Case Report

Osteogenesis Imperfecta with Associated Ostium Secundum Atrial Septal Defect: A Case Report from North Central Nigeria

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Abstract

Osteogenesis imperfecta (OI) is a group of inherited disorders of connective tissue characterized by increased bone fragility. The disease can manifest in a range of severities, from mild cases with few fractures and minor skeletal deformities to severe forms that may result in stillbirth or birth with multiple fractures and other complications. We report a case of OI (probably type III) with concomitant ostium secundum atrial septal defect in an 8-day male neonate who had no family history of the disease from North Central Nigeria. The baby had progressive respiratory distress with hypoxia from the 2nd day of life. He was managed conservatively, discharged after 7 days of hospitalization, and remained clinically stable on follow-up visits. This is to highlight the sporadic occurrence of Osteogenesis Imperfecta (OI), its co-occurrence with congenital heart disease, and the challenges in providing care.

Keywords: Bone, connective tissue, fractures, fragility, osteogenesis imperfecta

Introduction

Osteogenesis imperfecta (OI), otherwise known as "brittle bone disease," is a group of inherited disorders of collagen in the connective tissue characterized by increased bone fragility.[1] It is the most common genetic cause of osteoporosis.[2] The disease presents with varying degrees of severity, ranging from mild cases with minimal fractures and skeletal deformities to severe forms that may result in stillbirth or birth with multiple fractures and extraskeletal complications.[1,2] The overall incidence of all forms of OI diagnosed in infancy is 1 in 20,000, with no racial or ethnic predilection for the autosomal dominant forms.[2]

In most cases of OI, there is an underlying mutation of the COL1A1 and COL1A2 genes that code for type 1 collagen. Type I collagen is a heterotrimeric protein containing two α1 and one α2 chains, and the mutations cause negative shifts in these α-chains.[3] Consequently, there are qualitative (i.e., defective collagen due to disorders in posttranslational modification and cross-linking of collagen molecules into fibrils) and quantitative (i.e. reduced amount of collagen) abnormalities in the tissues (bones, sclera, ligaments, and teeth) containing type 1 collagen.[2,4] These mutations are spontaneous in the vast majority of cases, while familial mutations, if they occur, are inherited in an autosomal dominant pattern.[2,5] The disease severity is variable, and cases with milder manifestations have quantitative abnormalities unlike those with more severe manifestations with qualitative defects.

Based on disease severity, four phenotypes of OI (I–IV) were described in 1979, but this has recently been updated to seven with the inclusion of three additional distinct types with specific histologies (V–VII).[6,7] Type I is mild, type II is perinatal lethal, type III is progressive deforming, type IV is moderately severe, type V is hyperplastic callus, and type VI is hyperosteoidosis.[2] The characteristic features of the various types of OI are summarized in Table 1. Given the presence of type 1 collagen in different body tissues, extraskeletal manifestations are bound and include blue sclera, hearing impairment, dentinogenesis imperfecta, hyperlaxity of ligaments and skin, cardiac (e.g. valvular defects, septal defect, and aortic root dissection), and renal anomalies.[9-11]

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Table 1: Characteristics and Online Mendelian Inheritance in Man identification of most common types of osteogenesis imperfecta (types I–IV)[2,3,8]

Types	Alternative name	OMIM ID	Characteristics
I	Blue sclera	166200	Inheritance is autosomal dominant Quantitative disorder in collagen The mildest form often presents at preschool age Hearing deficit in 50% In general, the life span is normal
II	Perinatal lethal or congenital OI	166210	Inheritance is autosomal dominant Qualitative disorder in collagen Lethal in the perinatal period
III	Progressively deforming OI	259420	Inheritance is autosomal dominant Qualitative disorder in collagen It is the most severe survivable form Loose joints and respiratory problems due to low thoracic volume causing low lung volumes Delivered with multiple fractures with progressively short stature
IV	Normal sclerae	166220	Inheritance is autosomal dominant Qualitative disorder in collagen The severity is moderate. Typically associated with bowing bones and vertebral fractures Hearing is normal

OI: Osteogenesis imperfecta, OMIM: Online Mendelian Inheritance in Man

There are currently no commercially available diagnostic genetic tests for the disease; hence, diagnosis is based mainly on distinctive clinical and radiological features.[12,13] The severe form of OI can be detected *in utero* through ultrasonography as early as 16-week gestation. The disease currently has no cure, and management is multidisciplinary focusing on fracture prevention and reduction of pain with bisphosphonates, fracture management when present, and realignment osteotomies for long bone deformities.[8]

Case Report

The case was an 8-day-old term male neonate who was delivered per vaginam in a primary health-care facility at 38 weeks of gestation. Labor was not prolonged, and the baby cried soon after birth. The antenatal period was not adversely eventful, and there was no history of maternal exposure to radiation or known teratogenic medication.

