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Osteogenesis Imperfecta: A Case Report

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ABSTRACT

Background: Osteogenesis imperfecta (OI) comprises a heterogeneous group of diseases characterized by susceptibility to bone fractures with variable severity and, in most cases, with presumed or proven defects in collagen type I biosynthesis and an estimated prevalence of 1/15,000 births. Management is multidisciplinary involving mainly surgery, physiotherapy, and rehabilitation

Case Presentation: A young woman the age of 19 years old came to the Endocrine Polyclinic of H. Adam Malik Hospital, with a complaint of a fracture of the arm and left thigh for 4 years due to a slip. Since a small age, there was difficulty walking due to the twisted bones of the limbs, and surgery was performed. The conclusion of X-ray of right and left femur bones according to the description of osteogenesis imperfecta accompanied by a picture of fracture and osteomalasia and the conclusion of the whole body scan: pathological picture in the bones can be caused by osteogenesis imperfecta.

Conclusion: A young woman the age of 19 years old has been reported may have OI type 1, management is multidisciplinary involving mainly surgery, physiotherapy, and rehabilitation.

Keywords: Osteogenesis-imperfecta, A young woman

ABSTRAK

***Latar Belakang**: Osteogenesis imperfecta (OI) terdiri dari kelompok penyakit heterogen yang ditandai dengan kerentanan terhadap patah tulang dengan tingkat keparahan yang bervariasi, dan dalam kebanyakan kasus terbukti terdapat cacat dalam biosintesis kolagen tipe I, dan diperkirakan prevalensi kelahirannya 1/15.000. Manajemen bersifat multidisiplin yang melibatkan beberapa divisi terutama bidang operasi, fisioterapi, dan rehabilitasi*

***Presentasi Kasus**: Seorang wanita muda berusia 19 tahun datang ke Poliklinik Endokrin RSUP H. Adam Malik, dengan keluhan patah tulang pada lengan dan paha kiri selama 4 tahun karena terpeleset. Sejak usia kecil, ada kesulitan berjalan karena tulang anggota badan yang bengkok, dan sudah dilakukan tindakan operasi. Kesimpulan foto dari sinar-X tulang paha kanan dan kiri sesuai dengan deskripsi osteogenesis imperfecta disertai dengan gambaran fraktur dan osteomalasia. Hasil pemindaian seluruh tubuh adalah gambaran patologis pada tulang yang dapat disebabkan oleh osteogenesis imperfecta.*

***Kesimpulan**: Seorang wanita muda berusia 19 tahun telah dilaporkan menderita OI tipe 1, manajemen multidisiplin yang melibatkan multi disiplin terutama operasi, fisioterapi, dan rehabilitasi.*

***Kata kunci**: Osteogenesis-imperfecta, Seorang wanita muda*

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1 Introduction

Osteogenesis imperfecta (OI) comprises a heterogeneous group of diseases characterized by susceptibility to bone fractures with variable severity and, in most cases, with presumed or proven defects in collagen type I biosynthesis.[1] Other clinical manifestations include short stature, blue sclerae, dentinogenesis imperfecta, and hearing loss. Osteogenesis Imperfecta (OI) is an estimated prevalence of 1/15,000 births. The majority of OI cases (85–90%) are inherited in an autosomal-dominant manner and are mostly caused by mutations in COL1A1 and COL1A2 encoding type I collagen subunits, a major protein of the bone extracellular matrix.[2] "Several other genes have been identified more recently and the majority of them encode proteins involved in posttranslational modifications of type I collagen. Among them, IFITM5 c.-14C>T mutation in all patients is responsible for a rare form of dominant OI with hyperplastic callus (5%).[3] Diagnosis can be made clinically. Radiographic support and confirmation by collagen analysis of skin fibroblast culture or blood deoxyribonucleic acid analysis may be necessary in some cases.[4] This is important for genetic counseling and cases of suspected child abuse. Prenatal diagnosis for at-risk pregnancies by fetal ultrasonography in the early 2nd trimester is possible and enables care.[5] Management is multidisciplinary involving mainly surgery, physiotherapy, and rehabilitation. However, medical treatment, especially with bisphosphonate has shown good prospects.[4]

