: ruginirao@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Osteogenesis Imperfecta is a rare inherited disorder affecting connective tissue integrity, characterized by bone fragility of varying severity ranging from lethal forms to those with very minimal features. Here, we are presenting a case of 3 months old infant with multiple fractures sustained during routine handling. Baby was diagnosed as OI type III, which is the most severe non-lethal form of the disease. Early diagnosis and institution of new modalities of treatments like bisphosphonates and surgical stabilization gives better prognosis in these patients.

Keywords: Osteogenesis imperfecta type III, Recurrent fractures, Bisphosphonates

INTRODUCTION

OI is one of the most prevalent skeletal dysplasias and that it occurs in approximately 1 in every 20,000 births.¹ They are mainly inherited as autosomal dominant but recessive inheritance is also seen. Molecular defects in type I collagen genes, COL1A1 and COL1A2, were seen in 90% of cases.² 10-15% of all OI are linked to defects other than these two regions like CRTAP, LEPRE1, FKBP10, and SERPINF1.³ Mutations in the $\alpha 1(I)$ or $\alpha 2(I)$ chain, especially glycine (Gly) to cysteine or tryptophan substitutions in the Triple helix is usually seen.⁴

Apart from the striking osteoporosis and recurrent fractures, other features of the disease includes easily fractured bones, hypermobile joints, blue or gray sclera, skeletal deformities, and fragile skin.⁵

Dentinogenesis imperfecta leads to enamel breakage due to abnormal collagen in the dental pulp. The lower teeth are more severely affected than the upper teeth.⁶ Severe forms of the disease may have platelet dysfunction,

cardiac and respiratory difficulties due to rib cage deformities.⁵ A prevalence rate of hearing loss of 46% has been reported.⁷

Osteogenesis imperfecta was classified into four types based on clinical, radiological and genetic features.⁸ Novel types V, VI and VII in which type I collagen genes were not involved were later added. The sillece classification is the universally accepted to classify the degree of OI.⁹

CASE REPORT

4 months old female baby, born of a non-consanguineous marriage to a 30 year old mother was brought to us with complaints of inconsolable cry on touching the lower limbs and bowing of the extremities.

Baby was born at term by Caesarean section with indication as breech presentation with oligohydramnios. Birth weight was 2.5kg, at birth skeletal survey was done as the baby had short limb dwarfism. It showed B/L short humerus and B/L short and bowed femur and a fracture

clavicle on the right side. Antenatal period was uneventful with no history of any infections, radiation or drug intake. Two antenatal ultrasounds done failed to pick up the deformities.

On presentation at our institution baby had tenderness on touching both the lower limbs. There was no evidence of any inflammation. Baby's weight, length, head circumference, chest circumference were 3.3 kg, 50cm, 39cm, 35cm respectively. Upper segment (31 cm): lower segment (19 cm) ratio was 1.6. Arm (8 cm) was short compared to forearm (9 cm) bilaterally. There was rhizomelic dwarfism with thigh length of 9 cm and leg length of 12 cm with relative macrocephaly. There was bilateral bowing of lower limbs with varus deformity and proximally displaced first metacarpophalangeal joint with flexion deformity of the thumb. There was marked scoliosis with convexity towards left.

Figure 1: Baby showing features of OI type 111.

Baby had triangular facies, soft skull with sutural diastasis wide open anterior, posterior, mastoid fontanelles, frontal bossing, dilated veins over forehead, low set ears and high arched palate. Bilaterally eyes were small and sclera was blue. Two skin bands were present over right lower limb just above the ankle. There were no soft tissue injuries. Systemic examination was normal. Complete blood count, Serum electrolytes, urea, creatinine, serum calcium, phosphate and alkaline phosphatase were within normal limits. There was no similar history in the family.

Figure 2: Blue Sclera.

Figure 3: X ray taken on Day 1 of life showing multiple fractures and curved spine.

A clinical diagnosis of Osteogenesis imperfecta was made.

Skeletal survey showed diffuse osteopenia with cortical thinning and marrow expansion of all visualized bones.

Shortening and broadening of B/L humerus with pathological fractures at various stages of healing in the region of middle 1/3rd of diaphysis. B/L Radius and ulna has general features as mentioned above with bowing deformity and flexion of first metacarpophalangeal joint.

Shortening and broadening of B/L femur with pathological fractures at various stages of healing. B/L tibia and fibula has general features as mentioned above with bowing deformity. Scoliosis with convexity towards left, no vertebral changes was seen.

DISCUSSION

Our patient had features suggestive of Type III OI, like short stature, shortening of the long bones, significant bowing, and multiple prenatal and postnatal fractures, typical triangular facies, grey blue sclera and dilated veins over forehead suggestive of skin laxity. Striking feature was the scoliosis which is typical of Type 111. This baby continued to have fractures even with gentle handling.