The parents brought the baby to our facility due to noticeable limb abnormalities and rapid breathing observed on the second day of life. There was no fever, bluish extremities, or lips although the mother had observed worsening feeding difficulty 2 days before presentation. The parents had observed limb abnormalities at birth characterized by unusually short and bent limbs with multiple swelling across their length and associated crying when moving the limbs. There was no use of instruments at delivery or other forms of trauma around the time of birth.

The baby was the 4th of 4 children, with 2nd and 3rd children delivered as stillbirths. The stillbirths had no physical deformities. There was no history of consanguinity or family history of short stature or susceptibility to fractures. The father and the mother were 25 and 21 years old, respectively. The child had received the first doses of vaccination (BCG, oral polio vaccine, and hepatitis) and had been fed with breast milk and water. The review of other systems did not reveal additional symptoms.

On examination, the baby had fast breathing and was in respiratory distress. He had a blue sclera, low-set ears, frog-like leg posture, and widened anterior and posterior fontanelles with sutural diastasis. There were multiple abnormal angulations and tender swellings of the upper and lower limbs and a short thorax. He had anterior bowing of the leg (saber shins) and excessive mobility across the limb joints [Figures 1 and 2]. He weighed 2700 g, his occipitofrontal circumference measured 42 cm, and his length was 34 cm. These measurements corresponded to the 25th percentile for both weight and occipitofrontal circumference, while his length fell below the 2nd percentile. In addition, his vital signs were as follows: a respiratory rate of 70 breaths/min, a heart rate of 160 beats/min, and an oxygen saturation level of 90%. The oxygen saturation, however, improved to 95%–96% after the commencement of oxygen therapy.

Additional cardiorespiratory examination findings include grunting, moderate chest retractions, and first and second heart sounds. There were no crepitations or cardiac murmur. Furthermore, there were no abnormalities found on the examination of other systems. A presumptive assessment of OI was thus made, with a suspicion of concomitant acyanotic congenital heart disease. Echocardiography done 36 h into admission revealed a 0.43 cm ostium secundum atrial septal defect. We initiated intranasal oxygen at 2 L/min, administered intravenous furosemide at 1 mg/kg/dose every 12 hours, and fed him 27 ml of expressed breast milk through a nasogastric tube every 2 hours (120 ml/kg/day).

The baseline serum calcium, phosphorus, and alkaline phosphatase were within normal limits. A babygram [Figure 3] done on the 2nd day of admission revealed multiple long bone fractures in

the humerus, femur, and tibiae in various stages of healing with calluses noted which are consistent with the diagnosis of OI. The radiograph also revealed a normal-sized heart, and there were no opacities in the lung field. The orthopedic team reviewed him and decided that medical management would suffice now but recommended a start dose of intravenous zoledronic acid at 0.05 mg/kg, to be repeated every 6 months.

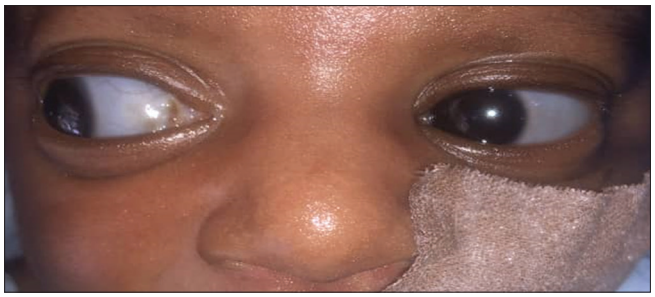

Figure 1: Photograph of the index case showing blue sclera

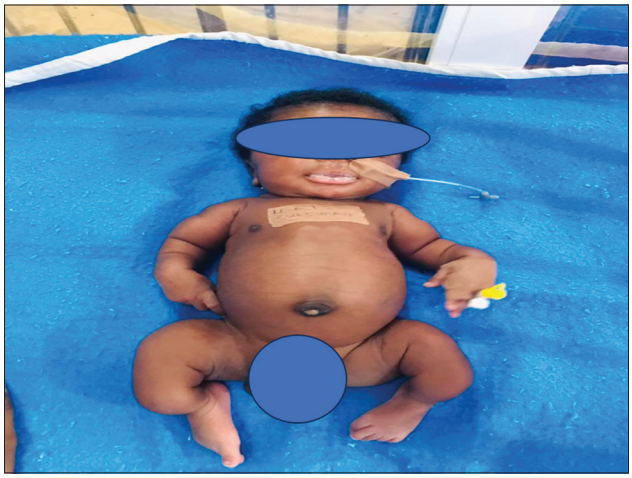

Figure 2: Photograph of the index case showing frog-like leg posture and anterior bowing of the leg