2 Case Presentation

A young woman the age of 19 years old came to the Endocrine Polyclinic of H. Adam Malik Hospital, with a complaint of a fracture of the left arm and thigh for 4 years due to a slip. From a small age, there was difficulty walking due to the twisted bones of the limbs, and surgery was performed. The patient has impaired height growth, impaired menstrual cycle, and secondary sex disorders. The onset of labor was spontaneous and the Apgar score was good. There was no history of the tendency to fractures in the family and no family history of any baby with a fracture at birth. There are fractures on 1/3 proximal os femur right and left with internal fixation attached. Bone density decreases with rough trabeculation of the femoral os and pelvis. Invisible formation of osteophytes. Conclusion: According to the description of Osteogenesis Imperfecta accompanied by a picture of fracture and osteomalacia (fig. 1)

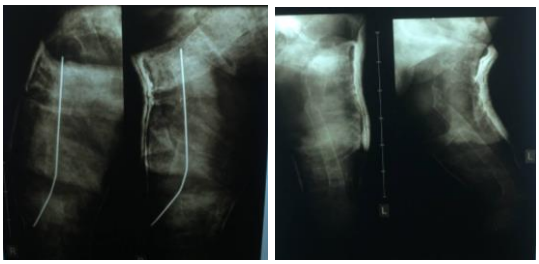

Figure 1 X-ray of Right and Left Femur bones

Whole body scan with with Radiopharmaceutical Tc-99m MDP, 18 MCI; there appears to be a pathologically increased radioactivity arrest (hot spot) on the frontal bone, parietal bone, sphenoidal bone, maxillary bone, vertebrae cervical I, VII, bilateral shoulder joint, 1/3 medial right humerus bone, bilateral wrist join, sternum bone, costae bone, bilateral VI, VII, left scapula, lumbar vertebrae I, II, vertebrae IV, V, sacrum bone, right pubic bone, left acetabulum, bilateral femur bone, bilateral genu, 1/3 proximal bilateral tibia bone, and 1/3 right distal tibia bone. From spect imaging of the head**:** the visible arrest of pathologically increased radioactivity (Hot spot) on the frontal bone, parietal bone, sphenoidal bone, maxillary, Bone vertebrae cervical I, VII, bilateral shoulder joint. From spect thorax imaging: It appears that the capture of radioactivity increases pathologically (Hot spot) in the bone sternum, costae bone. Bilateral, thoracal vertebrae VI, VII bone, left scapula bone, lumbar vertebrae I, II bone. From spect pelvic imaging: It appears that the capture of radioactivity increases pathologically (Hot spot) in the lumbar vertebrae bone I, II. Vertebrae IV, V bone, bone sacrum, bone pubis right, acetabulum left bone, and femur bilateral bone. Conclusion: Pathological picture in the bones can be caused by osteogenesis imperfecta (fig 2).

