DOI: 10.7860/IJNMR/2021/49205.2302

Case Report

Paediatrics Section

Multiple Bone Fractures in a Neonate with Osteogenesis Imperfecta: A Case Report

RAKESH KUMAR[1], PRERNA CHAMOLI[2]

ABSTRACT

Osteogenesis Imperfecta (OI) is characterised by increased bone fractures. It is clinically and genetically a heterozygous disease of connective tissues. OI type 3 is the most severe, non lethal form which is caused by the mutation of caused by mutation of procollagen type1 A1 or A2(COL1A1 or COL1A2) genes. A one-day-old male baby with respiratory distress and multiple limb deformities was presented to the paediatric emergency department. The head appeared unduly large in comparison to the body and the anterior, posterior and lateral fontanelle were wide open. Sclera did not appear blue. Both upper limbs appeared short and stubby with diffuse swelling in the left arm. Both lower limbs appeared curved and were held in a frog-like position. Infantogram showed multiple calvarial fractures in the skull, multiple rib fractures, fracture of left humerus, bilateral ulna, left femur and there were multiple areas with callus formation suggestive of intrauterine fractures. There was no history of trauma during birth. Clinical diagnosis of OI was made and the neonate was managed medically. Genetic analysis could not be done owing to financial constraints. In conclusion, a high index of suspicion and careful clinical and radiological evaluation can identify very rare hereditary abnormalities like OI.

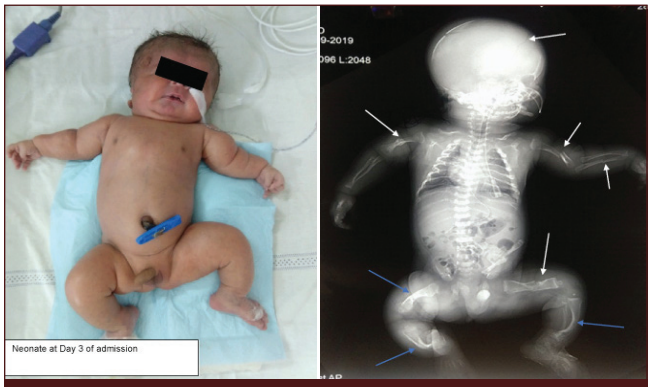
Keywords: Brittle bones, Connective tissues, Newborn

CASE REPORT

A one-day-old male neonate was referred to paediatric emergency with complaints of respiratory distress. The neonate was born to a 32-year-old P2L2 mother with no history of consanguinity. Mother had irregular antenatal visits without any iron/folic acid supplementation. Ultrasound examination was not done. There was no history of taking any teratogenic drug or exposure to radiation. There was no history of any bone disease or history of repeated fractures in the family. The baby was delivered at 37 weeks of gestation by spontaneous vaginal delivery with an Appearance Pulse Grimace (reflex) Activity Respiration (APGAR) score of 8,9,9 with a birth weight of 3000 grams. There was no history of birth trauma to the baby as described by parents.

At presentation baby was in a frog-like position and seemed in agony, colour was pink, temperature 36.8°C, respiratory rate of 72 breaths per minute with no signs of distress, heart rate of 136 per minute, capillary refill time was less than two seconds, and oxygen saturation of 74% by pulse oximetry on room air. The head appeared unduly large in comparison to the body and the anterior fontanelle was wide open measuring 4×4 cms and pulsatile. Posterior fontanelle was also wide and sutures were widely separated, lateral fontanelle was also open. Sclera did not appear blue. Both upper limbs appeared short and stubby with diffuse swelling in the left arm. Both lower limbs appeared curved with legs being more curved than the thighs, lower limbs were held in a frog-like position [Table/Fig-1]. Subcutaneous crepitus was present in the left arm and the neonate had a shrill cry on the movement of the left arm. The chest appeared normal. Pan systolic murmur was present with maximal intensity in the right parasternal area in the 4th intercostal space. The abdomen was protuberant with no organomegaly and the bilateral testis were undescended.

The baby was provisionally diagnosed with OI and relevant investigations were suggested. Infantogram showed multiple calvarial fractures in the skull, multiple rib fractures, fracture of left humerus, bilateral ulna, left femur and there were multiple areas with callus formation suggestive of intrauterine fractures [Table/Fig-2]. Blood tests revealed normal morphology and count of blood cells and the C-reactive protein was negative. Laboratory values for Calcium (C), Phosphorus (P) and Alkaline phosphatase (ALKP) (Ca: 7.2 mg/dL (range 8.8-10.6 mg/dL), PO4: 6.8 mg/dL (range 2.5-4.5 mg/dL), ALP-146 IU/L (range 30-120 IU/dL), 25-hydroxyvitamin D level was 38.5 nmol/L.



