International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

A Update Review Achrodogenesis is Disease of Cartilage Gene Defect and Skeletal Phenotype of Baby

Kishor Nivrutti Deshmukh[1], Jagruti Ravindra Patil[2], Shubham Prabhakar Chavan[3], Dinesh Ravindra Pawar[4]

[1,2,3,4]Dr. Uttamrao Mahajan College of B. Pharmacy, Chalisgaon

Abstract:
Achondrogenesis group OF Serve affect is a disorders that Cartilage and ment. It is dypalsia, bone develop-type of Skeletal Charecterised by the babis and Small Children's the developent and growth of organ's It Includes, extreme Short trunk and Small growth of in approximately births are Stops micromidia ungrowth and orgens- 40,000+ live. Achrododonogesis Classified into the two subclass. type IB and Type -2 Clinical & radiological histologicul LA based mainly Gerietarea Features. The disease when Zygote is produced with only genes. Occring a pare paternal nuclear. Standard Sextual reproduction One female and one make parent each produce gametes & Gromosomes.

KEYWORDS: Achrododonogesis ,Achromatopsia, Skeleton disorder, Genetic background, Clinical manifestation, Gene replacement therapy.

Introduction

Skeletal dysplasias are a heterogeneous collection of genetic disorders characterized by bone and cartilage abnormalities, and they encompass over 400 disorders. These disorders are rare individually, but collectively they are common, with an approximate incidence of one in 5000 births. Thus,radiologists occasionally encounter skeletal dysplasias in daily practice. Skeletal dysplasias that share similar radiologic patterns are grouped into a “skeletal dysplasia family” whose members generally have a common pathogenesis . This concept was originally proposed by Professor Juergen Spranger in the 1980s . He stated that different dysplasias that share similar skeletal patterns can be grouped into a “family”; on the basis of knowledge of the radiologic patterns of skeletal dysplasias, we can make the final diagnosis by means of provisional recognition of a pattern, followed by a more careful analysis; and bone dysplasia families may be the result of similar pathogenetic mechanisms.

The concept of a skeletal dysplasia family has been validated as it has been molecularly tested and refined. It allows a simple systematic stepwise approach to be applied to a spectrum of skeletal dysplasias. The modality of choice is radiography of the entire body, and a “babygram” is useful for pattern recognition. Prenatally, US together with CT or MRI is helpful for the diagnosis. The first step in the stepwise approach is the categorization of a certain case into a family based on pattern recognition. The second step, the final diagnosis, is based on more meticulous observations, such as the identification of different severities of the same pattern or of subtle but distinctive radiologic findings. The first step, based on pattern recognition,

is the key to making the right diagnosis. Since major skeletal dysplasia Androgenesis occurs when a zygote is produced with only paternal nuclear genes. During standard sexual reproduction, one female and one male parent each produce haploid gametes (such as a sperm or egg cell, each containing only a single set of chromosomes), which recombine to create offspring with genetic material from both parents. However, in androgenesis, there is no recombination of maternal and paternal chromosomes, and only the paternal chromosomes are passed down to the offspring the inverse of this is gynogenesis, where only the maternal chromosomes are inherited, which is more common than androgenesis. The offspring produced in androgenesis will still have maternally inherited mitochondria, as is the case with most sexually reproducing species.One of two things can occur to produce offspring with exclusively paternal genetic material: the maternal nuclear genome can be eliminated from the zygote, or the female can produce an egg with no nucleus, resulting in an embryo developing with only the genome of the male gamete.Androgenesis blurs the lines between sexual and asexual reproduction it is not strictly a form of asexual reproduction because both male and female gametes are required. However, it is not strictly a form of sexual reproduction because the offspring have uniparental nuclear DNA that has not undergone recombination, and the proliferation of androgenesis can lead to exclusively asexually reproducting species Androgenesis is a form of quasi-sexual reproduction in which a male is the sole source of the nuclear genetic material in the embryo. Two types of androgenesis occur in nature. Under the first type, females produce eggs without a nucleus and the embryo develops from the male gamete following fertilization. Evolution of this type of androgenesis is poorly understood as the parent responsible for androgenesis (the mother) gains no benefit from it. Ultimate factors driving the evolution of the second type of androgenesis are better understood. In this case, a zygote is formed between a male and a female gamete, but the female genome is eliminated. When rare, androgenesis with genome elimination is favoured because an androgenesis determining allele has twice the reproductive success of an allele that determines sexual reproduction. Paradoxically, except in hermaphrodites, a successful androgenetic strain can drive such a male-biased sex ratio that the population goes extinct. This likely explains why androgenesis with genome elimination appears to be rarer than androgenesis via non-nucleate eggs, although both forms are either very rare or remain largely undetected in nature. Nonetheless, some highly invasive species including ants and freshwater clams are androgenetic, for reasons that are largely unexplained. Researchers have described at least three forms of achondrogenesis, designated as type 1A, type 1B, and type 2. The types are distinguished by their signs and symptoms, inheritance pattern, and genetic cause. However, types 1A and 1B are often hard to tell apart without genetic testing.

Achondrogenesis type 1A, which is also called the Houston-Harris type, is the least well understood of the three forms. Affected infants have extremely short limbs, a narrow chest, short ribs that fracture easily, and a lack of normal bone formation in the skull, spine, and pelvis.

Achondrogenesis type 1B, also known as the Parenti-Fraccaro type, is characterized by extremely short limbs, a narrow chest, and a prominent, rounded abdomen. The fingers and toes are short and the feet may turn inward and upward . Affected infants frequently have a soft out-pouching around the belly-button (an umbilical hernia) or near the groin (an inguinal hernia).

Infants with achondrogenesis type 2, which is sometimes called the Langer-Saldino type, have short arms and legs, a narrow chest with short ribs, and underdeveloped lungs. This condition is also associated with a lack of ossification in the spine and pelvis. Distinctive facial features include a prominent forehead, a small chin, and, in some cases, an opening in the roof of the mouth . The abdomen is enlarged, and affected infants often have a condition called hydrops fetalis, in which excess fluid builds up in the body before

birth.Achondrogenesis refers to a group of fatal genetic disorders that affect the development of bone and cartilage.Babies with any of these disorders may have short limbs, small bodies, and cleft palate, as well as developmental differences.Most babies with achondrogenesis die before or shortly after birth because they are unable to breathe.There are three distinct types, and characteristics and inheritance patterns differ.