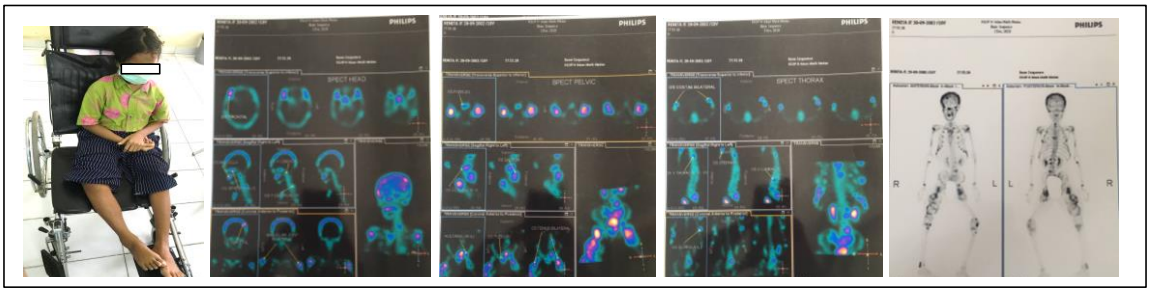

Figure 2 Scan Bones of Whole Body Scan

3 Discussion

Clinical types of OI as the phenotypic severity of OI vary widely, it can be useful to categorize individuals with similar clinical characteristics into more narrowly defined OI types. The 2015 Nosology and Classification of Genetic Skeletal Disorders distinguishes five clinically recognizable OI types.[7] OI type I is the mildest phenotype that is usually associated with straight limbs and a body height within or slightly below the reference range; median adult height Z-scores range between 1.1 and 1.5.[8] OI type II represents the most severe end of the phenotypic spectrum and usually leads to death from respiratory failure shortly after birth. OI type III is the most severe form of OI in individuals surviving the neonatal period. Individuals with OI type III almost always have restricted mobility, develop scoliosis, and are very short, with a final height Z-score typically between 8 and 9.[9] The disease severity of OI type IV is intermediate between OI types I and III. With adequate care, most individuals with OI type IV are ambulatory, but more than half develop scoliosis.[10] Short stature is very common in OI type IV, with mean adult height Z-scores between 3.6 and 4.6.[11] The skeletal features of the much rarer OI type V often resemble those of OI type IV, but OI type V is associated with additional distinctive

characteristics, such as hyperplastic callus formation (observed in about two-thirds of patients) and ossification of the interosseous membrane of the forearms (which eventually develops in almost all individuals with OI type V).[12] Among the various OI types, OI type I is by far the most prevalent, comprising 70% of the entire cohort in a population-based study.[13] In addition to OI types I to V, many higher-number OI types have been proposed based on genetic test results rather than phenotypic features. The drawback of this approach is that recoding the involved gene as an OI type with an arbitrary number adds a layer of complexity to the classification without providing additional information; it would be simpler to just state the name of the gene involved. Describing OI by a combination of the clinical OI phenotype (I to V) and the affected gene as proposed by the 2015 Nosology and Classification of Genetic Skeletal Disorders.[7] provides more useful information to clinicians.

Management. When the diagnosis OI has been established, the affected individual should preferentially be evaluated by a multidisciplinary team. Important members of the team would be orthopedic surgeons, rehabilitation physicians, endocrinologists, physical therapists, and pediatricians. Referral to other disciplines can take place upon individual needs and for routine surveillance such as dental controls. Management consists of pharmacological treatment, orthopedic treatment, physical medicine, dental treatment, treatment for hearing loss, and prevention of primary (e.g. basilar impression) and secondary (e.g. problems due to general medical disciplines) complications. [1]

Pharmacological Treatment. Oral and intravenous bisphosphonates are commonly prescribed for all OI types, adults and children since the first publication of the effect of bisphosphonate treatment in children with severe OI.[5] Nitrogenous bisphosphonates disrupt osteoclast formation, survival and cytoskeletal dynamics, and non-nitrogenous bisphosphonates initiate osteoclast apoptosis. A recently published systematic review of bisphosphonate treatment in OI concluded that in a relatively small group of patients, there is significant improvement in bone mineral density in individuals affected with OI and treated with oral or intravenous bisphosphonates.[13]

Orthopedic Treatment. In case of decreased bone mineralization, high fracture frequency and/or bone deformities, intramedullary rods will be placed in the majority of patients with OI types III and IV and sometimes in OI type I.[14] These rods are inserted in the bone marrow canal in the center of the long bones and are used to align and stabilize fractures. Severe scoliosis occurs most often in patients with OI type III and sometimes IV and appears not to be related to the number of vertebral compression fractures. Since severe scoliosis can lead to pulmonary insufficiency, corrective surgery is often performed when the curvature is less than 60°.[6] In case of anesthesia, precautions should be undertaken during intubation be- cause of possible cervical fragility, and the patient should be carefully monitored during surgery because of the (possibly weak)

association with hyperthermia during anesthesia. Nonsurgical management consists of bracing and splinting interventions. [14]

