Case Report

Osteogenesis imperfecta: a case report

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Abstract

Osteogenesis Imperfecta is a inherited disease of connective tissue. Its hallmark feature is bone fragility with a tendency to fracture from minimal trauma or from the work of bearing weight against gravity. The disorder may occur in one out of 20,000 to one out of 60,000 live births, affecting both male and female of all races. We present a 38 year lady who gave birth to baby with osteogenesis imperfecta in Sir Salimullah Medical College & Mitford Hospital, Dhaka. Both lower limbs appeared shortened with thick musculo-cutaneous folds. Both the femoral shafts were shortened, deformed and fragmented. Both the humeral and fibular shafts were deformed and the presentation was breech. Her sclerae was blue. X-ray showed multiple fractures in humerus, femur and ribs and also right sided pulmonary hypoplasia.

Key words: Osteogenesis Imperfecta, inherited disease, connective tissue disease

Introduction

Osteogenesis imperfecta, also known as brittle bone disease, is a inherited disease of connective tissue. Its hallmark feature is bone fragility with a tendency to fracture from minimal trauma or from the work of bearing weight against gravity. The disorder may occur in one out of 20,000 to one out of 60,000 live births, affecting both male and female of all races.[1] Due to the rarity of the disorder, the intrauterine diagnosis may be missed, resulting in misunderstanding between the obstetrician and parents of the affected babies. As the babies have disastrous outcome, early diagnosis of the cases and early termination of pregnancy are advisable. Pre-conception counseling is also very important.

Case Report

A 38 year old multiparous woman from middle class family conceived for 3rd time and remained under regular antenatal check-up throughout the pregnancy. Her previous babies were born by normal vaginal delivery. Her last menstrual period was on 17.01.2005 and the expected date of delivery was 24.10.2005. During antenatal period, her vital parameters were normal and routine investigations revealed normal values. Ultrasonogram done on 30.09.2005 showed biparital diameter 88 mm, corresponding to 35 weeks of pregnancy. Both lower limbs appeared shortened with thick musculo-cutaneous folds. Both the femoral shafts were shortened, deformed and fragmented. Both the humeral and fibular shafts were deformed and the presentation was breech. This time, the pregnancy ended up with a spontaneous vaginal delivery on 31.05.2005 at Sir Salimullah Medical College & Mitford Hospital, under supervision of a qualified obstetrician. The alive female baby weighed 2.5 kg with an APGAR score of 5 at 1 minute and needed active resuscitation. On examination, she was found to have multiple fractures in humerus and femur. Her sclerae was blue. She was shifted to paediatric ward on the same day where x-ray was done. X-ray showed multiple fractures in humerus, femur and ribs. X-ray also showed right sided pulmonary hypoplasia. She was diagnosed as a case of osteogenesis imperfecta type II and was being treated accordingly. The feeding of the baby was normal. Her 2nd baby, a female one, was also a case of osteogenesis imperfecta who died on 3rd March 2003, after struggling for 44 days. The family history revealed that a 22 years old cousin of the baby is also having the same disease and he is still alive.

Discussion

Osteogenesis imperfecta is a genetic disorder characterized by bones that break easily, often from little or no apparent cause.[2] Affected persons also exhibit an array of associated features, including short stature, macrocephaly, blue sclerae, dentinogenesis imperfecta, hearing loss and neurological and pulmonary complications. There is no preferential distribution of osteogenesis imperfecta by gender, race or ethnic group. Osteogenesis imperfecta is caused by a genetic defect that affects the body's production of collagen. One of the genes that tells the body how to make a specific protein (type I collagen) is defective in people with osteogenesis imperfecta. Type I collagen is a major component of the connective tissues in bones, ligaments, teeth and the white outer tissue of the eyeballs (sclerae). Structurally the protein is composed of a left-handed helix formed by COLIA1 on band 17q21 and COLIA2 on band 7q22.1, respectively cause osteogenesis imperfecta.[3] As a result of the defect, the body may not

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produce enough type I collagen or it may produce poor quality collagen. The result in both cases is the same, fragile bones that break easily. Most cases of osteogenesis imperfecta are caused by dominant genetic effect. If one parent has osteogenesis imperfecta, each child has 50 percent chance of being born with osteogenesis imperfecta.[4] But the child's symptoms and degree of disability could be very different from parents. In some cases, neither parent has osteogenesis imperfecta, and the genetic defect is a spontaneous mutation.

