Case Report

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Osteogenesis Imperfecta: A Rare Case Report

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Abstract

Introduction: Osteogenesis Imperfecta also known as brittle bone disease is a heterogeneous disorder which is rare and characterized by bone fragility, multiple fracture, bone deformity and short stature.[1] It has varying degree of classification based on varying degree of fragility and various clinical presentations.[2] Osteogenesis imperfecta (OI) is a rare skeletal dysplasia, with an incidence of 1/15,000–20,000.[3]

Case report: A 7-month-old male child visited our hospital for fever cough, cold & breathlessness. Ultrasonography at 8th month revealed mild polyhydramnios with Fetal growth retardation and shortening of fetal long bones of upper and lower limb & 9th month Ultrasonography revealed moderated Polyhydramnios with short limb Dwarfism. On head to toe examination, patient had triangular shaped face with broad forehead, blue sclera, short neck short statured limbs with cylindrical like appearance that is circumferential fat pads, both the hips and knees were flexed and rotated inwards. Barrel shaped rib cage was present.

Discussion: OI, commonly known as brittle bone disease, is a hereditary ailment that includes a diverse range of illnesses. It is characterised by a propensity for bone fractures, which can range in severity from a minor break to a prenatal fracture. Blue sclera, DI, hyperlaxity of ligaments and skin, hearing impairment, small height, and bone abnormalities are further characteristic clinical symptoms.[11] Sillence et al categorised OI into four kinds based on their clinical severity and genetic characteristics because OI is a diverse disease with different clinical presentations.[12]

Conclusion: In conclusion, experimental treatments including gene based therapy and bone marrow and stem cell transplantation offer prospective treatments for OI. But these methods are not yet prepared for clinical testing.[15] There should be availability of these approaches in each tertiary care center for better diagnosis & treatment of osteogenesis imperfecta.

Keywords: Osteogenesis; Brittle bone; Multiple fracture; Short stature; Blue sclera.

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INTRODUCTION

Osteogenesis Imperfecta also known as brittle bone disease is a heterogeneous disorder which is rare and characterized by bone fragility, multiple fracture, bone deformity and short stature.[1] It has varying degree of classification based on varying degree of fragility and various clinical presentations.[2] Osteogenesis imperfecta (OI) is a rare skeletal dysplasia, with an incidence

of 1/15,000–20,000.[3] As the production of type I collagen in various tissues is impaired, individuals with OI may also suffer from other clinical symptoms such as brittle teeth, blue sclerae, hearing loss, reduced respiratory function, and cardiac valvular regurgitation.[4]

The severity of OI varies from mild to extremely severe, with the most severe form being perinatally lethal.[5] Five clinical forms of OI are identified by the zrevised Nosology and Classification of Genetic Skeletal Disorders: OI type I, which is non-deforming with persistently blue sclera; type II, which is perinatally lethal; type III, which is gradually deforming; type IV, which is moderate; and type V, which has calcification of the interosseous membranes and/or hypertrophic callus.[6] Among patients who survive infancy, those with OI type III are the most seriously affected, with many fractures, scoliosis, small stature, and limited mobility. OI kind I possess the most modest phenotype. X-linked, dominant, or recessive inheritance patterns exist for OI.[7,8] Most frequently, pathogenic mutations in either COL1A1 or COL1A2 produce the dominant illness (encoding components of type I collagen).

Null alleles (i.e. deletions, splice variants that change the reading frame, or variations that are truncating) in COL1A1 result in haploinsufficiency that is typically associated with mild OI (type I). COL1A1 or COL1A2 missense mutations, which commonly result in glycine substitutions in a Gly-X-Y repeat, or splice mutations, which do not alter the reading frame, typically cause deadly, severe, or moderate OI (categories II, III, or IV, respectively) An OI type V recurrent pathogenic mutation in the 5 'untranslated region of IFITM5, which codes for the interferon induced transmembrane protein 5 (BRIL), causes the dominant form of the disease, which is rarer.[9] There is currently no known cure for OI, and available therapies do not deal with the underlying molecular illness.

The purpose of treatment is to retain mobility, encourage normal function, increase overall bone strength to prevent fractures, and enhance quality of life. Physiotherapy is used to build up the muscles and increase mobility, and lifetime orthopaedic procedures like rods in the long bones to rectify bone abnormalities are used to achieve this goal. Bisphosphonates are prescribed to treat osteoporosis and boost bone mineral density. The impact of bisphosphonates on OI has been debated, and a recent systematic review found that nonrandomized open label uncontrolled studies show that oral and intravenous bisphosphonate administration objectively improved function and mobility while randomised controlled trials did not show a significant improvement in function and mobility with oral bisphosphonate administration.[10]

CASE REPORT

A 7-month-old male child visited our hospital for fever cough, cold & breathlessness. The mother had non consanguineous marriage with 6 pregnancies out of which 2 were aborted and live births were 4. She was on calcium and iron supplements at the time of Pregnancy. No history of taking teratogenic drugs. No any illness to mother during pregnancy. She also had history of Polyhydramnios during the delivery. Ultrasonography at 8th month revealed mild polyhydramnios with Fetal growth retardation and shortening of fetal long bones of upper and lower limb & 9th month Ultrasonography revealed moderated Polyhydramnios with short limb Dwarfism. Baby was born full term normal delivery and cried immediately after birth. Birth weight was 2.5 kg & other anthropometry of at birth was not recorded. Now head circumference is 39 cm, chest circumference 33 cm and length from heel to crown was 45 cm. So patient had microcephaly & severely stunted. He was normally breastfed and had no history of NICU stay. Mild tachypnoea was present & rest vitals were stable. On auscultation of both lungs, crepts were heard, mild hypotonia was present & other systemic examination was normal. X ray lungs showed pneumonia. Patient also had history of recurrent respiratory tract infections.