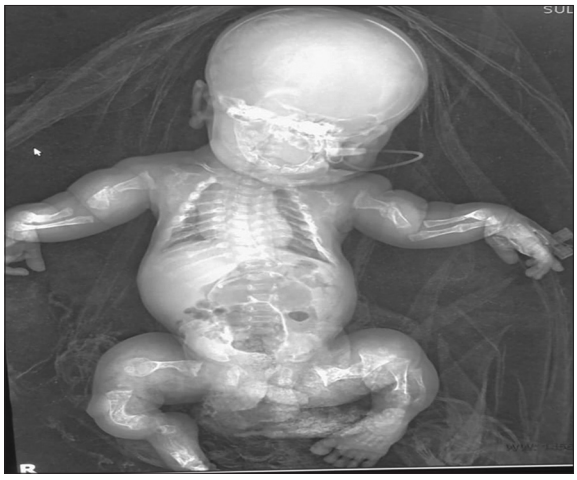

Figure 3: A babygram of the index case case showing multiple long bone fractures in the humerus, femur, and tibiae in various stages of healing with callus

The baby, however, did not receive the medication because the parents could not afford it.

The baby made a significant improvement in respiratory distress by the 3rd day of admission with reduced ranges of respiratory rate between 56 and 62 breaths/min, optimal oxygen saturation (>95%), and reduced chest retractions over 24 h. Consequently, he was weaned off oxygen therapy, and enteral feeding continued via cup and spoon at 34 ml/kg (150 ml/kg/day) on the 4th day. Furthermore, furosemide was converted to oral at the same intravenous dose. He remained clinically stable, and his mother was able to successfully breastfeed from the 5th day of admission. Thereafter, oral calcium (200 mg daily) and Vitamin D (400 IU) were added to the medications. He was discharged after 7 days of hospitalization on oral furosemide, calcium, and Vitamin D. The parents were counseled and educated on how to handle the baby to minimize fractures.

In addition to the pediatric cardiology clinic, the baby was scheduled for follow-up at the orthopedic clinic for long-term management of fractures (existing and future possible fractures) and joint hypermobility problems. The baby has been followed up for 5 months now during which he made a total of 3 clinic visits. Table 2 shows the anthropometric profile and the vital signs of the child over the first 5 months. There was no bony tenderness during the clinic visits, suggesting that there were no new fractures, but weight gain was less satisfactory as he weighed 4000 g at 5 months. Furthermore, he has persistent tachypnea despite normal oxygen saturation and hematocrit levels during the visits. The baby is yet to commence the prescribed zoledronic acid prophylaxis due to financial constraints.

Discussion

OI, also known as brittle bone disease, is a heterogeneous group of genetic disorders affecting connective tissue. It results from mutations in the COL1A1 or COL1A2 genes, leading to either quantitative or qualitative defects in type I collagen. The disease spectrum varies widely, ranging from mild cases with few fractures and skeletal deformities to severe forms associated with stillbirth, multiple fractures, and multisystemic complications.[10,11,13]

Table 2: Anthropometric profile and the vital signs of the child over the first 5 months

Anthropometry/vital signs	Visit at 5 weeks	Visit at 3 months	Visit at 5 months
Weight (kg)	3.1	3.45	4
Length (cm)	42	44	52
Head circumference (cm)	36	39	41
Respiratory rates	66	68	72
Heart rates	160	156	158
Oxygen saturation	95% (room air)	96% (room air)	96% (room air)

The index patient does not have a family history of bone disease or susceptibility to fracture which is consistent with the sporadic nature of the disease in the majority of the cases.[4,5] Furthermore, facilities for genetic studies are not available at the managing facility; hence, the diagnosis of the disease in the reported cases was based on the distinctive clinical and radiological features identified in the case, i.e. blue sclera, fractures, Saber shins, short thorax, and excessive mobility of the joints. The presence of multiple fractures, respiratory distress, hypoxia, and a cardiac defect at birth in this case suggests a more severe form of the disease, which is inconsistent with the milder manifestations typically seen in OI types I and IV. In addition, a blue sclera is uncommon in patients with type IV variants. Furthermore, given that type II is prenatally lethal, it contrasts the observation in the case presented that has lived till 5 months. Furthermore, the majority with OI have mutations in either the *COL1A1* or *COL1A2* genes which are exclusive to types I to IV disease; we, therefore, conclude that the index case fits into the type III form.[2,8]