Type 1A

Type 1A, sometimes called the Houston-Harris type, causes a baby to have:
Short limbs
Bones that easily fracture
Abnormal bone development in the spine, skull, and pelvis
Facial abnormalities
A baby born with this type may have a small, underdeveloped chest, leading to life threatening breathing difficulties.

Type 1B

Type 1B, also known as the Fraccaro type, causes a baby to have:
A short trunk and limbs
Short fingers
Unusually shaped toes
A large stomach

Type 2

Type 2, or Langer-Saldino type, causes a baby to have:
A narrow chest
Small bones in the legs or arms
Underdeveloped lungs
Abnormal bone growth in the pelvis and spine
Some babies with this type also have swelling because fluid has built up in their stomachs.

Symptoms

1. Premature birth
2. Cleft palate – Incomplete closure of the roof of the mouth
3. Abnormal or ossified head shape
4. The short size of neck, limbs, and ribs
5. Flat vertebrae
6. Hydrops fetalis – Abnormal accumulation of fluid in the body
7. Small thoracic cage
8. Ear deformities
9. Corneal clouding

Other symptoms that are associated with Achondrogenesis are specific to its type, here are some other signs of this medical condition.

1. Achondrogenesis type IA symptoms:

2. Flat face
3. Protruding eyes and tongue
4. Short trunk and limbs
5. Short beaded ribs
6. Ossification of the skull
7. Abnormality of spine, pelvis, and extremities
8. Small thorax which may lead to early death
9. Achondrogenesis type IB symptoms:
10. Short trunk and limbs
11. Narrow chest
12. Prominent abdomen
13. Umbilical or inguinal hernia
14. Inward turned feet with short fingers and toes
15. Flat face with short neck and cleft palate
16. Abnormal thickening of the soft tissue in the neck
17. Achondrogenesis type II symptoms:
18. Narrow chest
19. Smaller arms or legs
20. Thin ribs
21. Flat vertebra
22. Underdeveloped lungs
23. Small chin
24. Cleft palate
25. Clubfeet
26. Abnormal formation of spine and pelvis
27. Hydrops fetalis

Type 1A-

Dysostosis Multiplex Family

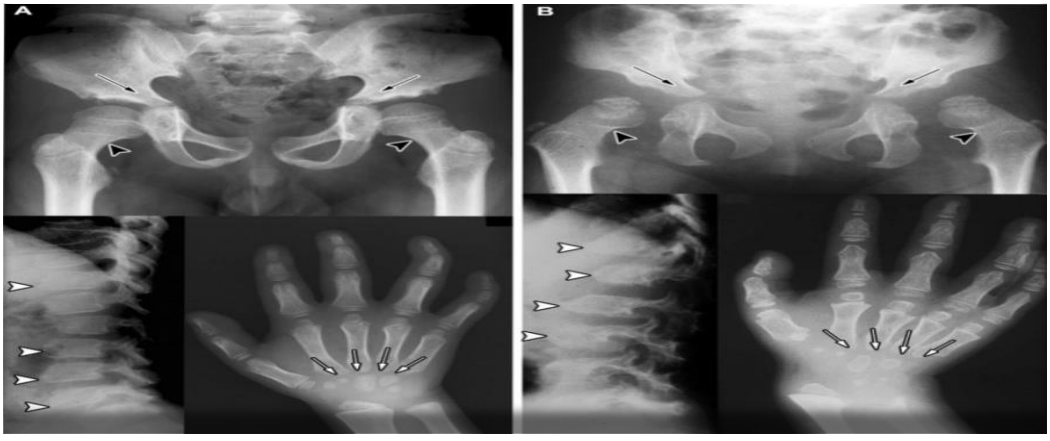
Dysostosis multiplex family refers to a heterogeneous group Of lysosome storage diseases (lysosomal enzyme deficien-Cies leading to accumulation of toxic large molecules) that Are caused by impaired degradation of glycosaminoglycans. This family includes mucopolysaccharidosis (MPS) (eg, Hurler syndrome [type I MPS], Hunter syndrome [type II MPS], Sanfilippo syndrome [type III MPS], Mosquito syndrome [type IV MPS], Maroteaux-Lamy syndrome [type VI MPS]), mucolipidosis (eg, I-cell disease [type II mucolipidosis], type III mucolipidosis), and oligosaccharidosis. Most Patients are asymptomatic at birth but develop physical and Mental disabilities in early childhood. Regardless of the ac-Cumulated substances, all of these disorders manifest with Similar skeletal changes, termed dysostosis multiplex.The pathogenesis underlying the findings of dysostosis Multiplex remains unknown. It is believed that exagger-Ation of eccentric bone modeling may account for most of The skeletal changes in this group of diseases. In tubular Bones, external bone resorption of the metaphysis is exces-Sive (excessive metaphyseal cutback), and internal bone re-Sorption of the diaphysis is augmented (excessive diaphyseal Drift). As a result, the metaphysis is constricted, while the Diaphysis is expanded. In general, the more prominent the Growth potential of a bone, the more severe its metaphyseal Constriction. However, it is

interesting that the short tubu-Lar bones show more conspicuous constriction at the ends Without a growth plate. Likewise, nontubular bones show Accentuation of their eccentric modeling. For example, thedistal ilia are constricted owing to a prominent cutback of The supra-acetabular region and greater sciatic notches, and Posterior scalloping of the vertebral body occurs as a result Of increased absorption on its posterior surface. Moreover, There are a few distinctive skeletal changes pinpointing to a Subtype of dysostosis multiplex.

Radiologic Approach

First Step.—Skeletal changes that can lead to a diagnosis of Dysostosis multiplex include macrocephaly, thick Calvaria, J-shaped sella, thick ribs with constriction of the Posterior costal end, thick clavicles with constriction of the Distal ends, hook-shaped vertebral bodies with pos-Terior vertebral scalloping, a flared iliac wing with overcon-Striction of the distal ilia (comma-shaped ilia and wine glass Appearance of the inner pelvic rim), coxa valga, metaphyseal Constriction and diaphyseal broadening of the long bones, Proximal metacarpal pointing and bullet-shaped Phalanges .

