A Review of the Principles of Radiological Assessment of Skeletal Dysplasias

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Introduction
Skeletal dysplasias are disorders associated with a generalized abnormality in the skeleton. Although individually rare, the overall birth incidence is estimated to be 1/5000 live births (1). Today, there are more than 450 well-characterized skeletal dysplasias classified primarily on the basis of clinical, radiographic, and molecular criteria (2). Half a century ago, in the 1960s, individuals with disproportionate short stature were diagnosed either as achondroplasia (short-limbed dwarfism) or Morquio syndrome (short-trunked dwarfism). In time, delineation of numerous entities not fitting these two “disorders” led experts to come up with a systematic approach. The “International Nomenclature of Constitutional Diseases of Bone” group, since its first publication in 1970, has intermittently classified these disorders (1970-1977-1983-1992-2001-2005-2009) (3). In the 1970s, the categories were purely clinical and descriptive. This later evolved into a combination of clinical, radiological and molecular knowledge as the pathogenetic mechanisms of various entities have been revealed. In the latest 2010 revision of the Nosology and Classification of Genetic Skeletal Disorders, an increase from 372 to 456 disorders was noted in the four years since the classification was last revisited in 2007 (2,4). Of these conditions, 316 are associated with one or more of 226 different genes. This increase reflects the
continuing delineation of unique phenotypes among short stature conditions, which in aggregate represent about 5% of children with birth defects (1). Some of the increase has also been driven by technological improvements in our ability to define the molecular genetic basis of these conditions, which is now known for 316 of the disorders (215 in the prior revision), with defects in 226 (140 previously) different genes. Table 1 provides a list of main groups in the latest published classification (2).

In daily practice however, clinicians dealing with patients with short stature may be confused with the molecular listings. It is therefore important to remember that an accurate diagnosis of a skeletal dysplasia is still based on detailed evaluation of clinical and radiographic [as well as chondro-osseous] findings. This review aims to outline the diagnostic approach to disproportionate short stature with special emphasis on radiological findings.

**Clinical Evaluation**

The accurate history regarding time of onset of short stature is essential prior to physical examination. Among the nearly 400 skeletal dysplasias, 100 or so have prenatal onset, while others may only present either as newborns or beyond 2 to 3 years of age (5). Individuals with disproportionate short stature are likely to be affected by a skeletal dysplasia. However, the abnormal proportions may not be readily recognizable. Therefore, whenever an individual presents with short stature, it is essential to measure body proportions. This should be done keeping in mind that some generalized bone mineralization abnormalities such as osteogenesis imperfects (OI), some osteosclerotic disorders, and hypophosphatasia may present with near normal proportions.

Anthropometric measurements such as upper/lower segment (U/L) ratio, sitting height, and arm span are routinely measured when a patient with short stature is evaluated. Sitting height is the measurement of head and trunk, and may be difficult to measure accurately due to the need of special equipment. The lower segment, however, is easier to measure (from symphysis pubis towards the floor medially to the heel). The upper segment can then be easily calculated by subtracting the lower segment from total height. Upper and lower segment measurements can be made in a standing or supine position. The mentioned ratios change with age. U/L ratio is 1.7 in the newborn; approximately 1.0 between ages 2-8 years; 0.95 as an adult. A short statured patient with short trunk will have decreased a U/L ratio, while an individual with normal trunk and relatively short limbs will have an increased U/L ratio (6).

Clinical evaluation also includes description of the limb involvement. Depending on the primarily involved segment of the limb, the condition can be described as rhizomelic (humerus and femur), mesomelic (radius, ulna, tibia and fibula) and acromelic (hands and feet). These descriptions help in differential diagnosis. It is noteworthy that a careful examination by an experienced clinical geneticist can sometimes narrow the list of dysmorphic entities to be considered even before the skeletal radiographs are analyzed (7).

Other clinical assessments such as immunological /hematological data as well as hair quality, cleft palate, eye abnormalities (myopia) and even internal organ abnormalities (cystic kidneys, hepatosplenomegaly) are important in skeletal dysplasia evaluation.

After obtaining a thorough family history, constructing a detailed pedigree and performing clinical examination, radiological assessment is likely to close the case in most skeletal dysplasias as many have distinctive radiological features in growing bones.

**Radiological Assessment**

Before giving details of the stepwise radiographic analysis for skeletal dysplasias, we would like to emphasize that a complete “genetic skeletal survey” is not necessary in patients with proportionate short stature, in which the differential diagnosis consists of constitutional delay, familial short stature, a small group of endocrinopathies and some dysmorphic syndromes. Their initial imaging assessment may warrant a left hand and wrist radiograph for bone age determination. This will protect children from unnecessary radiation exposure.

The “genetic skeletal survey” should include anteroposterior (AP), and lateral views of the skull, AP and lateral views of the entire spine, and AP views of the pelvis and all four extremities, with separate AP views of the hands and feet [A lateral view of the knee can be helpful to diagnose a recessive form of multiple epiphyseal dysplasia (MED) associated with multilayered patella] (7). In adult patients, it is mandatory to try to obtain prepubertal skeletal radiographs. Once the epiphyses have fused to the metaphyses, diagnosis may be very difficult. After obtaining the radiographs, a three-step assessment will be helpful in trying to make a specific diagnosis.