Previous researchers have reported cardiac anomalies among subjects with OI, mostly mitral valvular abnormalities, aortic root dilatation, and atrial septal defect.[10,11] The index case had a moderate-sized atrial septal defect which is consistent with previous observations. The persistent tachypnea, in this case, could reflect an attempt to compensate for the reduced lung capacity occasioned by the short thorax. Furthermore, recent studies have established a connection between reduced lung function in OI and structural distortions within the lung tissues caused by abnormal type I collagen.[14] Furthermore, the tachypnea may have resulted from the hypermetabolic state that has been reported among subjects with OI.[13]

At present, there is no cure for the disease, and the management is multidisciplinary emphasizing fracture management and prevention, respiratory, and counseling support. As highlighted in the report, we supported the respiration of the index case when he had respiratory distress. We also evaluated the child for the presence of cardiac anomaly, commenced prophylactic furosemide, and followed him up at the cardiology clinic. Furthermore, the child was evaluated by the orthopedic team. Although the parents could not yet afford zoledronic acid, we commenced the child on calcium and vitamin supplements. The parents were further counseled on the child's clinical condition and the need for cautious handling to avoid fractures.

Conclusion

Although rare, OI also occurs in Sub-Saharan Africa, and it is mostly sporadic. Cases could also present with associated cardiac anomaly, and hence, thorough cardiac evaluation is warranted in suspected cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given consent for images and other clinical information to be reported in the journal. The guardian understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Monsell F, Gargan M, Eastwood D, Turner J, Katchky R. Genetic disorders, skeletal dysplasias and malformations. In: Apley and Solomon's System of Orthopaedics and Trauma. 10th ed. Boca Raton: Taylor and Francis; 2017. p. 22.
2. Popkov OA, Shchurova DA, Ochirova EN, Ryabykh PV. Osteogenesis imperfecta: Current issues of etiology, pathogenesis, classification (systematic review). Genij Ortopedii 2021;27:453-60.
3. Mortier GR, Cohn DH, Cormier-Daire V, Hall C, Krakow D, Mundlos S, *et al.* Nosology and classification of genetic skeletal disorders: 2019 revision. Am J Med Genet A 2019;179:2393-419.
4. Augusciak-Duma A, Witecka J, Sieron AL, Janeczko M, Pietrzyk JJ, Ochman K, *et al.* Mutations in the COL1A1 and COL1A2 genes associated with osteogenesis imperfecta (OI) types I or III. Acta Biochim Pol 2018;65:79-86.
5. Zhytnik L, Maasalu K, Reimann E, Prans E, Kõks S, Märtson A. Mutational analysis of COL1A1 and COL1A2 genes among Estonian osteogenesis imperfecta patients. Hum Genomics 2017;11:19.
6. Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. J Med Genet 1979;16:101-16.
7. Fratzl-Zelman N, Misof BM, Roschger P, Klaushofer K. Classification of osteogenesis imperfecta. Wien Med Wochenschr 2015;165:264-70.
8. Wikipedia. Osteogenesis Imperfecta; 2024. Available from: https://en.wikipedia.org/wiki/Osteogenesis_imperfecta. [Last accessed on 2024 Jun 22].
9. Hortop J, Tsipouras P, Hanley JA, Maron BJ, Shapiro JR. Cardiovascular involvement in osteogenesis imperfecta. Circulation 1986;73:54-61.
10. Vetter U, Maierhofer B, Müller M, Lang D, Teller WM, Brenner R, *et al.* Osteogenesis imperfecta in childhood: Cardiac and renal manifestations. Eur J Pediatr 1989;149:184-7.
11. Folkestad L, Hald JD, Gram J, Langdahl BL, Hermann AP, Diederichsen AC, *et al.* Cardiovascular disease in patients with osteogenesis imperfecta – A nationwide, register-based cohort study. Int J Cardiol 2016;225:250-7.
12. Fajolu I, Ezeaka V, Elumelu O, Onabajo O, Ananti C, Iroha E, *et al.* Osteogenesis imperfecta in a set of Nigerian twins – A case report. Internet J Pediatr Neonatol 2012;14:1-5.
13. Sauder C. Orthobullets. Osteogenesis Imperfecta; 2022. Available from: https://www.orthobullets.com/pediatrics/4102/osteogenesis-imperfecta. [Last accessed on 2023 May 26].
14. Storoni S, Treurniet S, Micha D, Celli M, Bugiani M, van den Aardweg JG, *et al.* Pathophysiology of respiratory failure in patients with osteogenesis imperfecta: A systematic review. Ann Med 2021;53:1676-87.