European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 01, 2020

The First Report of Metaphyseal Dysplasia (Pyle's disease) in Iraq

Nawar N. Yaseen[1], Mohamed A. Mahdi[2]
[1]MBChB, ABHS, Senior Orthopedic surgeon, Fellowship in Hip and Knee reconstructive surgery
Division of Orthopedic Surgery, Department of surgery, Al-Sadir Medical City, Najaf, Iraq
[2]MBChB, FICMS, Consultant Radiologist, Division of Radiology, Department of surgery, Al-Sadir Medical City, Najaf, Iraq

Abstract: Metaphyseal dysplasia (Pyle's disease) is rare autosomal recessive disease. Only few cases were reported around the world since 1930 when Edwin Pyle, an orthopedic surgeon from United States, first describes the disease. Pyle's disease is asymptomatic; it may be diagnosed incidentally during routine radiological examination for a genu valgus deformity. From orthopedic point of view, Pyle's disease requires no treatment except for deformity correction or management of fractures. Orthodontic intervention may be required for malocclusion and abnormal dentation.
Keywords: Metaphyseal dysplasia, asymptomatic, orthopedic

1. Introduction

Metaphyseal dysplasia (Pyle's disease) is a very rare genetic disease of autosomal recessive inheritance. It was first described by Edwin Pyle (1891-1961), an American orthopedic surgeon, in 1931 [1]. The disease prevalence is less than 1 per million [2]. It is usually asymptomatic apart from apparent genu valgus. It is discovered incidentally during routine counseling for the deformity. Less than 30 cases were reported around the world, distributed in USA, Italy, France, Germany, India and South Africa [1]. This is the first case that I report in Iraq.

2. History and examination:

A 11 years old boy presented by his uncle to my private clinic for the complaint of bilateral knee deformities (genu valgus) associated with occasional pain during activities,He isthe second in the family after one normal sister and 2normal brothers (with another two brothers that died during infancy).He was delivered through uneventful vaginal delivery. His father killed duringa localwar.The parents were remote consanguineous with normal phenotype. His grandfather and grandmother of his father side were cousins. His mother was related remotely to the grandmother of the father side. On gross examination, there was normal statue, normal facial features apart from defective dentition and mild malocclusion,figure (1) and genus valgus,figure (2) with intermaleollar distance of 13 cm. there was no history of trauma or infection. There was normal range of motion of all joints. The intelligence was normal; there was no delay in the school.

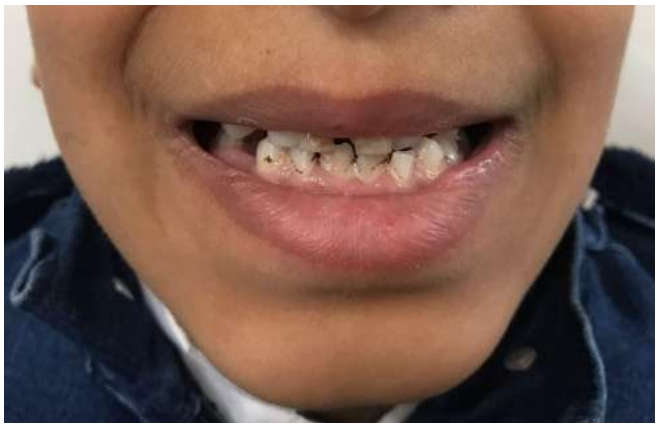

Figure (1): defective dentation and malocclusion

Figure (2): genu valgus

3. Laboratory investigations

All laboratory investigations including hematology, chemistry and immunology were normal except for low vitamin D which was treated accordingly by an orthopedic surgeon. DEXA scan of the spine and proximal femur showed marked decrease in the bone mineral density with a T-score less than -2.5.

4. Radiographic examination

The most striking feature of radiological examination of patients with Metaphyseal dysplasia is the typical Erlenmeyer flask deformity of the distal femora and proximal tibiae which is a Metaphyseal expansion and cortical thinning of the affected bones,figure (3).