Second Step.—The overall severity of the dysostosis multi-Plex phenotype can help predict the diagnosis of a subtype, Which is confirmed by using an enzyme assay and/or mo-Lecular analysis. Hurler syndrome (type I MPS) and Maro-Teaux-Lamy syndrome (type VI MPS) are the most severe, Hunter syndrome (type lI MPS) and Morquio syn-Drome (type IV MPS) are of intermediate severity, And Sanfilippo syndrome (type III MPS) is the mildest in se-Verity. Morquio syndrome has distinctive skeletal changes, Including platyspondyly and epiphyseal dysplasia . Epiphyseal dysplasia is also seen in type III mmucolipiDosis and Maroteaux-Lamy syndrome. Neonatal forms Of dysostosis multiplex (eg, I-cell disease) are associated With secondary hyperparathyroidism leading to generalized Osteopenia and subperiosteal resorption and/or periosteal Cloaking . Neonatal dysostosis multiplex is also associ-Ated with stippled epiphyses of the tarsal and sacrococcygeal Regions.



Type 1B

Achondroplasia Family-

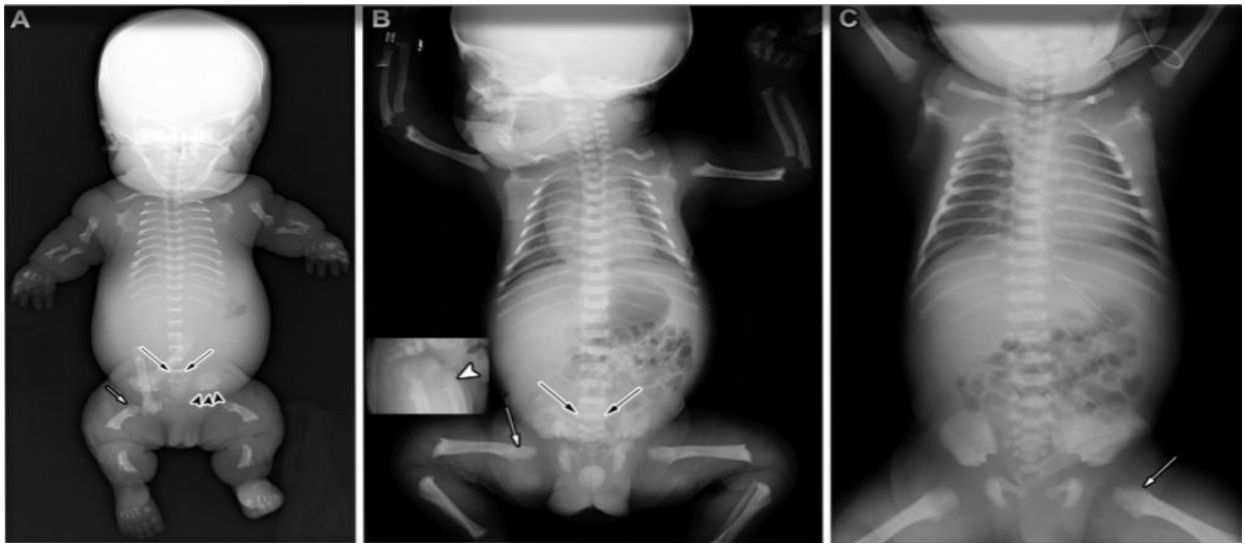
Achondroplasia family refers to a group of disorders that Are caused by abnormal activation of fibroblast growth fac-Tor receptor 3 (FGFR3) signaling . This family of skel-Etal dysplasias includes achondroplasia (prototype), than-Atophoric dysplasia (most severe), and hypochondroplasia (mildest in severity) . Normal FGFR3-mediated sig-Naling negatively regulates chondrogenesis owing to im-Pairment of chondrocyte proliferation and cartilage matrix Synthesis. The increased activity of FGFR3 inhibits longitu-Dinal endochondral bone growth but not transverse intram-Embranous bone formation . Affected individuals

have Short stature and short limbs, particularly of the proximal Segments (rhizomelic shortening). Achondroplasia is the Most common nonlethal short-limb skeletal dysplasia. Most Individuals with achondroplasia have only minor physical Morbidities. However, a small subset of affected infants and Young children have severe shortening of the skull base (where it grows by way of an endochondral process) with Foramen magnum stenosis that may cause apnea, qquadriPlegia, and even sudden death .
Thanatophoric (meaning "death bearing" in Greek) dysplasia is the most commonlethal skeletal dysplasia. Perinatal death is inevitable with Thoracic hypoplasia. Hypochondroplasia is a benign skeletal Dysplasia with moderate short stature.

Radiologic Approach-

First Step.—The radiologic hallmarks of the achondroplasia Family include shortening of the skull base; a narrow Thorax; platyspondyly; narrow caudal interpediculate dis-Tances; iliac hypoplasia with a trident appearance of the ac-Etabulum (trident ilia; corniculate protrusion of the lateral, Middle, and medial acetabulum); ovoid lucency of The proximal femora or proximal fem-Oral scooping (lateral view); and stubby tubular bones with Metaphyseal cupping, flaring, and corner spur.

Second Step.—The manifestations of thanatophoric dys-Plasia, achondroplasia and hypochondro-Plasia are quite homogeneous among themselves And readily distinguishable from each other. Intermediate Phenotypes are rare. Achondroplasia and thanatophoric Dysplasia manifest with all of the radiologic findings Just described. However, thoracic hypoplasia, platyspondyly, And shortening of tubular bones are more severe in thana-Tophoric dysplasia. The common subtype of thanatophoric Dysplasia manifests with distinctive French tele-Phone receiver–like bowing of the femurs, whereas type 2 Shows straight femurs and severe craniosynostosis with clo-Verleaf-shaped deformity. Hypochondroplasia demonstrates Only mild iliac hypoplasia and mild lucency of the proximal Femurs or mild proximal femoral scooping .