**Step I (Assessment of Disproportion):** An assessment of disproportion similar to the one made clinically is repeated looking at the radiographs. A quick look at the spine will readily help decide if there is platyspondyly leading to short-trunked disproportion. Similarly, looking at the
| Name of Disorder | Inheritance | MIM No. | Locus | Gene | Protein |
|------------------|-------------|---------|-------|------|---------|
| **1. FGFR3 group** |             |         |       |      |         |
| Thanatophoric dysplasia type 1 (TD1) | AD | 187600 | 4p16.3 | FGFR3 | FGFR3 |
| Thanatophoric dysplasia type 2 (TD2) | AD | 187601 | 4p16.3 | FGFR3 | FGFR3 |
| SADDAN (severe achondroplasia-developmental delay- acanthosis nigricans) | AD | 134934 |       |       |         |
| Achondroplasia | AD | 100800 | 4p16.3 | FGFR3 | FGFR3 |
| Hypochondroplasia | AD | 146000 | 4p16.3 | FGFR3 | FGFR3 |
| Hypochondroplasia-like dysplasia | AD, SP |       |       |       |         |
| Camptodactyly, tall stature, and hearing loss syndrome (CATSHL) | AD | 187600 | 4p16.3 | FGFR3 | FGFR3 |
| **2. Type 2 collagen group** |             |         |       |      |         |
| Achondrogenesis type 2 (ACG2; Langer-Saldino) | AD | 200610 | 12q13.1 | COL2A1 | Type 2 collagen |
| Platyspondylic dysplasia, Torrance type | AD | 151210 | 12q13.1 | COL2A1 | Type 2 collagen |
| Hypochondrogenesis | AD | 200610 | 12q13.1 | COL2A1 | Type 2 collagen |
| Spondyloepiphyseal dysplasia congenital (SEDC) | AD | 183900 | 12q13.1 | COL2A1 | Type 2 collagen |
| Spondyloepimetaphyseal dysplasia Strudwick type | AD | 184250 | 12q13.1 | COL2A1 | Type 2 collagen |
| Kniest dysplasia | AD | 156550 | 12q13.1 | COL2A1 | Type 2 collagen |
| Spondyloepiphyseal dysplasia | AD | 271700 | 12q13.1 | COL2A1 | Type 2 collagen |
| Mild SED with premature onset arthrosis | AD | 12q13.1 | COL2A1 | Type 2 collagen |
| SED with metatarsal shortening (formerly Czech dysplasia) | AD | 609162 | 12q13.1 | COL2A1 | Type 2 collagen |
| Stickler syndrome type 1 | AD | 108300 | 12q13.1 | COL2A1 | Type 2 collagen |
| **3. Type 11 collagen group** |             |         |       |      |         |
| Stickler syndrome type 2 | AD | 604841 | 1p21 | COL11A1 | alpha-1 chain |
| Marshall syndrome | AD | 154780 | 1p21 | COL11A1 | alpha-1 chain |
| Fibrochondrogenesis | AR | 288520 | 1p21 | COL11A1 | alpha-1 chain |
| Otospondyloepiphysseal dysplasia (OSMED), recessive type | AR | 215150 | 6p21.3 | COL11A2 | Type 11 collagen alpha-2 chain |
| Otospondyloepiphysseal dysplasia (OSMED), dominant type (Weissenbacher-Zweymüller syndrome, Stickler syndrome type 3) | AD | 215150 | 6p21.3 | COL11A2 | Type 11 collagen alpha-2 chain |
| **4. Sulphation disorders group** |             |         |       |      |         |
| Achondrogenesis type 1B (ACG1B) | AR | 600972 | 5q32-33 | DTDST | SLC26A2 sulfate transporter |
| Atelosteogenesis type 2 (AO2) | AR | 256050 | 5q32-33 | DTDST | SLC26A2 sulfate transporter |
| Diastrophic dysplasia (DTD) | AR | 226900 | 5q32-33 | DTDST | SLC26A2 sulfate transporter |
| MED, autosomal recessive type (rMED; EDM4) | AR | 226900 | 5q32-33 | DTDST | SLC26A2 sulfate transporter |
| SEMD, PAPSS2 type | AR | 603005 | 10q23-q24 | PAPSS2 | PAPS-Synthetase 2 |
Table 1. (continued)

| Disorder                                                                 | Type       | Chromosome | Genes or Proteins | Conditions                          |
|--------------------------------------------------------------------------|------------|------------|-------------------|-------------------------------------|
| Chondrodysplasia with congenital joint dislocations, CHST3 type          | AR         | 10q22.1    | CHST3             | Carbohydrate sulfotransferase 3; Chondroitin 6-sulfotransferase |
| Ehlers-Danlos syndrome, CHST14 type ("musculo-skeletal variant")         | AR         | 15q14      | CHST14            | Carbohydrate sulfotransferase 14; Dermatan 4-sulfotransferase |

5. Perlecan group

| Disorder                                                                 | Type       | Chromosome | Genes or Proteins | Conditions                          |
|--------------------------------------------------------------------------|------------|------------|-------------------|-------------------------------------|
| Dyssegmental dysplasia, Silverman-Handmaker type                          | AR         | 1q36-34    | PLC (HSPG2)       | Perlecan                            |
| Dyssegmental dysplasia, Roland-Desbuquois                                  | AR         | 1q36-34    | PLC (HSPG2)       | Perlecan                            |
| Schwartz-Jampel syndrome (myotonic chondrodystrophy)                      | AR         | 1q36-34    | PLC (HSPG2)       | Perlecan                            |

6. Aggrecan group

| Disorder                                                                 | Type       | Chromosome | Genes or Proteins | Conditions                          |
|--------------------------------------------------------------------------|------------|------------|-------------------|-------------------------------------|
| Dyssegmental dysplasia, Silverman-Handmaker type                          | AR         | 1q36-34    | PLC (HSPG2)       | Perlecan                            |
| Dyssegmental dysplasia, Roland-Desbuquois                                  | AR         | 1q36-34    | PLC (HSPG2)       | Perlecan                            |
| Schwartz-Jampel syndrome (myotonic chondrodystrophy)                      | AR         | 1q36-34    | PLC (HSPG2)       | Perlecan                            |

7. Filamin group and related disorders

| Disorder                                                                 | Type       | Chromosome | Genes or Proteins | Conditions                          |
|--------------------------------------------------------------------------|------------|------------|-------------------|-------------------------------------|
| Frontometaphyseal dysplasia                                              | XLD        | Xq28       | FLNA              | Filamin A                           |
| Osteodysplasty Melnick-Needles                                           | XLD        | Xq28       | FLNA              | Filamin A                           |
| Otopalatodigital syndrome type 1 (ODP1)                                  | XLD        | Xq28       | FLNA              | Filamin A                           |
| Otopalatodigital syndrome type 2 (ODP2)                                  | XLD        | Xq28       | FLNA              | Filamin A                           |
| Atelosteogenesis type 1 (AO1)                                             | AD         | 3p14.3     | FLNB              | Filamin B                           |
| Atelosteogenesis type 3 (AO3)                                             | AD         | 3p14.3     | FLNB              | Filamin B                           |
| Larsen syndrome                                                          | AD         | 3p14.3     | FLNB              | Filamin B                           |
| Spondylo-carpal-tarsal dysplasia                                         | AR         | 5q35.1     | SH3PD28           | TKS4                                |
| Franck-ter-Haar syndrome                                                  | AD         | 5q35.1     | SH3PD28           | TKS4                                |

