Introduction to the Assessment of Skeletal Dysplasias

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Bone & Calcium Disorders Annual Study Day
28th Sept’12
• Introduction and overview
• Assessment – before x-rays
• The basics of radiological interpretation
• Cardinal clues
• X-rays
• Who to involve – the MDT
• Tools of the trade
Introduction

• Skeletal dysplasias are conditions with generalised skeletal abnormalities

• Usually associated with disproportionate short stature, normal intelligence

• Incidence 1/5000 live births

• Classified on clinical, radiological and molecular criteria and sometimes histology
Overview

• 2010 Nosology and Classification of Genetic Skeletal disorders

• >450 different dysplasias, >220 genes

• ~100 have prenatal onset

• remainder presenting in infancy or age 2-3 years

• In some conditions, features disappear with time and therefore are more difficult to diagnose retrospectively in adults.
Radiological diagnostic groupings

- Achondroplasia group
- Metatropic dysplasia group
- Short-rib polydactyly (SRP) group
- Diastrophic dysplasia (DD) group
- Type II Collagenopathies
- SEMDs
- Multiple epiphyseal dysplasia (MED) and pseudoachondroplasia group
- Chondrodysplasia punctata (CDP) group
- Metaphyseal chondrodysplasia (MCD)
- Spondylometaphyseal dysplasia (SMD) group
- Mesomelic dysplasia
- Acromelic / acromesomelic group
- Dysplasias with prominent membranous bone involvement – CCD
- Bent bone dysplasia – Campomelic
- Dysostosis multiplex group
- Decreased bone density dysplasias – OI
- Increased bone density dysplasias – osteopetrosis, pyknodysostosis
- Defective mineralisation dysplasias – Hypophosphatasia
- Craniotubular dysplasias – Pyle
- Disorganised cartilagenous development – enchondrodysplasias
- Osteolysis group
- Patellar dysplasia – nail-patella syndrome
Assessment I - disproportion

Upper/lower segment ratio:
• 1.7 newborn
• 1.0 ages 2-8yrs
• 0.95 adult

Sitting height: ascertains trunkal shortening

Limb lengths:
• Rhizomelia (humerus and femur)
• Mesomelia (radius, ulna, tibia and fibula)
• Acromelia (Hands and feet)

Body asymmetry

Spine: assess for scoliosis, kyphosis and lordosis
Assessment II – General examination

• General examination: facial features, hair quality, dental health, nails
• Systemic features: renal problems, cardiac abnormalities
• Developmental history: Most normal
• Family history
• Ethnicity: CHH in Amish, SEMD with joint laxity in SA
• Joint pain
Assessment III - Radiology

Skeletal survey:
1. Skull AP & Lateral
2. Spine AP & Lateral
3. Pelvis AP
4. 4 Limbs AP, occasional lateral Knee (assessment of patella)
5. Hands
6. Feet
Radiological assessment I

- Epiphyseal dysplasia – small under ossified epiphyses
- Metaphyseal dysplasia – widened, flared or irregular metaphyses
- Diaphyseal dysplasia – cortical thickening or marrow space expansion or reduction
Radiological assessment II

- Epiphyseal dysplasia
- Metaphyseal dysplasia
Radiological assessment III

- Vertebral (spondylo) abnormalities

- Combinations:
  - Spondylo-epiphyseal dysplasia (SED)
  - Spondylo-metaphyseal dysplasia (SMD)
  - Metaphyseal-epiphyseal dysplasia (MED)
  - Spondylo-epiphyseal-metaphyseal dysplasia (SEMD)
Question - Is it acquired?