On head to toe examination, patient had triangular shaped face with broad forehead, blue sclera, short neck short statured limbs with cylindrical like appearance that is circumferential fat pads, both the hips and knees were flexed and rotated inwards. The baby also had long flexible fingers and toes. Barrel shaped rib cage was present

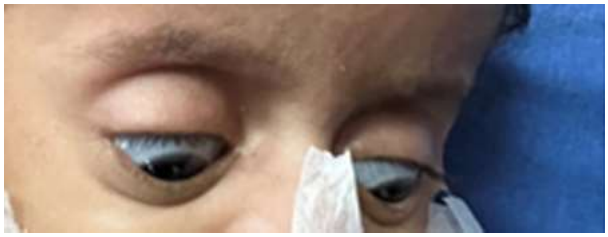
All routine investigations sent & were normal. In order to confirm diagnosis, genetic sequencing of the most common problematic genes, COL1A1, COL1A2, and IFITM5 was planned but patient was unaffordable.

Calcium, phosphorous & vit D levels were low for which appropriate supplements started.

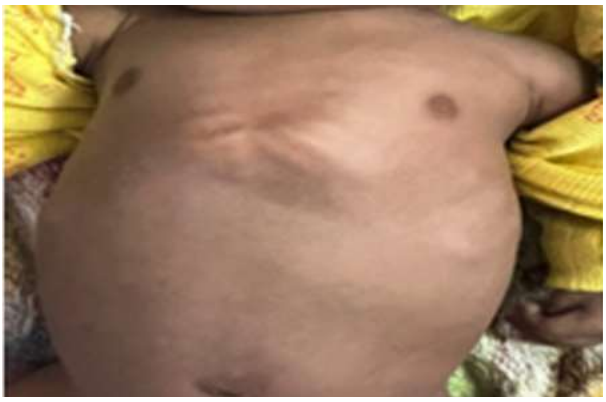
Limb physiotherapy was started & advised to continue after discharge.

Patient was given IV antibiotics, oxygen by nasal prongs, nebulization & patient responded to treatment for pneumonia. At last patient was referred to higher centre for further management of

osteogenesis imperfecta.



Picture 1: Osteogenesis imperfecta patient showing BLUE SCLERA



Picture 2: Osteogenesis imperfecta patient showing *Barrel Shaped Chest*

DISCUSSION

OI, commonly known as brittle bone disease, is a hereditary ailment that includes a diverse range of illnesses. It is characterised by a propensity for bone fractures, which can range in severity from a minor break to a prenatal fracture. Blue sclera, DI, hyperlaxity of ligaments and skin, hearing impairment, small height, and bone abnormalities are further characteristic clinical symptoms.[11] Sillence et al. categorised OI into four kinds based on their clinical severity and genetic characteristics because OI is a diverse disease with different clinical presentations.[12] Type I, mild nondeforming; type II, prenatal deadly; type III, severely deforming; and type IV, moderately deforming were the categories used. However, more OI cases have since been discovered and looked into. As a result, OI categories V through VIII have been added to the original Sillence classification based on the unique clinical, radiological, and molecular aspects.[13] There are four of these: type V, which is moderately deforming and has normal teeth and sclera; type VI, which is moderately ill and has a fishscale pattern of bone lamellation, normal sclera, and teeth; type VII, which is clinically similar to type II but the patients have a smaller head and normal sclera; and type VIII, in which the patients have defects in growth and mineralization.[14] Type I collagen, a main and predominate extracellular matrix protein in bone tissues, is synthesised with a quantitative or qualitative deficiency, causing OI, an autosomal dominant condition.[15] The mutation could be in either of the two COL1A1 or COL1A2 genes, which produce the pro-I or pro-II chains of type I collagen, respectively.[16] However, depending on which chains are impacted, where in the collagen structure the mutation occurs, and the type of amino acid substitute used, different phenotypes are produced.[11] In this instance, the patient had a history of recurrent respiratory tract infections, which could range in severity from mild symptoms to life-threatening discomfort. The physical examination revealed a triangular shaped face, blue sclera, and hypermobile joints.

DNA or collagen protein analysis can be used to confirm an OI diagnosis, but in many cases, the presence of other clinical signs including blue sclera and the occurrence of bone fractures with little damage is enough to make the diagnosis. A multidisciplinary team evaluation of the patient is required following the confirmation of the OI diagnosis. The cornerstones of OI management include orthopedic surgery, physical therapy, and rehabilitation. In this example of mild type I OI, the aim was also to provide a normal quality of life for the patient. The purpose of multimodality therapy is to maximise the mobility and functional capabilities of patients.[16] For the treatment of all forms of OI, oral and intravenous bisphosphonates (BPs) and strong antiresorptive medicines are frequently used. Although BPs cannot treat OI, they are a useful supplement to complete therapy. The best way to utilise BPs, whether those with lesser symptoms should use them, and any negative effects are still unknown. To improve their therapeutic applicability, a sizable randomised double blind placebo controlled experiment is needed. There are other medicinal treatments available, like GHs and PTHs, but their results and side effects need to be assessed and analysed further.[15] When medicinal treatments are ineffective, surgical surgery is a backup plan. No surgical intervention was necessary in the present case because no abnormalities were seen and the response to pamidronate was positive. In order to avoid contractures and immobility related bone loss, it was also essential to implement monitored, moderate physical activity regimens after the patient was discharged from the hospital.[17]

CONCLUSION

In conclusion, experimental treatments including gene based therapy and bone marrow and stem cell

transplantation offer prospective treatments for OI. But these methods are not yet prepared for clinical testing.[15] There should be availability of these approaches in each tertiary care center for better diagnosis & treatment of osteogenesis imperfecta.

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