Type-2

Achondrogenesis is a very rare group of severe disorder that affects cartilage and Bone development . Achondrogenesis was described in 1925 by Donath and Vogl, and was first used in the medical literature in 1952 by an Italian patholo-Gist named Marico Fraccaro. By the 1970s, researchers concluded that achondrogenesis was a heterogeneous group of chondroplasia lethal to Neonate. Achondrogenesis type I and II were distinguished on the bases of radi-Ological and histological criteria. In 1983, a new

radiological classification of Achondrogenesis type I- ||by Whitley and Gorlin was adopted in the McKusick Criteria.Achodrogenesis was derived from Greek word meaning "not producing carti-Lage". It is a lethal disorder characterized by extreme micromelia, short Trunk, a disproportionately large cranium, and anasarca. Radiological Features are characteristic, with virtual absence of ossification of the vertebral Column, sacrum, pelvic bone, poor ossification of the skull, multiple rib fracture (Type IA and Type IB), and very short, broad bones of the extremities with Marked bowing.There are two types of Achondrogenesis. Type I is of an autosomal recessive Inheritance with subtype IA (Houston-Haris type) and type IB (Parenti-Fraccaro Type), and are often hard to tell apart without genetic testing. Type IA is the least well understood one of the three forms of achondrogenesis. It re-Sults from mutation in TRIP II gene which provides instructions for making a Protein GMAP-210. This protein plays a critical role in Golgi apparatus, a cell Structure in which newly produced proteins are modified so they can carry out Their function, while type IB results from mutation of SLC26A2 gene which Provides instructions for making a protein that is essential for the development Of cartilage and for its conversion to bone .Achondrogenesis type II (Langer-Saldino) is mostly sporadic and was initially Described by Langer et al. and Saldino. Achondrogenesis type II is Caused by de novo dominant mutations in collagen type II-I COL2AI gene. A transition of G2853 to A in axon 41 produced a substitution of Gly769 by Sir within the triple helical domain of the αI(II) chain type II collagen, inter-Rupting the mandatory Gly-X-Y triple sequence required for the normal forma-Tion of stable triple helical type II collagen molecules resulting in the complete Absence of type II collagen in the cartilage, which had a gelatinous composition. This type II collagen is essential for normal development of bones and oth-Er connective tissue that form the body's supportive framework .The children with achondrogenesis are usually born premature, stillborn or Die in the neonatal period mostly from respiratory failure . The incidence Is rare, most cases reported are delivered as stillbirth. Type I achondrogenesis is An autosomal recessive disorder, the risk of having another affected child is 25% For couple who had a first child with this condition . Type II incidence rate is Approximately 1/40,000 – 1/60,000 births.We reported this case study of a live term newborn infant with achondroge.