Rule out acquired causes of bone problems:
- Neuromuscular disorders
- Chronic diseases – JIA
- Poorly healed fractures
- Metabolic bone problem
Achondroplasia

INHERITANCE
Autosomal dominant (but 50% new mutations) FGFR3

CLINICAL FEATURES
Megalocephaly  Short limbs
Prominent forehead  Thoracolumbar kyphosis
Midfacial hypoplasia  Short stature

RADIOLOGY
Diminishing interpeduncular distances between L1 and L5

COMPLICATIONS
Short stature  Dental malocclusion
Hydrocephalus  Repeated otitis media
Cardinal clues – cleidocranial dysostosis

- Large head
- Delayed suture closure
- Hypertelorism, small face
- Dental dysplasia – multiple teeth
- Hypoplasia / aplasia of the clavicles
Cardinal clues – cartilage-hair hypoplasia

- McKusick type metaphyseal chondrodysplasia
- Short limbed dwarfism
- Sparse hair
- Autosomal recessive \( RMRP \) gene
- T-cell and B-cell immunodeficiency
- Dysplastic nails and brachydactyly
- Notched incisors
Cardinal clues – Ellis van Creveld (chondroectodermal dysplasia)

- Short stature, mesomelia
- Narrow chest and short ribs
- Polydactyly
- Dysplastic nails
- Dental abnormalities – missing teeth, lip fusion to gingiva
- Cardiovascular abnormalities
- AR – *EVC1* & *EVC2*
Cardinal clues - Trichorhinophalyngeal syndrome (TRP) Type II / Langer-Giedion syndrome

- Short stature
- Unusual facies – long bulbous nose
- Developmental delay

- Cone epiphyses of the metacarpals
- Bony exostoses especially distal tibia and ulna
- Ear cysts
- Hitchhiker thumb – shortened 1\textsuperscript{st} metacarpal

\textbf{Diastrophic dysplasia}

- Pierre Robin sequence – midface hypoplasia, high arched palate, micrognathia
- Myopia
- Hearing problems

\textbf{Type II Collagenopathies}
Cardinal clues - Osteopoikilosis

- Dalmation disease – AD, *LEMD3 & EXT1*
- small round or oval foci of bone sclerosis located in the trabecular bone
- particularly in the pelvis, metaphyses and epiphyses of long bones, tarsals, and carpals
Cardinal clues - Melorheostosis

- Dripping wax appearance
- *LEMD3* mutations
- Linked to osteopoikilosis
- Buschke-Ollendorff syndrome – dermatofibrosis lenticularis
Cardinal clues - osteopetrosis

- Extra dense bone
- ‘Bone in bone’ appearance
- Failure of normal osteoclast activity
- May lead to marrow suppression – pancytopenia
- Neural foramina stenosis
Cardinal clues - Enchondromatosis

• Ollier’s syndrome
• Not inherited
• central expansile pattern or linear metaphyseal lucencies
• 5-30% malignant degeneration to chondrosarcoma
• higher risk if associated with soft tissue haemangiomas (Mafucci's syndrome)
Who to involve - The MDT

- Geneticist
- Radiographer
- Metabolic bone doctor
- Orthopaedic surgeon
- Spinal surgeon
- Physiotherapist
- Occupational therapist
Tools of the trade

• A good atlas – Spranger, Brill and Poznanski


Phone or e-mail a friend!

- The European Skeletal Dysplasia network (ESDN) – usually accessed by the radiologists or genetists
- The North-western Skeletal Dysplasia Group
• SEMD – Pseudoachondroplasia (PSACH)
Vertebrae

- Double hump vertebrae – Dgyvve-Melchior-Clausen syndrome
- Platyspondyly, ovoid vertebrae, gibbus, dysostosis multiplex, J shaped sella - MPS
Hand x-rays

- Cone epiphyses of the metacarpals
- Bony exostoses esp distal tibia and ulna

Trichorhinophalyngeal syndrome (TRP) Type II / Langer-Giedion syndrome

- Osteolysis of distal phalanges

Pycnodysostosis
Hand x-rays

- Proximal pointing of distal phalanges
- Bullet shaped

Hurlers disease (MPS)
IMAGING SKELETAL DYSPLASIAS

Musa Kaleem (MBBS, MRCPCH, FRCP)
Constitutional disorders of bone

**osteochondrodysplasias**

- Dysplasias (growth)
- Osteodystrophies (texture)
  - Failure of gene expression
  - Phenotype usually continues to evolve