David Sillence[5] formulated the classification for osteogenesis imperfecta in 1979. The patients had been classified into four groups, depending on the severity of clinical features and radiological findings. Over the years, new manifestations were discovered and as a result, the present classification is a modified one (Table-1). Type II is the most severe form of osteogenesis imperfecta. The collagen is improperly formed. Bones may break even while the fetus is in the womb, and many infants are still-born or die shortly after birth. In addition to complete medical history and physical examination, diagnostic procedures for osteogenesis imperfecta may include a skin biopsy to evaluate the amount and structure of collagen. However, this test is complicated and not many quality laboratories are available to perform the procedure. It is not unusual for results of the biopsy to take up to six months. Additional diagnostic tests may include:

Lab Studies

Results from routine laboratory studies usually are within reference ranges.

Collagen synthesis analysis by culturing dermal fibrobalsts obtained by skin biopsy. It is useful for prenatal screening, genetic counseling, and differentiating osteogenesis imperfecta from child abuse. False-negative results are obtained in 13.6% cases.

Prenatal DNA analysis can be performed in pregnancies with risk of osteogenesis imperfeta by analyzing uncultured chorionic villus cells obtained by chorionic villus sampling that is performed under sonographic guidance. Bone mineral density analysis is still experimental.

Dual-energy x-ray absorptiometry (DEXA) or lumbar spine quantitative CT scan is used. Mean bone mineral density (BMD) is 77% of normal in the lumbar spine and 71% of normal in the femoral neck.

Imaging Studies

- Post-natal x-ray: Obtain skull, chest, long bones and pelvis x-ray films. (Figure-1)

Table- I : Classification of Osteogenesis imperfecta

OI Type	Clinical Features	Inheritance
I	Most common and mildest type, normal or near normal stature, little or no deformity, blue sclerae, hearing loss in 50% of families. Triangular face, tendency toward spinal curvature. Dentinogenesis imperfecta is rare. Collagen structure is normal, but the amount is subnormal	AD**
II	Most severe form, lethal in the perinatal period; numerous fracture, beaded ribs, compressed femurs, marked long bone deformity, short stature with underdeveloped lungs. Collagen is improperly formed.	AD (new mutations) Parental mosaicism
III	Progressively deforming bones, usually with moderate deformity at birth. Bones fracture easily. Triangular face, spinal curvature. Dentinogenesis imperfecta common, hearing loss common. Stature very short. Collagen is imperfectly formed.	AD, AR*** Parental mosaicism
IV	Mild moderate bone deformity and variable short stature; between type I and III in severity, dentinogenesis imperfecta is common and hearing loss occurs in some families. White or blue sclerae, Triangular face and barrel shaped rib case. Collagen is improperly formed.	AD Parental mosaicism

* Modified from Sillence et al, 1979

** AD = Autosomal Dominant ***AR = Autosomal Recessive

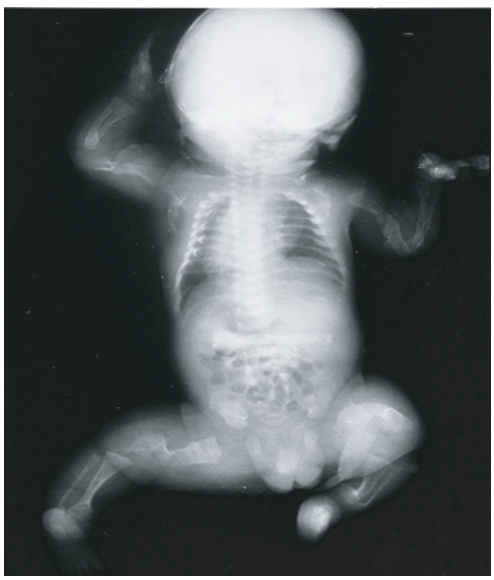

Figure-1 : Osteogenesis imperfecta

An examination of the ear, nose and throat should be done to detect hearing loss. However, the symptoms of osteogenesis imperfecta may resemble other medical conditions or problems such as camptomelic dysplasia, achondrogenesis type I, congenital hypophosphatasia, steroid induced osteoporosis, battered child syndrome (Syndrome X) and copper deficiency. So, it is always better to consult physicians of other disciplines for a diagnosis.[7]
For the first case of moderate to severe osteogenesis imperfecta in a family, prenatal diagnosis will probably occur during ultrasound at 14 to 16 weeks gestation. Detecting recurrence of osteogenesis imperfecta prenatally is easiest if the exact collagen mutation in the affected child is known. In that case, a potential mutation in the current pregnancy can be detected early and with confidence.[8]