This type involved in tree condition

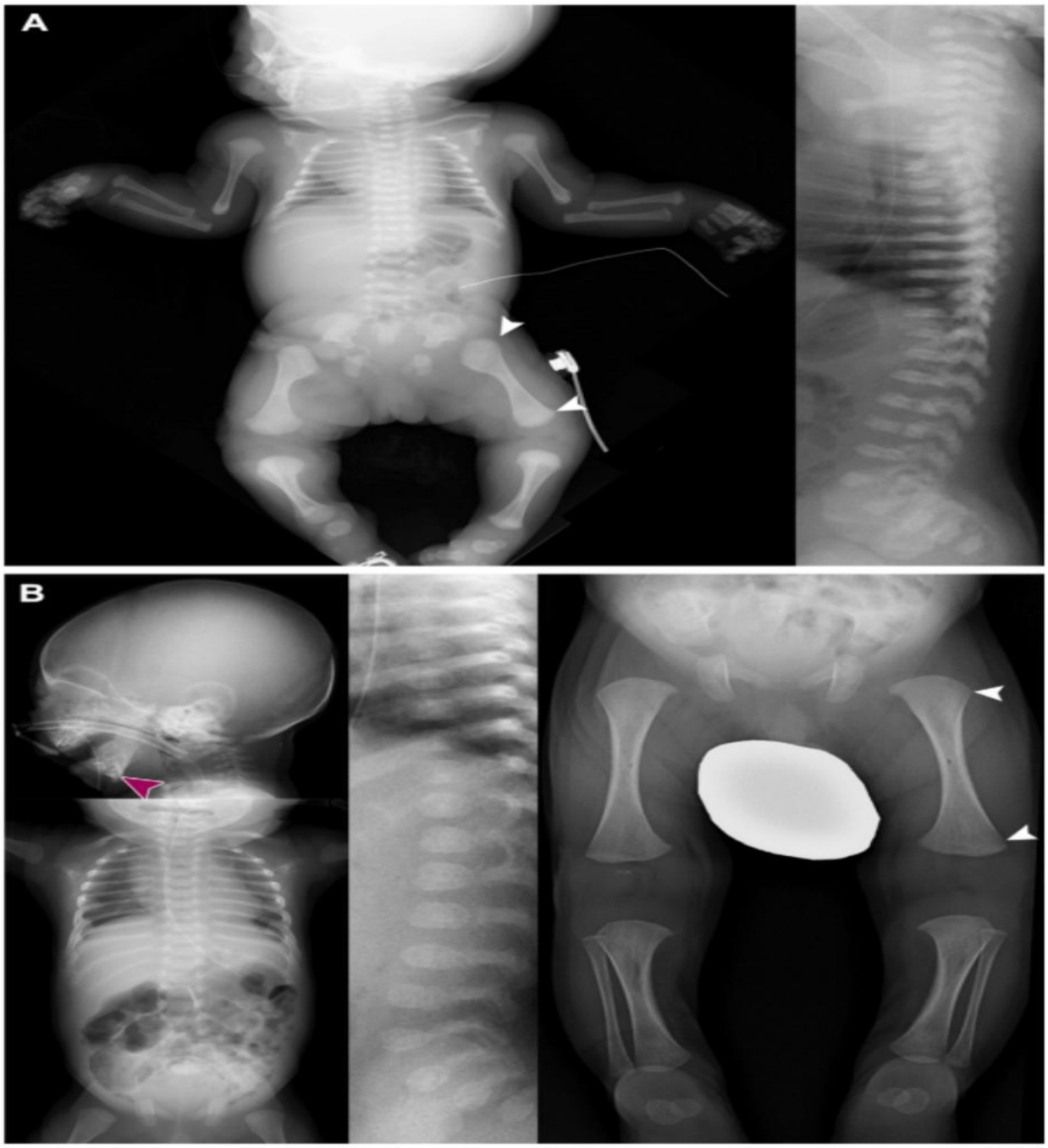
Diastrophic Dysplasia Family

The diastrophic dysplasia family comprises a spectrum of dis-Orders that are due to impairment of sulfate transport at the Cell membrane, and consequently intracellular sulfate deple-Tion and undersulfation of proteoglycans. This family Includes (in descending order of severity) achondrogenesis Type 1B, atelosteogenesis type 2, diastrophic dysplasia (proto-Type), and autosomal recessive multiple epiphyseal dysplasia. Undersulfated proteoglycans in the cartilage matrix And other connective tissues interfere with endochondral Bone growth and joint development. The interference of joint Development leads to contractures of the large joints, symph-Alangism, and characteristic hitchhiker thumbs (proximally Set, hypermobile, and abducted thumbs). Spontaneous hem-Orrhage of the auricular cartilage occasionally occurs in dia-Strophic dysplasia.Radiologic Approach

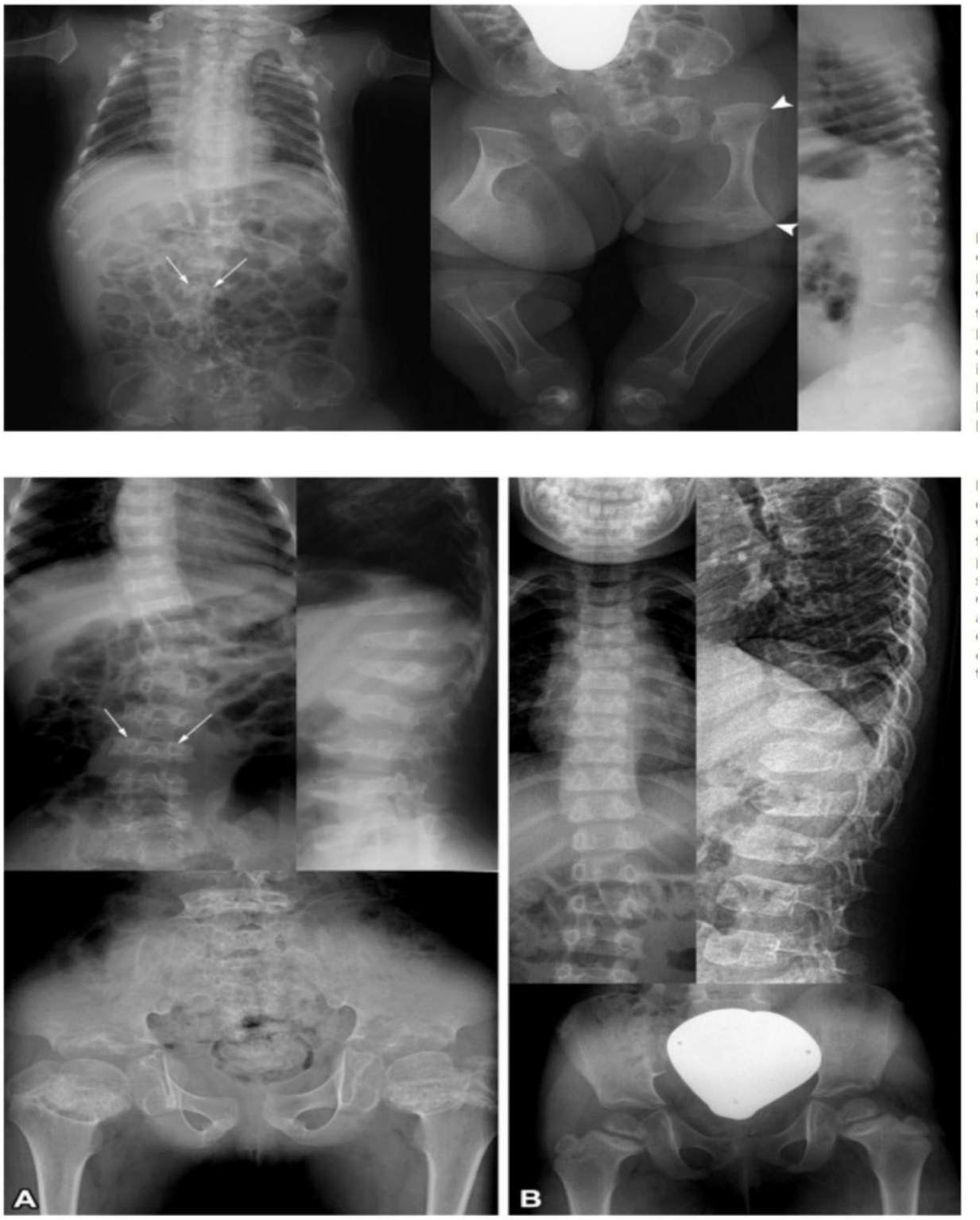
First Step-

The manifestation of diastrophic dysplasia represents an essential radiologic pattern of this familyThe hallmark findings include hitchhiker thumbs Due to laxity of the first carpometacarpal joint; short and Ovoid first metacarpals; irregular ossification of the short tubular bones, occasionally associated with proximal sympha-Langism; cervical kyphosis with hypoplasia of the midcervical Bodies; hypoplasia of the distal humeri (tapering on the lat-Eral view or bifid appearance on the frontal view); Elbow dislocation;

metaphyseal cupping of the tubular bones. Kniest and Stickler dysplasias. (A) Frontal And lateral radiographs of Kniest dysplasia in a newborn Show a broad thorax, platyspondyly with squared elon-Gated vertebral bodies, broad iliac crests and acetabula With constricted iliac bodies, and broad pubic and ischial Bones. The long bones show metaphyseal broadening With convex bone ends, resulting in the characteristic Dumbbell deformity of the long bones (arrowheads). The Distal femoral and proximal tibial epiphyses are not ossi-Fied. Coronal clefts in the L2 and L3 vertebral bodies also Are noted. (B) Frontal and lateral radiographs of Stickler Dysplasia in a newborn show micrognathia (red arrow Hrequirianasalairway),mildlydelayed vertebral Ossification, mild metaphyseal broadening of the tibiae.