8. TRPV4 group

| Disorder                                                                 | Type       | Chromosome | Genes or Proteins | Conditions                          |
|--------------------------------------------------------------------------|------------|------------|-------------------|-------------------------------------|
| Metatropic dysplasia                                                    | AD         | 12q24.1    | TRPV4             | Transient receptor potential cation channel, subfamily V, member 4 |
| Spondyloepimetaphyseal dysplasia, Maroteaux type (Pseudo-Morquio syndrome type 2) | AD         | 12q24.1    | TRPV4             | Transient receptor potential cation channel, subfamily V, member 4 |
| Spondylometaphyseal dysplasia, Kozlowski type                           | AD         | 12q24.1    | TRPV4             | Transient receptor potential cation channel, subfamily V, member 4 |
| Brachyolmia, autosomal dominant type                                     | AD         | 12q24.1    | TRPV4             | Transient receptor potential cation channel, subfamily V, member 4 |
| Familial digital arthropathy with brachydactyly                         | AD         | 12q24.1    | TRPV4             | Transient receptor potential cation channel, subfamily V, member 4 |

9. Short-rib dysplasias (with or without polydactyly) group

| Disorder                                                                 | Type       | Chromosome | Genes or Proteins | Conditions                          |
|--------------------------------------------------------------------------|------------|------------|-------------------|-------------------------------------|
| Chondroectodermal dysplasia (Ellis-van Creveld)                          | AR         | 4p16       | EVC1, EVC2        | EvC gene 1, EvC gene 2              |
| SRP type 1/3 (Saldino-Noonan/Verma-Naumoff)                             | AR         | 4p16       | DYNC2H1           | Dynein, cytoplasmic 2, heavy chain 1 |
| SRP type 1/3 (Saldino-Noonan/Verma-Naumoff)                             | AR         | 3q25.33    | IFT80             | Intraflagellar transport 80 (homolog of) |
| SRP type 1/3 (Saldino-Noonan/Verma-Naumoff)                             | AR         | 3q25.33    | IFT80             | Intraflagellar transport 80 (homolog of) |
| SRP type 2 (Majewski)                                                   | AR         | NEK1       | Nima related kinase 1 |
| SRP type 4 (Beemer)                                                     | AR         | 269860     |                  |                                     |
Table 1. (continued)

| Condition                                                                 | Mode | Chromosome  | Gene (Gene ID) | Description                                                                 |
|---------------------------------------------------------------------------|------|-------------|----------------|----------------------------------------------------------------------------|
| Oral-Facial-Digital syndrome type 4 (Mohr-Majewski)                        | AR   | 11q22.3     | DYNC2H1        | Dynein, cytoplasmic 2, heavy chain 1                                        |
| Asphyxiating thoracic dysplasia (ATD; Jeune)                              | AR   | 3q25.33     | IFT80          | Intraflagellar transport 80 (homolog of)                                    |
| Asphyxiating thoracic dysplasia (ATD; Jeune)                              | AR   | 208500      |                |                                                                            |
| Thoracolaryngopelvic dysplasia (Barnes)                                   | AD   | 187760      |                |                                                                            |

10. Multiple epiphyseal dysplasia and pseudoachondroplasia group

| Condition                                                                 | Mode | Chromosome | Gene (Gene ID) | Description                                                                 |
|---------------------------------------------------------------------------|------|------------|----------------|----------------------------------------------------------------------------|
| Thoracolaryngopelvic dysplasia (Barnes)                                   | AD   | 187760     |                |                                                                            |

11. Metaphyseal dysplasias

| Condition                                                                 | Mode | Chromosome | Gene (Gene ID) | Description                                                                 |
|---------------------------------------------------------------------------|------|------------|----------------|----------------------------------------------------------------------------|
| Tiefenbacher type                                                          | AD   | 156500     | COL10A1        | Collagen 10 alpha-1 chain                                                   |
| Cartilage-hair-hypoplasia (CHH; metaphyseal dysplasia, McKusick type)     | AR   | 250250     | RMRP           | RNA component of RNase H                                                   |
| Metaphyseal dysplasia, Jansen type                                         | AD   | 156400     | PTH1R          | PTH/PTHrP receptor 1                                                        |
| Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (Shwachman-Bodian-Diamond syndrome, SBDS) | AD   | 260400     | SBDS           | SBDS gene, function unclear                                                |
| Metaphyseal anadysplasia type 1                                           | AD/AR| 309645     | MMP13          | Matrix metalloproteinase 13                                                |
| Metaphyseal anadysplasia type 2                                           | AR   | 20q13.12   | MMP9           | Matrix metalloproteinase 9                                                  |
| Metaphyseal dysplasia, Spahr type                                         | AR   | 250400     |                |                                                                            |
| Metaphyseal acrocephalodyplasia (various types)                           | AR   | 250215     |                |                                                                            |
| Genochondromatosis (type1/type 2)                                         | AD/SP| 137360     |                |                                                                            |
| Metaphyseal chondromatosis with D-2-hydroxyglutaric aciduria              | AR/SP| 271550     |                |                                                                            |

12. Spondylometaphyseal dysplasias (SMD)

| Condition                                                                 | Mode | Chromosome | Gene (Gene ID) | Description                                                                 |
|---------------------------------------------------------------------------|------|------------|----------------|----------------------------------------------------------------------------|
| Odontoachondrodysplasia (OCCD)                                           | AR   | 184260     |                |                                                                            |
| Spondylometaphyseal dysplasia Kozlowski type                             | AD   | 184252     |                |                                                                            |
| Spondylometaphyseal dysplasia, Sutcliffe/corner fracture type             | AD   | 184255     |                |                                                                            |
| SMD with severe genu valgum                                              | AD   | 184253     |                |                                                                            |
| SMD with cone-rod dystrophy                                              | AR   | 608940     |                |                                                                            |
| SMD with retinal degeneration, axial type                                 | AR   | 602271     |                |                                                                            |
| Dysspondylochondromatosis                                                | SP   |            |                |                                                                            |
| Chietro-spondylochondromatosis                                           | SP   |            |                |                                                                            |
### Table 1. (continued)