[Table/Fig-1]: Image showing limb deformity, lower limbs are curved and swollen left upper limb; **[Table/Fig-2]:** X-ray on day 1 of admission showing multiple fractures (white arrows) of limb bones and deformed bones (blue arrows). (Images from left to right)

A 2D echocardiography was suggestive of tiny patent ductus arteriosus, dilated right atrium and right ventricle, severe tricuspid regurgitation, and severe pulmonary arterial hypertension.

Ultrasonography of cranium was suggestive of mild prominence of cortical sulci of the bilateral cerebral hemisphere which was planned for further follow-up with Magnetic Resonannce Imaging (MRI) brain but was refused by attendants. A further genetic analysis was also declined for the reason of economic constraints.

The baby was stabilised under a radiant warmer in emergency and oxygen via hood was provided at 5 liters, intravenous fluids were started to maintain euglycaemia, and was shifted to neonatal intensive care unit for further management. Orthopaedic consultation was taken, the left arm was braced and paracetamol at 10 mg/kg/dose 8th hourly was started as an analgesic. Brainstem Evoked Response Audiometry (BERA) was planned. Calcium gluconate 10% was added at a dose of 8 mL/kg in intravenous fluids. Oral sildenafil 1 mg/kg/dose 8th hourly was added for severe pulmonary arterial hypertension. As the baby's general condition improved, Orogastric (OG) feeds were started on day 3 and progressed to bowl spoon feeds on day 5 of life and intravenous fluids were stopped. Neonate was started on oral calcium (80mg/kg) and 1000 IU/day of vitamin D3. The baby remained stable till day 10 of life when he developed multifocal seizures which were managed with injection midazolam 0.1 mg/kg stat and injection calcium gluconate 2 mL/kg stat followed by 8 mL/kg/day 48 hourly was given. Neonate was euglycaemic at the time and serum electrolytes were in the normal range except for hypocalcaemia (6.7 mg/dL). Neonate developed repeated episodes of apnoea requiring bag and mask ventilation on day 11, so was intubated and mechanically ventilated. The sepsis screen was negative. Calcium supplements were increased to 100 mg/kg/day. The baby was stabilised and OG feeds were restarted on day 11 of life. Neonate gradually improved in the subsequent days, but the attendant refused treatment citing familial problems, and took the neonate home against medical advice on day 16 of life. Neonate was advised to continue calcium and vitamin D3 supplementation at home. Neonate was followed up telephonically on day 20 and was fed on cow's milk by feeding bottle which he was able to suck. Telephonic call on day 25 revealed that the neonate expired on day 23 of life after developing breathing difficulty and no medical aid was sought.

DISCUSSION

The OI is a hereditary condition characterised by increased bone fragility and varied clinical features. It is caused by a defect in type I collagen which synthesises skin, bone, and other connective tissue [1]. The incidence of OI is 6-7 per 100000 [2]. Sillence et.al., classified OI into four groups namely I to IV but with further research and genetic testing, groups V to XI were also incorporated in the classification by Cole WG [3]. Type 1 is the most common and type 2 is the most severe form [4].

OI should be considered in the differential diagnosis of non-accidental trauma presenting with multiple fractures. Rickets, child abuse, osteomalacia, and other skeletal syndromes with bone fragility and deformity should also need to be thought of. The most common clinical feature is bone fragility which is present in most of the subtypes. Specific clinical features as described by Van Dijk FS and Sillence DO [5] are present. However, correct subtype diagnosis clinically remains difficult. Diagnosis remains simple whenever most of the clinical features of a subtype are present in a case. A high index of suspicion needs for suspecting a diagnosis. In a case series reported by John BM et al., clinical presentation can vary and includes frog-leg attitude, protuberant abdomen, macrocephaly, large anterior fontanel, short limbs with marked bowing, and a blue sclera [6]. A case reported by Bhat YR and Prakashini K also presented with similar findings [7] Bayram S et al., reported a case who became distressed during handling and had multiple atraumatic fractures which were managed clinically [8]. Similarly in the present study, the baby moaned and cried whenever handled.