Second Step.—2



Lethal variants of the diastrophic dysplasia Family, atelosteogenesis type 2 and achondrogene-Sis type 1B, recapitulate the pattern of diastrophic Dysplasia. However, shortening of the tubular bones is Much more severe and ossification of the short tubular bones Is irregular. The defective distal iliac ossification manifests as Inferiorly concave parachute-shaped ilia. An increased inter-Pedicular distance of the cervical and lumbar spine (“cobra” Sign]) is a useful sign to distinguish achondrogenesis

Larsen Dysplasia Family

The Larsen dysplasia family, or filaminopathy B ,(Comprises a group of disorders that are caused by defects of Filamin B, an anactin-binding cytoskeletal protein. This fam-Ily includes (in descending order of severity) atelosteogenesis type 1, atelosteogenesis type 3, and Larsen syndrome (proto-Type) (36–40). The clinical hallmarks of this family include Multiple joint dislocations, cylindric digits with broad tips, And facial abnormalities (prominent forehead, hypertelorism, Midface flattening, micrognathia). The skeletal changes are Probably due to anomalous skeletal patterning.

11. Diastrophic dysplasia family (in three stillborns).

(A) Frontal and lateral radiographs show diastrophic dyspla-Sia, with tapering (blue arrowheads) on the lateral views of The distal humeri or a bifid appearance on the frontal view (white arrowhead); elbow dislocation; tapered distal femurs (frontal view); stubby long tubular bones with metaphy-Seal broadening; shortening of the short tubular bones, Particularly of the second and fifth middle phalanges; and "hitchhiker" abducted thumbs (arrows) with short ovoid First metacarpals.

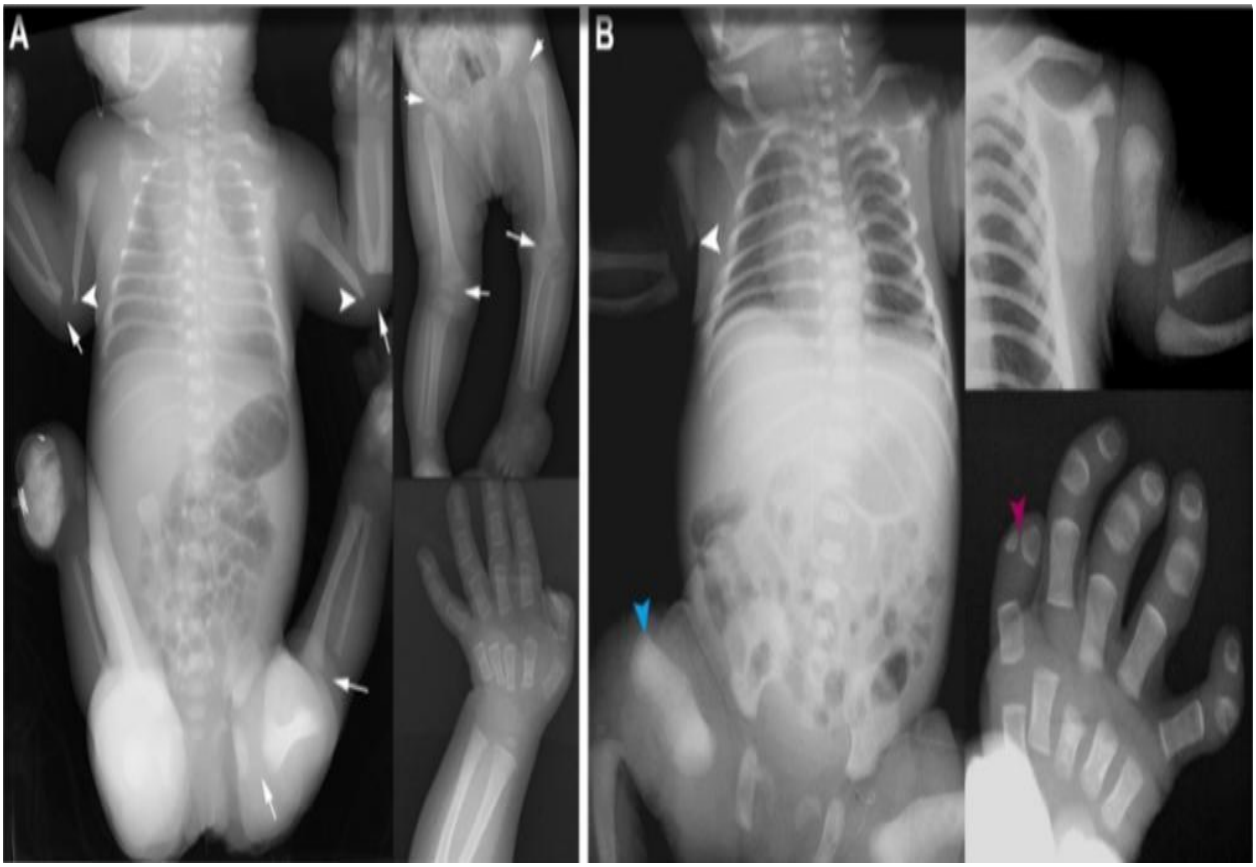
(B) Frontal and lateral radiographs show Atelosteogenesis type 2, with the same pattern of skeletal Changes as that of diastrophic dysplasia, including hitch-Hiker abducted thumbs (arrows); however, the overall find-Ings are much more severe and include platyspondyly and Defective ossification of the distal ilia. © Frontal radiograph Shows achondrogenesis type 1B, with much more severe Skeletal changes, including absence of vertebral ossification And abnormal tubulation of the long bones. However, distal Humeral tapering (arrowheads) and defective ossification Of the distal ilia (very short with inferiorly concave para-Chute-shaped ilia) are similar to those of atelosteogenesis Type 2. Increased interpedicular distance of the cervical and Lumbar spine (ie, "cobra" sign) (arrows) is distinctive.

Radiologic Approach

First Step.—The hallmarks of the Larsen dysplasia family (Fig 12) include dislocated large joints, particularly the knee joints (39). The tubular bones show undertubulation. In particular, the distal phalanges, particularly those of the thumbs, are short and broad. Distal humeral tapering (Fig 12A) and cervical kyphosis are also characteristic and are similar to those in The diastrophic dysplasia family.