#### 13. Spondylo-epi(-meta)physeal dysplasias (SE(M)D)

| Type                                                                 | Mode | Chromosome | Gene/Location                                                                 | Description                                                                 |
|----------------------------------------------------------------------|------|------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Dyggve-Melchior-Clausen dysplasia (DMC)                               | AR   | 18q12-21.1 | DYM                                                                          | Dymeclin                                                                    |
| Immuno-osseous dysplasia (Schimke)                                    | AR   | 2q34-36    | SMARCAL1                                                                     | SWI/SNF-related regulator of chromatin subfamily A-like protein 1           |
| SED Wolcott-Rallison type                                            | AR   | 2p12       | EIF2AK3                                                                      | Translation initiation factor 2-alpha kinase-3                              |
| SEMD Matrilin type                                                   | AD   | 11q22.3    | MMP13                                                                        | Matrix metalloproteinase 1                                                  |
| Metatropic dysplasia (various forms)                                 | AD/AR| 156530     |                                                                              |                                                                             |
| SED tarda, X-linked (SED-XL)                                         | XLR  | Xp22       | SEDL                                                                         | Sedlin                                                                      |
| SPONASTRIME dysplasia                                                | AR   | 271510     |                                                                              |                                                                             |
| SEMD short limb - abnormal calcification type                        | AR   | 1q23       | DDR2                                                                         | Discoidin domain receptor family, member2                                   |
| SEMD with joint laxity (SEMD-JL) Beighton type                       | AR   | 271640     |                                                                              |                                                                             |
| Spondylo-megaepiphyseal-metaphyseal dysplasia (SMMD)                 | AR   | 4p16.1     | NKX3                                                                         | NK3 Homeobox                                                                 |
| Spondyloepiphyseal Ehlers-Danlos syndrome                            | AR   | 11p.11.2   | SLC39A13                                                                     | Zinc transporter ZIP13                                                      |
| SEMD with joint laxity (SEMD-JL) leptodactylic or Hall type          | AD   | 603546     |                                                                              |                                                                             |
| Platyspondly (brachyolmia) with amelogenesis imperfecta               | AD   | 601216     |                                                                              |                                                                             |
| Late onset SED, autosomal recessive type                              | AR   | 609223     |                                                                              |                                                                             |
| Brachyolmia, Hobaek, and Toledo types                                | AR   | 271530, 271630 |                                                                              |                                                                             |

#### 14. Severe spondylodyplastic dysplasias

| Type                                                                 | Mode | Chromosome | Gene/Location                                                                 | Description                                                                 |
|----------------------------------------------------------------------|------|------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Achondrogenesis type 1A (ACG1A)                                       | AR   | 14q32.12   | TRIP11                                                                       | Golgi-microtubule-associated protein, 210-kDa; SMAP210                      |
| SMD Sedaghatian type                                                 | AR   | 250220     |                                                                              |                                                                             |
| Severe SMD Sedaghatian-like                                          | AR   | 7q11       | SBDS                                                                         | SBDS gene, function still unclear                                          |
| Opsismodyplasia                                                      | AR   | 258480     |                                                                              |                                                                             |
| Schneckenbecken dysplasia                                            | AR   | 269250     | 1p31.3                                                                       | SLC35D1                                                                     |

#### 15. Acromelic dysplasias

| Type                                                                 | Mode | Chromosome | Gene/Location                                                                 | Description                                                                 |
|----------------------------------------------------------------------|------|------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Trichorhinophalangeal dysplasia types 1/3                            | AD   | 8q24       | TRPS1                                                                        | Zinc finger transcription factor                                           |
| Trichorhinophalangeal dysplasia type 2 (Langer- Giedion)             | AD   | 8q24       | TRPS1, EXT1                                                                  | Zinc finger transcription factor                                           |
| Acrocapitofemoral dysplasia                                          | AR   | 2q33-q35   | IHH                                                                           | Indian hedgehog                                                            |
| Cranioectodermal dysplasia (Levin-Sensenbrenner) type 1              | AR   | 218330     |                                                                              |                                                                             |
| Cranioectodermal dysplasia (Levin-Sensenbrenner) type 2              | AR   | 2p24.1     | WDR35                                                                        | WD repeat-containing protein 35                                            |
| Geleophysic dysplasia                                                | AR   | 9q34.2     | ADAMTS2                                                                      | ADAMTS-like protein 2                                                      |
| Geleophysic dysplasia, other types                                   | AR   |            |                                                                              |                                                                             |
| Acromicric dysplasia                                                 | AD   | 102370     |                                                                              |                                                                             |
| Acrodysostosis                                                      | AD   | 101800     |                                                                              |                                                                             |
| Angel-shaped phalangeopiphysal dysplasia (ASPED)                     | AD   | 105835     |                                                                              |                                                                             |
| Acrolaryngeal dysplasia                                             | AD   |            |                                                                              |                                                                             |
| Craniofacial conodysplasia                                          | AD   |            |                                                                              |                                                                             |
| Familial digital arthropathy with brachydactyly                     | AD   | 606835     |                                                                              |                                                                             |
| Saldino-Mainzer dysplasia                                           | AR   | 266920     |                                                                              |                                                                             |
| 16. Acromesomelic dysplasias |  |
|-------------------------------|------------------|
| Acromesomelic dysplasia type Maroteaux | AR 602875 9p13-12 NPR2 Natriuretic peptide receptor 2 |
| Grebe dysplasia | AR 200700 20q11.2 GDF5 Growth and differentiation factor 5 |
| Fibular hypoplasia and complex brachydactyly (Du Pan) | AR 228900 20q11.2 GDF5 Growth and differentiation factor 5 |
| Acromesomelic dysplasia with genital anomalies | AR 609441 4q23-24 BMPR1B Bone morphogenetic protein receptor 1B |
| Acromesomelic dysplasia, Osebold-Remondini type | AD 112910 |

| 17. Mesomelic and rhizo-mesomelic dysplasias |  |
|-----------------------------------------------|------------------|
| Dyschondrosteosis (Leri-Weill) | Pseudo-AD 127300 Xpter-p22.32 SHOX Short stature - homeobox gene |
| Langer type (homozygous dyschondrosteosis) | Pseudo-AR 249700 Xpter-p22.32 SHOX Short stature - homeobox gene |
| Robinow syndrome, recessive type | AR 268310 9q22 ROR2 Receptor tyrosine kinase-like orphan receptor 2 |
| Robinow syndrome, dominant type | AD 180700 |
| Mesomelic dysplasia, Korean type | AD 2q24-32 |
| Mesomelic dysplasia, Kantaputra type | AD 156232 2q24-32 |
| Mesomelic dysplasia, Nievergelt type | AD 163400 |
| Mesomelic dysplasia, Kozlowski-Readon type | AD 249710 |
| Mesomelic dysplasia with acral synostoses (Verloes-David-Pfeiffer type) | AD 600383 8q13 SULF1 and SLCOSA1 Heparan sulfatase 6-O-endosulfatase 1 and solute carrier organic anion transporter family member SA1 |
| Mesomelic dysplasia, Savarirayan type (Triangular Tibia-Fibular Aplasia) | SP 605274 |

| 18. Bent bones dysplasias |  |
|--------------------------|------------------|
| Campomelic dysplasia (CD) | AD 114290 17q24.3-25.1 SOX9 SRY-box 9 |
| Stüve-Wiedemann dysplasia | AR 601559 5p13.1 LIFR Leukemia inhibitory factor receptor |
| Cumming syndrome | 211890 |
| Kyphomelic dysplasia, several forms | 211350 |