The main radiographic features of OI are osteopenia, bone fractures and bone deformities [9,10]. In our case, considering the clinical presentation and radiological findings, it fits more with type III. A genetic test would have helped in reaching a correct diagnosis but was not feasible owing to financial constraints. A multidisciplinary team comprising of neonatologists, orthopaedician, physiotherapists, audiologists, and dieticians is required for management [11]. Bisphosphonates are used in OI to increase bone mass and reduce the risk of fractures, long bone deformities, and increasing mobility [12].

Delivery of the baby should be gentle, if diagnosed antenatally with minimal manipulation at birth to avoid the risk of fractures. Due to respiratory distress and limited mobility of the thoracic cavity, baby needs to be feed through the OG route and appropriate calorie and protein intake should be maintained. Patients who are discharged from the hospital need special care at home to avoid fractures. Physiotherapy remains an important intervention to achieve improvement of muscle strength and ability [13].

CONCLUSION(S)

Osteogenesis imperfecta is an uncommon diagnosis and a high index of suspicion is required for detecting early. A multidisciplinary team is required for management. Genetic counseling should be offered to parents to avoid recurrence of the disease which remains a lethal condition in most cases.

REFERENCES

[1] Beary JF, Chines AA. Osteogenesis imperfecta: Clinical features and diagnosis. 2019. https://www.uptodate.com/contents/osteogenesis-imperfecta-clinical-features-and-diagnosis.

[2] Tauer J, Robinson M, Rauch F. Osteogenesis imperfecta: New perspectives from clinical and translational research. JBMR Plus. 2019;3(8):e10174.

[3] Cole WG. The Nicholas Andry Award-1996. The molecular pathology of osteogenesis imperfecta. Clin Orthop Relat Res. 1997;(343):235-48.

[4] Marini JC. Osteogenesis Imperfecta. In Kliegman RM, Stanton BF, Nina FS, Joseph WS, editors. Nelson Textbook of Paediatrics, 20th ed. Philadelphia: WB Saunders, 2016:3380-3384.

[5] Van Dijk FS, Sillence DO. Osteogenesis imperfecta: Clinical diagnosis, nomenclature and severity assessment. Am J Med Genet A. 2014;164A(6):1470-81.

[6] John BM, Patnaik SK, Thergaonkar RW. Multiple fractures in neonates and Osteogenesis Imperfecta. Medical Journal Armed Forces India. 2006;62:73-74.

[7] Bhat YR, Prakashini K. A neonate with multiple fractures. J Clin Diagn Res. 2009;3(1):1326-28.

[8] Bayram S, Mert L, Anarat FB, Chodza M, Ergin ÖN. A newborn with multiple fractures in osteogenesis imperfecta: A case report. J Orthop Case Rep. 2018;8(3):71-73.

[9] Renaud A, Aucourt J, Weill J, Bigot J, Dieux A, Devisme L, et al. Radiographic features of osteogenesis imperfecta. Insights Imaging. 2013;4(4):417-29.

[10] Mbono Betoko RC, Ngo Um Sap S, Ngo Yamben MA, Tony Nengom J, Koki Ndombo P. Osteogenesis Imperfecta in neonatal period in Cameroon: A case report. Clin Case Rep. 2021;9:526-30.

[11] Marr C, Seasman A, Bishop N. Managing the patient with osteogenesis imperfecta: A multidisciplinary approach. J Multidiscip Healthc. 2017;10:145-55. Doi: 10.2147/JMDH.S113483.

[12] Graaff F, Verra W, Pruijs J. Decrease in outpatient department visits and operative interventions due to bisphosphonates in children with osteogenesis imperfect. J Child Orthop. 2011;5(2):121-25.

[13] Binder H, Conway A, Gerber LH. Rehabilitation approaches to children with osteogenesis imperfecta: A ten-year experience. Arch Phys Med Rehabil. 1993;74:386-90.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Paediatrics, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India.
2. Junior Resident, Department of Paediatrics, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Rakesh Kumar,
Department of Paediatrics, Himalayan Institute of Medical Sciences,
Dehradun, Uttarakhand, India.
E-mail: drrakesh99@yahoo.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Mar 03, 2021
- Manual Googling: Jun 11, 2021
- iThenticate Software: Jul 16, 2021 (4%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 02, 2021**
Date of Peer Review: **Apr 20, 2021**
Date of Acceptance: **Jun 29, 2021**
Date of Publishing: **Sep 30, 2021**