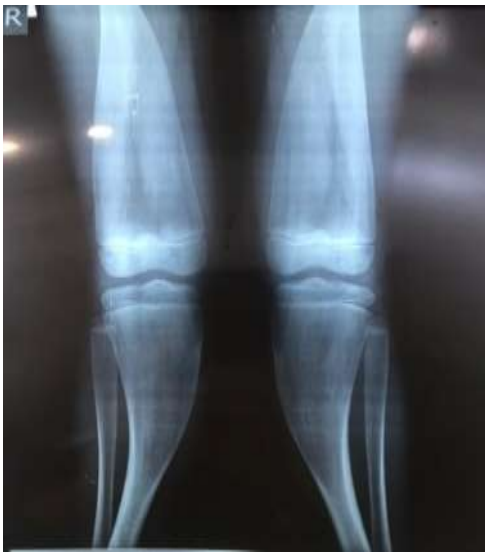

Figure (3): Erlenmeyer flask deformity of the distal femora and proximal tibiae

The Metaphyseal expansion also affects the proximal hummers bilaterally and medial ends of clavicles with poor pneumatization of the paranasal sinusesfigure (4), distal radius and ulna bilaterally, proximal metacarpals, proximal and middle phalanges of both hands (Fig.5), and the proximal femora and pubicrami,figure (6).

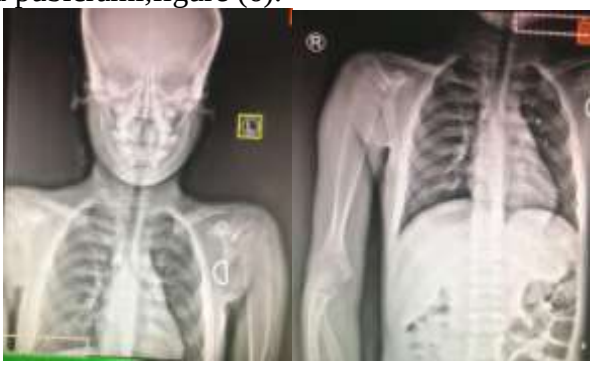

Figure (4): Metaphyseal expansion of the proximal hummers bilaterally and medial ends of clavicles withpoor pneumatization of the paranasal sinuses

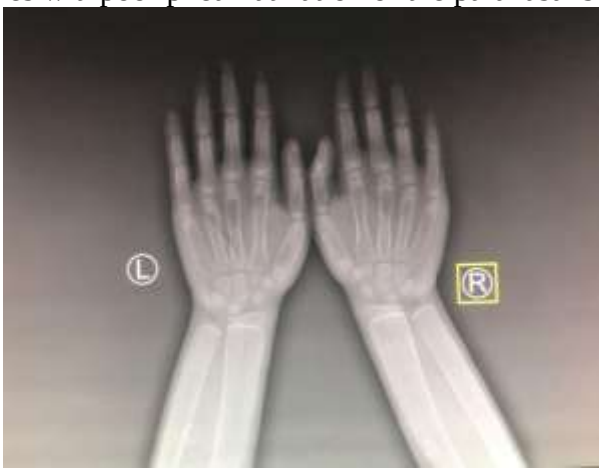

Figure (5): Metaphyseal expansion of distal radius and ulna bilaterally, proximal metacarpals, proximal and middle phalanges of both hands

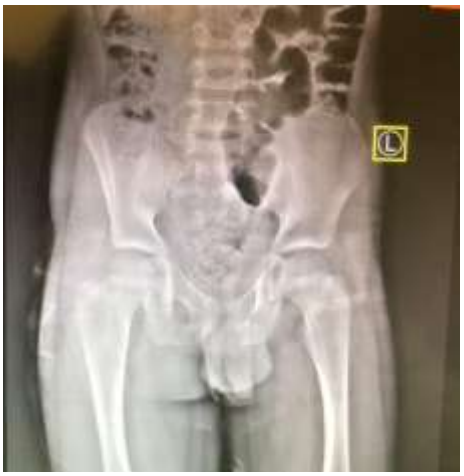

Figure (6): Metaphyseal expansion of the proximal femora and pubic rami

5. Discussion:

Metaphysealdysplasia (Pyle's disease) is a very rare genetic disease with a prevalence of less than one case per million. Until the 1980s, there were only 20 cases described in the literature, distributed in USA, France, Germany, South Africa, India, and Italy [1]with fewer than 30 casesreported to date [3]. No cases were reported from Middle East including Iraq.