Bent bones at birth can be seen in a variety of conditions, including Antley-Bixler syndrome, cartilage-hair hypoplasia, hypophosphatasia, osteogenesis imperfecta, dyssegmental dysplasia, and others

| 19. Slender bone dysplasia Group |  |
|----------------------------------|------------------|
| 3-M syndrome (3M1) | AR 273750 6p21.1 CUL7 Cullin 7 |
| 3-M syndrome (3M2) | AR 619921 2q35 PBSL1 Obscurin-like 1 |
| Kenny-Caffey dysplasia type 1 | AR 244460 1q42-q43 TBCE tubulin-specific chaperone E |
| Kenny-Caffey dysplasia type 2 | AD 127000 |
| Microcephalic osteodysplastic primordial dwarfism type 1/3 (MOPD1) | AR 210710 2q |
| Microcephalic osteodysplastic primordial dwarfism type 2 (MOPD2; Majewski type) | AR 210720 21q PCNT2 Pericentrin 2 |
| Microcephalic osteodysplastic dysplasia, Saul-Wilson type | AR |
| IMAGE syndrome (Intrauterine Growth Retardation, Metaphyseal Dysplasia, Adrenal Hypoplasia, and Genital Anomalies) | XL/AD 300290 |
extremities may help defining rhizomelia, mesomelia, and acromelia. It should be noted that these descriptive terms of limb segments may be more correct radiologically as the clinical visualization is accentuated by skin folds or other tissues rather than the length of the underlying bone. Rhizomelic chondrodysplasia punctata (CDP) is a good example of a rhizomelic skeletal dysplasia diagnosed with the additional radiological findings of punctate calcifications (stippling) and coronal clefted vertebrae (Figure 1). Mesomelia alone will suggest a long heterogeneous differential diagnosis list of mesomelic dysplasias. Presence of acromelia is important to recognize, as it may be an isolated finding. Presence of isolated acromelia may suggest skeletal dysplasias such as acromicric dysplasia, acrodysostosis, geleophysic dysplasia or nonskeletal dysplasias such as the brachydactilies. Brachydactyly type E, characterized by a short fourth metacarpal bone may support clinical or laboratory findings in Turner syndrome and pseudohypoparathyroidism, respectively. The absence of proportional acromelic shortening is also very important to remember in spondyloepiphyseal dysplasia congenita (and most forms of type II collagenopathies) (7).

Step II (Assessment of Epiphyseal/Metaphyseal/ Diaphyseal Ossification): Abnormal development of epiphyses, metaphyses, and diaphyses has given rise to the original nomenclature using those site names (Figure 2). An overall look at the radiological survey will suggest epiphyseal dysplasias by the presence of very small (delayed ossification) and/or irregularly ossified epiphyses (Figure 3a). If the metaphyses are widened, flared, and/or irregular, the diagnosis of a form of metaphyseal dysplasia is established (Figure 3b, 3c and Figure 4). Diaphyseal dysplasia is present when there is diaphyseal widening and/or cortical thickening or marrow space expansion or restriction. Isolated vertebral involvement without changes in the growth plate region in a patient with short-trunked

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Table 1. (continued)

| Dysplasias with multiple joint dislocations |
|--------------------------------------------|
| Desbuquois dysplasia (with accessory ossification center in digit 2) | AR | 251450 | 17q25.3 | CANT1 |
| Desbuquois dysplasia with short metacarpals and elongated phalanges | AR | 251450 | 17q25.3 | CANT1 |
| Desbuquois dysplasia (other variants with or without accessory ossification center) | AR | 264180 |

| Pseudodiastrophic dysplasia |
|-----------------------------|
| AR | 264180 |

Modified and reproduced from Warman ML et al. Nosology and Classification of Genetic Skeletal Disorders: 2010 Revision. Am J Med Genet 155A:943-988.
short stature should suggest brachyolmia (Figure 5a and 5b). Figure 3 helps to combine the aforementioned skeletal involvement, such as forms of spondyloepiphyseal dysplasia and the group of spondylo-epi-(meta)-physeal dysplasias.

Figure 3. a,b,c. Radiographic manifestations of the dysplasias

Figure 4. Radiographic abnormalities helpful in classification of skeletal dysplasias

Figure 5. a,b. Brachyolmia. Note platyspondyl and overfaced pedicles

Figure 6. Fractures in Osteogenesis Imperfecta

Figure 7. Osteopetrosis, generalized osteosclerosis
dysplasias [SEiMDs]. Fractures can be seen in all types of OI (Figure 6), osteosclerotic disorders including osteopetrosis (Figure 7) and severe hypophosphatasia (Figure 8) (7).

Following the evaluation of limb segments and the epiphyseal growth plate, focus on all the skeletal structures available in the genetic skeletal survey is mandatory to recognize a well-described skeletal dysplasia from a previous broad categorization into a specific group. This precise evaluation will include a search for pathognomonic findings, such as snail-shaped iliac bones of Schneckenbecken dysplasia (Figure 9), “lacy” appearance of iliac crest in Dyygve-Melchior-Clausen syndrome (Figure 10), and loss of mandibular angle accompanied by wormian bones and acroosteolysis in pycnodysostosis (Figure 11 a,b,c) (7).

Step III (Differentiation of Normal Variants from Pathological Abnormalities): This last step requires experience in the field of pediatric radiology. It essentially involves recognition of normal variation from pathological abnormalities in the growing skeleton. Every portion of every bony structure should be looked at in an effort to combine the clinical, often dysmorphic findings previously noted in evaluation of the patient. Pathognomonic findings help to narrow the group of differential diagnosis leading to a specific entity.

At this point, having had a thorough clinical and radiographic assessment, even a simple radiographic grouping can be helpful to the clinician for the establishment of clinical care and follow-up. Table 2 provides a list of the grouping mentioned with common specific entities to consider (7). If a specific diagnosis cannot be made, it is expedient to send the case to a local expert, or an expert group in Skeletal Dysplasias such as the International Skeletal Dysplasia Registry at Cedars Sinai MC [www.csmc.edu/skeletaldysplasia].