To date, there is no known treatment option that will cure osteogenesis imperfecta. Early-termination is preferable. The goal of treatment is to prevent deformities and fractures and allow the child to function as independently as possible.[9]

Management of osteogenesis imperfecta can be either non-surgical or surgical. Non-surgical interventions may include one or more of the following

- Physical therapy
- Positioning aids (to help sit, lie or stand)
- Braces and splints (to prevent deformity and promote support or protection)
- Medications-bisphosphonates, growth hormone
- Psychological counseling
- Gene therapy

Surgical interventions may be considered to manage the following conditions

- Fractures
- Scoliosis
- Heart problem
- Bowing of bone
- Dental procedures

Research into other treatment methods is continuing. Several clinical trials are focused on the use of medications to improve bone strength and decrease fracture rates.[10] Pamidronate (a bisphosphonate) has been found to inhibit bone resorption. As a result, chronic bone pain lessens, bone density increases, fewer fractures occur and mobility improves.[11] More promising research is being done in the area of gene therapy. It may be possible to replace the damaged cells with normal cells or to suppress the mutation completely.

Osteogenesis imperfecta is a progressive condition thatneeds life-long management to prevent deformity and complications.[13] The prognosis of an individual with osteogenesis imperfecta varies greatly depending on the number and severity of symptoms. The interdisciplinary healthcare team helps the family to improve the functional outcomes and to provide support. The Osteogenesis Imperfecta Society can also be an important resource.[14]

References

1. Marini JC. Osteogenesis Imperfecta. In: Behrman editor. Nelson's Textbook of Pediatrics. Elsevier: Atlanta1; 1999. p. 2128-2130.
2. Marini JC. Heritable Collagen Disorders. In: Klippel J, Dieppe P editors. Rheumatology. 2nd edi. London: Gower; 1998.p.833-836
3. Dawson PA, marini JC. Osteogenesis Imperfecta. In: Econs MJ editor. The Genetics of Osteoporosis and Metabolic Bone Disease. New Jeresy: The Humna Press Inc; 2002. p. 75-95.
4. Kururila K. Grenman R, Johansson R, Kaitila I. Hearing loss in children osteogenesis imperfect. European journal of Pediatrics. 2000; 259(7): 515-519
5. Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfect. Journal of Medical Genetics. 1979; 16(2): 101-116
6. Ablin DS. Osteogenesis Imperfecta: a review. Can Assoc Radiol J. 1998; 49(2): 110-123
7. Chapman S. Hall CM. Non-accidental injury or brittle bones. Pediatr Radiol. 1997; 27(2): 106-110
8. Delatycki M, Rogers JG: The genetics of fibrodysplasia ossificans progressiva. Clin Orthop.1998; 346: 15-18
9. Engelbert RH, Prujus HE, Beemer FA, Helders PJ.Osteogenesis imperfect in childhood: treatment strategies. Arch phys Med Rehabil. 1998; 79(12): 1590-1594
10. Minch CM, Kruse RW: Osteogenesis imperfect: a review of basic science and diagnosis Orthopedics. 1998 ; 21(8): 842.
11. Roughley PJ, Rauch D, Glorieux FH: Osteogenesis imperfect – clinical and molecular diversity. Eur Cell mater. 2003; 5: 41-47.
12. Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. J Med Genet. 1979; 16(2): 101-116.
13. Taitz LS: Child abuse and osteogenesis imperfect. Br Med J. (Clin Res Ed) 1987; 295: 1082-1083
14. Tiley F, Albright JA. Osteogenesis imperfecta-treatment by multiple osteotomy and intramedullary rod insertion: Report on thirteen patients. J Bone Joint Surg. 1973; 55(4): 701-713.