Genu valgus deformity is the most obvious sign in patients with Pyle's disease. Defects in dentation, prominent mandibles and malocclusion are other characteristic features. Skeletal survey shows widening of metaphysis and cortical thinning of distal and proximal femur, proximal tibia, proximal hummers, medial clavicle, distal radius and ulna, metacarpals and phalanges, pubic rami and ischium. There is decrease in pneumatization of paranasal sinuses.

Gorlin et al established imaging criteria to differentiate craniometaphysealdysplasia from Pyle's disease including more pronounced Metaphyseal widening, as well as costoclavicular and ischiopubic rami widening in Pyle's disease [4]. These were similar to the present case.

Metaphyseal dysplasia is an autosomal recessive disease. Recently, a mutation in the gene encoding secreted frizzled-related protein 4 (SFRP4), which is a soluble Wnt inhibitor, was discovered. Pelin et al (2016) found that mice deficient in SFRP4, like persons with Pyle’s disease, have increased amounts of trabeculae bone and thin cortices, as a result of differential regulation of Wnt and bone morphogenetic protein (BMP) signaling in these two bone compartments.[5]Loss-of-function mutations in the SFRP4gene lead to the protein deficiency causing skeletal phenotype typical for Pyle disease [6].

Pyle's disease is diagnosed mainly radio graphically due to it very characteristic radiographic features. When the radiologist evaluates such a common deformity as genu valgum with Erlenmeyer flask deformity, it may be the first clue to suspect the diagnosis of this extremely rare disease.[2]

Pyle's diseaseis asymptomatic and does not require treatment. Orthopedic intervention restricted to correction of genu valgus (by epiphysiodesis or osteotomies) and treatment of fractures [4-7].

6. References

(1)Beighton P. Pyle disease (metaphyseal dysplasia). J Med Genet 1987; 24:321-4.

(2)Diego XimenesSoares, AmaliaMapurunga Almeida, Andre Rodrigues Fac¸anhaBarreto, IlzeJucaAlencare Silva, Jose Daniel Vieira de Castro, Francisco Jose Magalhaes Pinto,

Daniel Aguiar Dias, Lindenberg Barbosa Aguiar. Pyle disease (metaphyseal dysplasia) presenting in two adult Sisters. Radiology Case Reports 11 (2016); 405-410.

(3)Wonkam A, Makubalo N, Roberts T, Chetty M. Pyle metaphyseal dysplasia in an African child: case report and review of the literature. S Afr Med J 2016;106(Suppl 1):S110e3.

(4)Gorlin RJ, Koszalka MF, Spranger J. Pyle's disease (familial metaphyseal dysplasia). A presentation of two cases and argument for its separation from craniometaphyseal dysplasia. J Bone Joint Surg 1970;52:347-54.

(5)Pelin O. SimsekKiper, Hiroaki Saito, Francesca Gori, Sheila Unger, Eric Hesse, Ph.D., Kei Yamana, RikuKiviranta, Ph.D., Nicolas Solban, Jeff Liu, Robert Brommage, KorayBoduroglu, Luisa Bonafé, Belinda Campos-Xavier, EsraDikoglu, Richard Eastell, FatmaGossiel, Keith Harshman, Gen Nishimura, Katta M. Girisha, Brian J. Stevenson, Hiroyuki Takita, Carlo Rivolta, Andrea Superti-Furga, and Roland Baron. Cortical-Bone Fragility — Insights from sFRP4 Deficiency in Pyle's Disease. N Engl J Med. 2016 June 30; 374(26): 2553–2562.

(6)Sowin´ ska-Seidler A,Sztromwasser P, Zawadzka K,Sielski D, Bukowska-Olech E,Zawadzki P, Kozłowski K andJamsheer A (2020) The First Reportof Biallelic Missense Mutationsin the SFRP4 Gene Causing PyleDisease in Two Siblings.Front. Genet. 11:593407.doi: 10.3389/fgene.2020.593407.

(7)Gupta N, Kabra M, Das CJ, Gupta AK. Pyle metaphyseal dysplasia. Indian Pediatr 2008;45:323-5.