Figure 8. Infantile hypophosphatasia

Figure 9. Schneckenbecken dysplasia. Note severe platyspondyly, thin ribs and snail-shaped iliac bones

Figure 10. Dyygve-Melchior-Clausen syndrome. Note “lacy” iliac crest

Figure 11. a,b,c. Pycnodysostosis. Loss of mandibular angle with wormian bones, large fontanelle and acroosteolysis in distal phalanges of hand
| Radiological Groups | Common Entities | Radiological Findings |
|---------------------|----------------|-----------------------|
| **Achondroplasia**  | **Thanatophoric Dysplasia** | Skull: Proportionately large skull, narrow skull base, kleeblattschadel<br>Spine: flat, small vertebral bodies with rounded anterior ends<br>Pelvis: small, flared iliac bones; very narrow sacrosciatic notches; flat, dysplastic acetabula<br>Extremities: generalized micromelia: French telephone receiver femurs, round proximal femoral metaphyses with medial spike |
|                     | **Achondroplasia** | Skull: enlarged, midface hypoplasia; rarely hydrocephalus, tight foramen magnum<br>Thorax: small; shortened and anteriorly splayed ribs<br>Spine: slight platyspondyly, short and anteriorly round vertebral bodies that normalize from childhood on; very short pedicles with decreased interpedicular distance marked in lumbar spine; posterior vertebral scalloping that persists through life<br>Pelvis: flared, superiorly and laterally flattened ilia (elephant ear-shaped iliac wings), narrow sacrosciatic notches, flat acetabular roofs<br>Extremities: rhizo-, meso-, and acromelia<br>Hands: brachydactyly, metacarpal metaphyseal cupping, phalangeal metaphyseal widening<br>Knees: proximal femoral fade-out (infancy); hemispheric capital femoral epiphyses, short femoral necks<br>Arms: prominent deltoid insertion area |
|                     | **Hypochondroplasia** | The radiological findings are identical to achondroplasia but to a milder degree. All cases exhibit interpedicular narrowing in the lumbar spine. There may be brachydactyly, fibular overgrowth, short femoral necks. Other achondroplasia-like changes may or may not be present. |
| **Metatropic Dysplasia** | **Metatropic Dysplasia** | Thorax: small; short ribs<br>Spine: dense wafer vertebral bodies (newborn), platyspondyly (child, adult), scoliosis (adult)<br>Pelvis and Hips: short, squared iliac wings; flat irregular acetabular roof; narrow sacrosciatic notches; halberd (hunting ax)-shaped proximal femurs<br>Extremities: trumpet-shaped metaphyses (newborn), dumbbell-shaped short tubular bones of hand and feet |
| **Short-Rib Polydactyly** | **Short-Rib (With or Without)-Polydactyly Dysplasia** | Thorax: small; extremely short horizontal ribs<br>Spine: relatively normal<br>Pelvis: small, dysplastic ilia<br>Extremities: micromelia; round-ended femora; ovoid or tiny normal-shaped tibiae; severe brachydactyly with hypoplastic middle and distal phalanges; polydactyly common, not essential |
|                     | **Asphyxiating Thoracic Dysplasia (Jeune’s syndrome)** | Thorax: long and barrel shaped, handlebar clavicles, short horizontal ribs with bulbous anterior ends<br>Pelvis: normal<br>Extremities: generalized shortening, precocious proximal femoral epiphyseal ossification, cone-shaped epiphyses in hand |
|                     | **Chondroectodermal Thorax (Ellis van Creveld) Dysplasia** | Thorax: small, moderately short ribs<br>Pelvis: small; short, flared iliac wings; Trident acetabula; narrowed sacrosciatic notches<br>Spine: normal<br>Extremities: generalized shortening with meso- and acromelia; premature ossification of capital femoral epiphyses, humeral and femoral bowing<br>Hands: characteristic-postaxial polydactyly, capitate/hamate (and other carpal) fusions, extra carpal bone, cone-shaped epiphyses<br>Arms: polydactyly |
### Table 2. (continued)