Even though, these cases are frequently diagnosed on prenatal ultrasound due to the intranatal fractures and scoliosis. In our case it was not evident antenatally. Skeletal survey on day 1 showed bending of tibia and clavicular fracture. All other fractures were sustained later in life. There was no classic "popcorn epiphyses" of long bones which may develop later.¹⁰ The fractures were reduced and limbs were immobilized.

Intravenous pamidronate (Bisphosphonate) given cyclically is advised in this baby as there were recurrent fractures.

Bisphosphonates increases cortical thickness. They improve comfort and function but they do not remodel pre-existing bony deformity. It improves vertebral height and development in children with compressed vertebral bodies. These effects are found to be maximum in the first 2-4 years of therapy. Zoledronic acid is a more potent bisphosphonate, which requires only one intravenous treatment per year. Lifestyle modifications, such as use of orthotics and physiotherapy, should be considered.¹¹

Splinting of the long bones with the use of intramedullary implants in order to prevent recurrent fractures and allow correction of deformities is advised in these children at the age when they attempt to stand.¹²

Positioning of the patient, securing an airway, preventing haemorrhage due to platelet dysfunction and tackling breathing difficulties due to abnormal thoracic cage is important while doing surgery. Oakley, Reece suggested to rule out cardiac abnormalities in high risk patients prior to surgery.⁵

Stem cell therapy and gene therapy are being investigated as potential treatments. Gene-based therapy presently remains in the early stages of preclinical research.¹³

O type III can be prenatally be diagnosed with ultrasonogram as early as 18 weeks or by abnormal production of collagen type I by cultured chorion villi cells. Fetal DNA molecular analysis for genes involved in OI is confirmatory.¹³

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Marini JC. Osteogenesis imperfecta. In: Nelson WE, Behrman RE, Kliegman RM, Arvin AM, editors. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: W.B. Saunders Company; 2007:2887-90.
2. Steiner RD, Adsit J, Basel D. COL1A1/2-Related Osteogenesis Imperfecta. *Gene Reviews*. 1993-2015.2005 Jan 28 [updated 2013 Feb 14].
3. Kelley BP, Malfait F, Bonafe L, Baldrige D, Homan E, Symoens S, et al. Mutations in FKBP10 cause recessive osteogenesis imperfecta and Bruck syndrome. *J Bone Miner Res*. 2011;26(3):666-72.
4. Starman BJ, Eyre D. Osteogenesis imperfecta. The position of substitution for glycine by cysteine in the triple helical domain of the pro alpha 1(I) chains of type I collagen determines the clinical phenotype. *J Clin Invest*. 1989;84(4):1206-14.
5. Oakley I, Reece L. Anesthetic implications for the patient with osteogenesis mperfecta. *AANA Journal*. 2010;78(1):47-53.
6. Beattie ML, Kim JW, Gong SG, Murdoch-Kinch CA, Simmer JP, Hu JC. Phenotypic variation in dentinogenesis imperfecta/dentin dysplasia linked to 4q21. *J Dent Res*. 2006;85(4):329-33.
7. Pillion JP, Vernick D, Shapiro J. Hearing loss in osteogenesis imperfecta: Characteristics and treatment considerations. *Genetics Research International*. 2011;2011:1-6.
8. Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. *J Med Genet*. 1979;16:101-6.
9. Roughley PJ, Rauch F, Glorieux FH. Osteogenesis imperfecta - clinical and molecular diversity. *European Cells and Materials*. 2003;5:41-7.
10. Obafemi AA, Bulas DI, Troendle J, Marini JC. Popcorn calcification in osteogenesis imperfecta: incidence, progression, and molecular correlation. *Am J Med Genet A*. 2008;146A(21):2725-32.
11. Shaw NJ. Management of Osteoporosis in children. *European Journal of Endocrinology*. 2008;159:S33-9.
12. Nicolao N, Bowe J, Wilkinson J, Bell MJ. Use of the Sheffield Telescopic Intramedullary Rod System for the management of osteogenesis imperfecta. *Journal of Bone and Joint Surgery American*. 2011;93(21):1994-2000.
13. Van Dijk FS, Cobben JM, Kariminejad A, Maugeri A, Nikkels PG, van Rijn RR, et al. Osteogenesis Imperfecta: A Review with Clinical Examples. *Molecular syndromology*. 2011;2(1):1-20.

Cite this article as: Kamalammal R, Venkatamurthy M, Bandari AK. Osteogenesis imperfecta type 111. *Int J Contemp Pediatr* 2016;3:268-70.