Second Step.—Larsen syndrome manifests with mod-Est undertubulation (39). Atelosteogenesis type 1 (Fig 12B) and Atelosteogenesis type 3 show more severe undertubulation and Distal femoral tapering, as well as distal humeral shortening (36). The striking broadening of the short tubular bones in ate-Losteogenesis type 3 is termed tombstone appearance. Atelosteo-Genesis type 1 may manifest with a misshapen boomerang-like Deformity and absent ossification of the long bones. The short Tubular bones and the distal phalanges may be unossified in Atelosteogenesis type 1. The distal phalanges of the thumb may Be bifid. Given the malformed bones in atelosteogenesis type 12. Larsen dysplasia family (in two neonates). (A) Frontal radiographs in a neonate with Larsen dysplasia show multiple joint dislocations (arrows), Distal humeral tapering (arrowheads), and broadening of the short tubular bones. (B) Frontal radiographs in a neonate with atelosteogenesis type 1 show The same pattern of skeletal changes seen in A, including distal humeral tapering (white arrowhead) and broadening of the short tubular bones with Malaligned fingers. However, the long bones are also severely broad, and distal femoral tapering (blue arrowhead) is still seen. A bifid distal phalanx the undertubulation seen in Larsen dysplasia family disor-Ders may be the result of anomalous patterning rather than an Abnormal modeling process. With Larsen dysplasia family dis-Orders in general, the vertebral bodies are better ossified. How-Ever, the most severe

form of this family, atelosteogenesis type 1 (alternatively termed boomerang dysplasia), shows defective Vertebral ossification. Multiple coronal clefts are common in Atelosteogenesis types 1 and 3.



Otopalatodigital Syndrome Family

Otopalatodigital syndrome family, or filaminopathy A (Fig 13), Is a group of X-linked disorders caused by defects of another Actin-binding cytoskeletal protein, filamin A. This family in-Cludes otopalatodigital syndrome types 1 and 2, frontometaph-Yseal dysplasia, and Melnick-Needles syndrome (41–45). As a Rule with regard to X-linked disorders, males who have these Anomalies are severely affected and Melnick-Needles syndrome Is lethal for them. Filaminopathy A shares clinical features (fa-Cial abnormalities and cylindrical digits with broad tips) and Skeletal changes (undertubulation and anomalous skeletal pat-Terning) with filaminopathy B. However, joint dislocation is not A cardinal feature of filaminopathy A.

Radiologic Approach

First Step.—The skeletal hallmarks of the otopalatodigital syn-Drome family (Fig 13) include not only undertubulation and Bowing but also cortical irregularity of bones (43). The latter Is prominent in frontometaphyseal dysplasia and Melnick-Nee-Dles syndrome. The anomalous skeletal patterning primarily af-Fects the hands and feet. The craniofacial bones show variable Hyperostosis. The vertebral bodies are well ossified, and widen-Ing of the interpediculate distance is a distinctive finding.

Second Step.—Otopalatodigital syndrome type 1 (Fig 13A) Shows only mild undertubulation and bowing of the long Bones (43). By contrast, the hands and feet show striking Anomalies, including severe hypoplasia of the halluces; broad, Occasionally bifid distal phalanges of the thumbs; proximal Ulnar projection of the second metacarpal with large pseudo-Epiphysis; and deformed occasionally

supernumerary carpal And tarsal bones. Otopalatodigital syndrome type 2 (Fig 13B) Has a similar but more severe pattern of skeletal alterations (46). Thoracic hypoplasia with wavy ribs is related to the early Mortality with this disorder.

Frontometaphyseal dysplasia and Melnick-Needles syn-Drome share common manifestations, including twisted ribs And conspicuous undertubulation and bowing. Abnormal Skeletal patterning is not overt in these disorders. Supraorbital Hyperostosis and arachnodactyly are distinctive in frontome-Taphyseal dysplasia. Melnick-Needles syndrome manifests With a wavy appearance of the long bone.

REFERENCE -

1. Mortier GR, Cohn DH, Cormier-Daire V, et al. Nosology and classifi- cation of genetic skeletal disorders: 2019 revision. Am J Med Genet A 2019;179(12):2393-2419.
2. Spranger J. Pattern recognition in bone dysplasias. Prog Clin Biol Res 1985:200:315-342.
3. Spranger J. Bone dysplasia 'families.' Pathol Immunopathol Res 1988;7(1- 2):76-80.
4. Palmucci S, Attinà G, Lanza ML, et al. Imaging findings of mucopolysac- charidoses: a pictorial review. Insights Imaging 2013;4(4):443-459.
5. Lachman RS. Burton BK, Clarke LA, et al. Mucopolysaccharidosis IVA (Morquio A syndrome) and VI (Maroteaux-Lamy syndrome): un- der-recognized and challenging to diagnose. Skeletal Radiol 2014;43(3): 359-369.
6. Oussoren E, van Eerd D, Murphy E, et al. Mucolipidosis type III, a series of adult patients. J Inherit Metab Dis 2018;41(5):839-848.
7. Lai LM, Lachman RS. Early characteristic radiographic changes in muco- lipidosis II. Pediatr Radiol 2016;46(12):1713-1720.
8. Sargar KM, Singh AK, Kao SC. Imaging of Skeletal Disorders Caused by Fibroblast Growth Factor Receptor Gene Mutations. RadioGraphics 2017;37(6):1813-1830.
9. Langer LO Jr, Baumann PA, Gorlin RJ. Achondroplasia, Am J Roentgenol Radium Ther Nucl Med 1967;100(1):12-26.
10. Maroteaux P, Lamy M, Robert JM. Thanatophoric dwarfism [in French]. Presse Med (1893) 1967;75(49):2519-2524.
11. Hall BD, Spranger J. Hypochondroplasia: clinical and radiological aspectsIn 39 cases. Radiology 1979;133(1):95-100. 12. Fairbank HA. Dysplasia epiphysealis multiplex. Proc R Soc Med 1946:39:315-317.
12. Unger SL, Briggs MD, Holden P, et al. Multiple epiphyseal dysplasia: radiographic abnormalities correlated with genotype. Pediatr Radiol 2001;31(1):10-18.
13. Unger S, Bonafé L, Superti-Furga A. Multiple epiphyseal dysplasia: clinical and radiographic features, differential diagnosis and molecular basis. Best Pract Res Clin Rheumatol 2008;22(1):19-32.
14. Maroteaux P. Lamy M. Pseudo-achondroplastic forms of spondylo-epiphy- seal dysplasias [in French]. Presse Med (1893) 1959;67(10):383-386.
15. Narla A, Ebert BL. Ribosomopathies: human disorders of ribosome dys- function. Blood 2010;115(16):3196-3205.
16. Hästbacka J, Superti-Furga A, Wilcox WR, Rimoin DL, Cohn DH, Lander ES. Atelosteogenesis type II is caused by mutations in the diastrophic dys- plasia sulfate-transporter gene (DTDST): evidence for a phenotypic series involving three chondrodysplasias. Am J Hum Genet 1996;58(2):255-262.
17. Lamy M, Maroteaux P. Diastrophic nanism [in French]. Presse Med (1893) 1960;68:1977-1980.