| **Diastrophic Dysplasia Group** | **Diastrophic Dysplasia** | **MED-Multilayered Patellae/Brachydactyly/Clubfeet** | **Type II Collagenopathies** | **Spondyloepiphyseal Spine: mild platyspondyly with centrally humped end plates with intervertebral disc space narrowing** | **Kniest Dysplasia** | **Other Spondylo-Epi-(Meta)Physeal Dysplasias** | **Multiple Epiphyseal Dysplasia and Pseudoachondroplasia Group** | **Chondrodysplasia Punctata Group** |
|---------------------------------|---------------------------|-----------------------------------------------------|-----------------------------|--------------------------------------------------------------------------------|------------------|------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| **Diastrophic Dysplasia**       | Head: ear pinna calcification | Thorax: moderately small | Spine: oval vertebral bodies (newborn), anteriorly rounded platyspondyly (later) | Thorax: small, short ribs | Spine: mild platyspondyly with centrally humped end plates with intervertebral disc space narrowing | Skull: microcephaly | Skull: normal | Skine: coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| **Dysplasia**                   | Thorax: moderately small | Head: ear pinna calcification | Pelvis: absent pubic ossification (newborn and infancy) | Spine: oval vertebral bodies (newborn), anteriorly rounded platyspondyly (later) | Extremities: mild-moderate “epiphyseal dysplasia” (small and irregular epiphyseal centers), sparing hands and feet | Thorax: broad; anterior rib widening | Thorax: mild anterior rib widening | Extremities: small, irregular, flattened ossification centers (epiphyses); small, irregular carpal (and tarsal) centers |
| **Diastrophic**                 | Spine: progressive scoliosis, kyphosis, odontoid hypoplasia, cervical kyphosis | Extremities: micromelia; short, thick tubular bones; generalized bony dystrophy-short ovoid first metacarpal, twisted metatarsal, accessory and irregular carpal bones; epiphyseal dysplasia, joint dislocations | Pelvis: small, rounded posteriorly convex vertebrae with anterior central tongue, mild anterior rib widening | Spine: double-humped vertebral bodies with end plate notching and posterior scalloping | Extremities: moderate shortening with epiphysis/metaphysis changes, generalized brachydactyly with cone-shaped epiphyses and small carpal bones | Pelvis: small iliac wings with irregularly calcified “lacy” manubrium | Pelvis: rounded iliac wings, hypoplastic, poorly formed acetabular roofs | Extremities: mini-epiphyses in the hips, moderate-severe generalized epiphyseal dysplasia (small, irregular, poorly ossified), metaphyseal widening and irregularity in the knees, proximally rounded metacarpals with mini-epiphyses in the hands, irregular carpal/tarsal bones |
| **Dysplasia**                   | Extremities: micromelia; short, thick tubular bones; generalized bony dystrophy-short ovoid first metacarpal, twisted metatarsal, accessory and irregular carpal bones; epiphyseal dysplasia, joint dislocations | Epiphyseal dysplasia especially at hips (half/quarter moon shaped) | Extremities: normally modeled but shortened long bones, significant generalized ossification delay (early) and hypoplastic/dysplastic epiphyses (later), unossified talus/calcaneus in the newborn, normal hands and feet with ossification delay | Extremities: small to normal | Extremities: double-layered patella (lateral knee radiograph) | Extremities: mild brachydactyly | Extremities: twisted metatarsals |
| **Diastrophic Head: ear pinna calcification** | Patellae/Brachydactyly/Clubfeet | Mild brachydactyly | Thorax: small, short ribs | Thorax: broad; anterior rib widening | Double layered patella (lateral knee radiograph) | Clubfeet/ twistetmetatarsals |
| **Dysplasia Thorax: moderately small** | **Kniest Dysplasia** | **Other Spondylo-Epi-(Meta)Physeal Dysplasias** | **Spondyloepiphyseal** | **Dyggve-Melchior-Clausen Syndrome** | **Multiple Epiphyseal Dysplasia and Pseudoachondroplasia Group** | **Chondrodysplasia Punctata Group** | **Multiple Epiphyseal Dysplasia** | **Pseudoachondroplasia** | **Rhizomelic Chondrodysplasia** |
| **Spine:** progressive scoliosis, kyphosis, odontoid hypoplasia, cervical kyphosis | **Spondyloepiphyseal** | **Dyggve-Melchior-Clausen Syndrome** | **Spondyloepiphyseal** | **Multiple Epiphyseal Dysplasia** | **Pseudoachondroplasia** | **Rhizomelic Chondrodysplasia** |
| **Extremities:** micromelia; short, thick tubular bones; generalized bony dystrophy-short ovoid first metacarpal, twisted metatarsal, accessory and irregular carpal bones; epiphyseal dysplasia, joint dislocations | **Congenita** | **Skull:** microcephaly | **Tarda** | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | **Thorax:** moderately small | **Thorax:** broad; anterior rib widening | **Skull:** microcephaly | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | **Spine:** progressive scoliosis, kyphosis, odontoid hypoplasia, cervical kyphosis | **Thorax:** broad; anterior rib widening | **Skull:** microcephaly | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | **Extremities:** micromelia; short, thick tubular bones; generalized bony dystrophy-short ovoid first metacarpal, twisted metatarsal, accessory and irregular carpal bones; epiphyseal dysplasia, joint dislocations | **Spine:** double-humped vertebral bodies with end plate notching and posterior scalloping | **Skull:** microcephaly | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | **Pelvis:** small iliac wings with irregularly calcified “lacy” manubrium | **Skull:** microcephaly | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | **Extremities:** moderate shortening with epiphysis/metaphysis changes, generalized brachydactyly with cone-shaped epiphyses and small carpal bones | **Skull:** microcephaly | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | | **Skull:** normal | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | | | **Skull:** normal | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | | | | **Skull:** normal | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | | | | | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| | | | | | | | **Skine:** coronal clefs (newborn), platyspondyly with end plate irregularity (later) |
| Table 2. (continued) |
|----------------------|
| **Conradi-Hünermann Syndrome/Dysplasia** | Spine: diffuse stippling, scoliosis in childhood, abnormal vertebral body formation Extremities: mild symmetric or asymmetric shortening, diffuse generalized stippling in epiphyseal areas; hands and feet-normal aside from stippling **stippling resolves during infancy to develop normal or malformed epiphyseal centers** |
| **Brachytelephalangic Chondrodysplasia Punctata** | Spine: hypoplastic vertebral bodies with posterior scalloping and anterior rounding; stippling, especially in the sacrococcygeal area Extremities: normal length (mildly short), brachydactyly with hypoplastic tufts and deformed hypoplastic proximal phalanx of the second digit in the hand and first metatarsal of the foot |
| **Jansen-Type Metaphyseal Chondrodysplasia** | Skull: Brachycephaly, platybasia, small mandible Thorax: normal size; expanded irregular anterior rib ends Extremities: extensive irregularity of markedly expanded metaphyses- wide separation of epiphyses from metaphyses |
| **McKusick-Type Metaphyseal Chondrodysplasia** | Skull: Brachycephaly, platybasia, small mandible Thorax: normal size; expanded irregular anterior rib ends Extremities: extensive irregularity of markedly expanded metaphyses- wide separation of epiphyses from metaphyses |
| **Schmid-Type Metaphyseal Chondrodysplasia** | Skull: Brachycephaly, platybasia, small mandible Thorax: normal size; expanded irregular anterior rib ends Extremities: extensive irregularity of markedly expanded metaphyses- wide separation of epiphyses from metaphyses |
| **Kozlowski-Type Spondylometaphyseal Dysplasia** | Spine: severe platyspondyly, anteriorly rounded/wedged vertebral bodies, increased intervertebral disc spaces, overfaced pedicles Pelvis: short, flared iliac wings; irregular hypoplastic acatabular roof Extremities: widening, sclerosis and irregularity of metaphyses; hemispheric capital femoral epiphysis and widened proximal femoral growth plate with irregularity on both sides; hands-mild shortening with metaphyseal cupping and irregularity , marked carpal ossification delay |
| **Dyschondrosteosis** | Extremities: symmetrical bowing and shortening of both radii, shortened ulnae, radiographic Madelung’s deformity changes, variable tibial and fibular shortening |
| **Trichorhinophalangeal Syndrome Type I and II Acromesomelic Dysplasia of Maroteaux** | Spine: oval vertebral bodies (early), anterior beaking and posterior wedging (later), gibbus and/or kyphoscoliosis ultimately Extremities: shortening of all tubular bones, especially radius/ulna and tibia/fibula; very short tubular bones of hand and feet with cone-shaped epiphyses and large great toes |
| **Cleidocranial Dysplasia** | Skull: large, brachycephalic; wormian bones; wide sutures; persistently open anterior fontanelle Thorax: absence/hypoplasia of clavicles, mildly shortened ribs with downward slope, 11 ribs Spine: significant posterior wedging of thoracic vertebrae Pelvis: high narrow iliac wings, absence/hypoplasia of pubic bones Extremities: numerous pseudoepiphyses of metacarpals and tapered distal phalanges in the hands |
| **Table 2. (continued)** |  |
|---------------------------|---|
| **Bent Bone Dysplasia**  |  |
| **Group**                |  |
| Campomelic Dysplasia     | Skull: enlarged, narrow with a small face  
|                          | Thorax: mildly short ribs, 11 ribs; severe hypoplasia of the bodies of scapulae  
|                          | Spine: nonossification of thoracic pedicles, cervical kyphosis, hypoplasia of cervical vertebral bodies  
|                          | Pelvis: narrow, tall, iliac wings  
|                          | Extremities: proportionately long, bowed femurs, short tibiae; short long bones of upper extremity  |
| **Dysostosis Multiplex** |  |
| **Group**                |  |
| Dysostosis Multiplex     | Skull: enlarged neurocranium, abnormal J-shaped sella  
|                          | Thorax: short, thick clavicles; paddle (oar)-shaped ribs; hypoplastic glenoid  
|                          | Spine: gibbus, superior notched (inferior beaked) thoracolumbar vertebral bodies, upper cervical subluxation  
|                          | Pelvis: flared, small iliac wings with inferior tapering, steep acetabular roofs  
|                          | Extremities: diaphyseal widening of long bones (marrow expansion); dysplastic epiphyses; characteristic hand-brachydactyly, proximal metacarpal “pointing” diaphyseal widening of metacarpals and proximal/middle phalanges, small irregular carpal bones  |
| Morquio’s Syndrome       | Skull: no J-shaped sella  
| (MPS IVA, B)             | Thorax: widened, not oar shaped ribs  
|                          | Spine: middle tonguing, not inferior beaking  
|                          | Pelvis: no tapering of ileum  
|                          | Extremities: proximal metacarpal rounding, not pointing, of hands  |
| Mucolipidosis II         | Extremities: severe osteopenia, poorly defined cortices, “periosteal cloaking” (newborn); rickets-like appearance in distal ulna and radius (infancy)  
| (I Cell Disease)         | Dysostosis multiplex occurs later  |
| **Dysplasias With Decreased Bone Density** |  |
| Osteogenesis             | Skull: very poor to no ossification  
| imperfecta               | Thorax: small, narrow chest; beaded ribs  
| type II, perinatal lethal| Spine: severe deossification, collapsed vertebral bodies  |
| Osteogenesis             | Skull: wormian bones (>8 to 10), variable decreased ossification  
| Imperfecta-other types   | Spine: wedged or collapsed vertebrae  
|                          | Remaining skeleton: osteoporosis and pathological fractures  |
| **Dysplasias With Defective Mineralization** |  |
| Hypophosphatasia         | Perinatal lethal/Infantile:  
|                          | Skull: decreased ossification with single island-like centers for frontal occipital and parietal bones  
|                          | Thorax: poorly ossified ribs; sporadic dropout of ribs; thin, wavy, fractured ribs  
|                          | Spine: sporadic ossified vertebral bodies, dense and osteopenic vertebrae, butterfly shaped vertebral bodies  
|                          | Extremities: generalized decreased ossification, chromosome-shaped femurs, metaphyseal cupping and irregularity, central lucent defect, bowed femora  
|                          | *clavicles are not affected; infantile form is less severe  
|                          | Adult  
|                          | Generalized osteopenia  
|                          | Extremities: metaphyseal widening (rickets-like chages), punched-out metaphyseal lesions, pathologic fractures  |
| **Increased Bone Density Without Modification of Bone Shape Group** |  |
| Osteopetrosis            | Generalized increased bone density  
|                          | Skull: thick and dense, especially at the base  
|                          | Thorax: splayed anterior ribs  
|                          | Spine: “sandwich” vertebral bodies  
|                          | Extremities: splayed metaphyses, bone-within-bone configuration, dense metaphyseal bands  |
Table 2. (continued)