Physical Medicine Treatment (Rehabilitation). An intensive rehabilitation program is necessary especially in OI types III and IV.[14] with early intervention such as correct positioning of the child and proper head support, muscle strengthening (isotonic) and aerobic conditioning. [6]

Future prospects for OI therapy is gene therapy: silencing or replacement of the allele containing the causative variant

4 Conclusion

Osteogenesis imperfecta is a complex hereditary disease with (i) a remarkable clinical variability warranting a logical classification system; (ii) causative recessive or dominant variants in 8 different genes with 6 of 8 genes encoding proteins involved in collagen type I biosynthesis; (iii) a need for multidisciplinary management and further investigations of therapeutic approaches such as bisphosphonates, growth hormone therapy and gene therapy.

REFERENCES

[1]. van Dijk FS, Cobben JM, Kariminejad A, Maugeri A, Nikkels PGJ, van Rijn RR, et al. Osteogenesis Imperfecta: A Review with Clinical Examples. Molecular Syndromology. 2011;

[2]. Moller. UK, Streym SV, Mosekilde L, Rejnmark L.Changes in bone mineral density and body composition during pregnancy and postpartum. A controlled cohort study. Osteoporos Int . 2012;23:1213–23.

[3]. Rauch F, Moffatt P, Cheung M, Roughley P, Lalic L, Lund AM, et al. Osteogenesis imperfecta type V: marked phenotypic variability despite the presence of the IFITM5 c.−14C>T mutation in all patients. J Med Genet. 2013;50(1):21–4.

[4]. Marini JC. Osteogenesis imperfecta. In Nelson Textbook of Pediatrics. 18th ed. 2007. 2887–90.

[5]. Glorieux FH, Rauch F, Plotkin H, Ward L, Travers R, Roughley P, et al Type V osteogenesis imperfecta: A new form of brittle bone disease. J Bone Miner Res. 2000;15:1650–8.

[6]. Marini JC CWBA. Marini JNull mutations in LEPRE1 and CRTAP cause severe recessive osteogenesis imperfecta. Cell Tissue Res. 2010;339:59–70.

[7]. Bonafe L, Cormier-Daire V, Hall C, et al. Nosology and classification of genetic skeletal disorders. Am J Med. 2015;167A:2869–92.

[8]. Jain M, Tam A, Shapiro JR, Steiner RD, Smith PA, Bober MB, et al. Growth characteristics in individuals with osteogenesis imperfecta in North America: results from a multicenter study. Genetics in Medicine. 2019 Feb;21(2):275–83.

[9]. Barber LA, Abbott C, Nakhate V, Do AND, Blissett AR, Marini JC. Longitudinal growth curves for children with classical osteogenesis imperfecta (types III and IV) are caused by structural pathogenic variants in type I collagen. Genetics in Medicine. 2019 May;21(5):1233–9.

[10]. Anissipour AK, Hammerberg KW, Caudill A, Kostiuk T, Tarima S, Zhao HS, et al. Behavior of Scoliosis During Growth in Children with Osteogenesis Imperfecta. Journal of Bone and Joint Surgery. 2014 Feb 5;96(3):237–43.

[11]. Germain-Lee EL, Brennen FS, Stern D, Kantipuly A, Melvin P, Terkowitz MS, et al. Cross-sectional and longitudinal growth patterns in osteogenesis imperfecta: implications for clinical care. Pediatric Research. 2016 Mar 5;79(3):489–95.

[12]. Lindahl K, Åström E, Rubin CJ, Grigelioniene G, Malmgren B, Ljunggren Ö, et al. Genetic epidemiology, prevalence, and genotype–phenotype correlations in the Swedish population with osteogenesis imperfecta. European Journal of Human Genetics. 2015 Aug 6;23(8):1042–50.

[13]. Philippi CA RTSR. Bisphosphonate therapy for osteogenesis imperfecta. The Cochrane Collaboration. England: John Wiley & Sons Ltd; 2009.

[14]. Monti E, Mottes M, Fraschin. Current and emerging treatments for the management of osteogenesis imperfecta. Ther Clin Risk Manag. 2010;6:367–81.