18. Langer LO Jr. Diastrophic Dwarfism in Early Infancy. Am J Roentgenol Radium Ther Nucl Med 1965;93:399-404.
19. Ballhausen D. Bonafé L, Terhal P, et al. Recessive multiple epiphyseal dysplasia (rMED): phenotype delineation in eighteen homozygotes for DTDST mutation R279W. J Med Genet 2003;40(1):65-71.
20. Maroteaux P, Spranger J, Stanescu V, et al. Atelosteogenesis. Am J Med Genet 1982;13(1):15-25.
21. Stern HJ, Graham JM Jr, Lachman RS, et al. Atelosteogenesis type III: a distinct skeletal dysplasia with features overlapping atelosteogenesis and oto-palato-digital syndrome type II. Am J Med Genet 1990;36(2):183-195.
22. Farrington-Rock C, Firestein MH, Bicknell LS, et al. Mutations in two regions of FLNB result in atelosteogenesis I and III. Hum Mutat 2006;27(7):705-710. 39. Larsen LJ, Schottstaedt ER, Bost FC. Multiple congenital dislocations asso-ciated with characteristic facial abnormality. J Pediatr 1950;37(4):574-581.
23. Krakow D, Robertson SP, King LM, et al. Mutations in the gene encoding filamin Bdisruptvertebral segmentation, joint formation ands ntation, joint formation and skeletogenesis. Nat Genet 2004;36(4):405-410.
24. Gorlin RJ, Winter RB. Frontometaphyseal dysplasia: evidence for X-linked inheritance. Am J Med Genet 1980;5(1):81-84.
25. Melnick JC, Needles CF. An undiagnosed bone dysplasia. A 2 family study of 4 generations and 3 generations. Am J Roentgenol Radium Ther Nucl Med 1966;97(1):39-48.
26. Langer LO.Jr. The roentgenographic features of the oto-palato-digital (OPD) syndrome. Am J Roentgenol Radium Ther Nucl Med 1967;100(1):63-70.
27. Kozlowski K, Turner G, Scougall J, Harrington J. Oto-Palato-Digital syndrome with severe X-ray changes in two half brothers. Pediatr Radiol 1977;6(2):97-102.
28. Robertson SP. Otopalatodigital syndrome spectrum disorders: otopala- todigital syndrome types 1 and 2, frontometaphyseal dysplasia and Mel-Nick-Needles syndrome. Eur J Hum Genet 2007;15(1):3-9.
29. Savarirayan R, Cormier-Daire V, UngerS, etal. Oto-palato-digital syndrome,Type II: report of three cases with further delineation of the chondro-osseous morphology. Am J Med Genet 2000;95(3):193-200
30. Verma, A. (2008) Achondrogenesis. Spotters in Pediatrics, Jaypee Brothers Medical Publishers Ltd, New Delhi, 186-187.
31. Yadav, A. and Yadav, M. (2014) Achondrogenesis: A Lethal Chondrodystrophy IISS Case Reports and Reviews, 1, 1-3.
32. Saldino, R.M. (1971) Lethal Short Limbed Dwarfism: Achondrogenesis and Thana Tophoric Dwarfism, https://www.ajronline.org/
33. Genetic Home Reference (2008) Achondrogenesis. https://ghr.nlm.nih.gov/condition/achondrogenesis
34. Swarr, D.T. and Sutton, V.R. (2018) Skeletal Dysplasias in the Newborn: Diagnostic Evaluation and Developmental Genetics http://neareviews.aappublications org/cgi/content/full/ncoreviews
35. Chen, H. (2013) Achondrogenesis. (https://emedicine staging.medscape.com/article/941176-overview
36. Lee, H.S., Doh, J.W., Kim, C.J. and Chi, J.G. (2000) Achondrogenesis Type II (Lan ger-Saldino Achondrogenesis): A Case Report, Journal of Korean Medical Science, 15.604-608. https://doi.org/10.33-46//kims 2000.15.5.604

37. Jones, K.L. (2006) Achondrogenesis: Smith's Recognizable Patterns of Human Mal Formation. 6th Edition, Elsevier Saunders Publisher. Philadelphia, PA 11] NORD (National Organization for Rare Disorder (2017) Achondrogenesis [https://rarediscasem.org/rare-disease/achondrogenesis]
38. Maroteaux P. Brachytelephalangic chondrodysplasia punctata: a possible X-linked recessive form. Hum Genet 1989;82(2):167-170. 58. Happle R. X-linked dominant chondrodysplasia punctata: review of liter- ature and report of a case. Hum Genet 1979;53(1):65-73.
39. Gilbert EF, Opitz JM, Spranger JW, Langer LO Jr, Wolfson JJ, Viseskul C. Chondrodysplasia punctata-rhizomelic form: pathologic and radiologic studies of three infants. Eur J Pediatr 1976;123(2):89-109.
40. Franco B, Meroni G, Parenti G, et al. A cluster of sulfatase genes on Xp22.3: mutations in chondrodysplasia punctata (CDPX) and implications for warfarin embryopathy. Cell 1995;81(1):15-25.