| Condition | Description |
|-----------|-------------|
| Pyknody sostosis | Generalized osteosclerosis<br>Skull: marked delay in closure of fontanelles and sutures, wormian bones, obtuse or absent mandibular angle, dense skull<br>Thorax: resorbed acromial ends of clavicles<br>Extremities: resorbed phalangeal tufts |
| Craniotubular Dysplasias | |
| Craniodiaphyseal Dysplasia | Skull: marked thickening and sclerosis of calvarium and facial bones, obliteration of foramina and sinuses<br>Thorax: diffusely widened, sclerotic ribs and clavicles<br>Extremities: straightened, undermodeled long bones diaphyses with metaphyseal sparing; sclerosis (cortical thickening) of the short tubular bones of hands |
| Craniometaphyseal Dysplasia | Skull: diffuse hyperostosis of cranial vault base and facial bone, obliterated dysplasia paranasal sinuses<br>Extremities: sclerosis of diaphyses (early), undermodeled flared metaphyses of long bones (later) |
| Pyle Disease | Skull: Mild skull and facial involvement, minimal base-of-skull sclerosis, prominent supraorbital ridging<br>Thorax: mildly thick clavicles and ribs<br>Pelvis: thickened ischium and pubis<br>Extremities: marked undertubulation of long bones, especially distal femurs (Erlenmeyer flask deformity); distal flaring of metacarpals and proximal flaring of phalanges |
| Disorganized Development of Cartilaginous Bony and Fibrous Components of the Skeleton | |
| Spondyloenchondrodysplasia | Spine: severe platyspondyly with end plate irregularity<br>Extremities: enchondromata at distal and proximal ends of long bones, hands and feet are rarely affected |
| Dysspondyloenchondromatosis | Spine: vertebral anomalies, hemivertebrae, anisospondyly and end plate irregularity<br>Extremities: typical enchondromata, including hands and feet, with long bone asymmetry |
| Osteolysis Group | |
| Multicentric Carpal/Tarsal Osteolysis With or Without Nephropathy | Extremities (wrist and ankles): deossification of carpal bones, loss of carpal/tarsal contours, bone resorption and collapse, sclerosis sometimes extending into adjacent short tubular bones |
| Patellar Dysplasia Group | |
| Nail-Patella Syndrome | Spine: normal<br>Pelvis: iliac horn in the center of the iliac wing extending posteriorly<br>Extremities: (knees and elbows) hypoplastic or absent patella’s, radial head and capitellum hypoplasia/effusion dislocation |

Conclusion

The complete group of osteochondrodysplasias, although individually rare, is an important group of disorders for healthcare providers who deal with individuals with short stature. These individuals present with significant morbidities due to destruction of bone and cartilage caused by defects in linear growth, bone modeling and regeneration. Regardless of the specific diagnosis, skeletal dysplasias in general share clinical and radiological findings helping us to group them in several ways. In this review, we aimed to focus on the radiological aspect of assessment of skeletal dysplasias. We also included an outline of the basic clinical approach to an individual with a suspected skeletal dysplasia. The recent advances in the field of molecular pathogenetic mechanisms underlying skeletal dysplasias are beyond the scope of this review. However, we would like to emphasize that accurate clinical, radiological and finally molecular diagnosis of skeletal dysplasias is more important than ever in this era of up-to-date genetic counseling, prenatal, preimplantation genetic diagnoses and hopefully, molecularly targeted therapeutics in the future.
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