**dysostoses**

- Defective bone formation due to a defect in blastogenesis
  - Remain static
  - do not spread to involve normal bones

Offiah et al; Pediatr Radiol 2003
Zones
- Resting
- Proliferating cartilage
- Hypertrophic cartilage
- Provisional calcification
- Ossification
Genetics Skeletal Survey

- Skull (AP & Lat)
- Spine (AP & Lat)
- Chest
- Pelvis
- One upper limb
- One lower limb
- Left hand (bone age)

- Additional views
  - Lateral knee for assessment of patella
  - Lateral foot (for calcaneum)

- Foetogram/ babygram
  - AP
  - Lateral
Radiological assessment – stepwise approach

- Step 1 – assessment of disproportion
  - Spine
  - limb segments (rhizo/ meso/ acro)

- Step 2 – assessment of epiphyses, metaphyses and diaphyses

- Step 3 – assessment of bone density / texture
Radiological assessment (2)

- Step 4 – search for other clues
  - Skull
  - Cranio-cervical junction
  - Spine
  - Ribs/ clavicles
  - Pelvis
  - Long bones
  - Hands and feet

- Step 5 – Seek help from colleagues/ refer to textbook/ Electronic database
Radiological assessment (3)

- **Epiphyseal dysplasia**
  small/ under ossified/ irregular epiphyses

- **Metaphyseal dysplasia**
  widened /irregular metaphyses

- **Diaphyseal dysplasia**
  cortical thickening or marrow space changes
Radiological assessment (4)

- **Vertebral (spondylo) abnormalities**

- Combinations:
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DIASTROPHIC DYSPLASIA
Radiological hints to diagnoses

Skull
- Changes in density, size and shape
- Wormian bones
  - OI
  - Cleidocranial dysostosis
  - Pyknodysostosis
- Craniosynostosis
  - Crouzon’s/ Pfeiffer’s
- Skull base/ midface hypoplasia
- Basilar invagination
Achondroplasia
Mucopolysaccharidosis
Generalised reduced density: Osteogenesis Imperfecta (OI)
Wormian bones...

They are named after Ole Worm, a Danish anatomist who described them

From radiopedia.org
Generalised reduced bone density: HYPOPHOSPHATASIA
Increased density: osteopetrosis

- AR
- Benign vs malignant forms
- Presents with infection/ cranial nerve palsies
Increased density: generalised

Pycnodysostosis
Frontometaphyseal dysplasia

Spine

- Odontoid hypoplasia/ atlanto-axial subluxation
- Kyphoscoliosis (gibbus)
- Pedicles (length/ interpediculate distance)
- Vertebral body shape abnormalities
  - Platyspondyly
  - Bullet shaped vertebrae/ vertebral beaking
  - Scalloped vertebrae
  - Humps
  - Cleft vertebrae (sagittal/ coronal)
MPS – dysostosis multiplex
Achondroplasia
CDPX2
Chondrodysplasia Punctata (x-linked)
SED Tarda

- Short trunk
- Humped vertebrae
- Proximal epiphyseal irregularities
dd:
Chondrodysplasia Punctata
Atelosteogenesis
Kniest dysplasia
Short rib polydactyly
OI
Pelvis and Lower limbs

- Iliac shape / horns
- Pubis/ischium ossification
- Sacro-sciatic notches
- Acetabulum orientation and shape
- Femoral head abnormalities
  - Delayed ossification
  - Abnormal ossification
- Metaphyseal irregularities
- Shortening of long bones
- Layered patella
- Multiple calcaneal ossifications
Newborn with abnormally soft head

- **Hypophosphatiasia**

- Heterogenous disorder
- Low or absent Alk Phos due to lack of tissue non-specific alk phosphatase
- AR: congenital form (lethal)
- AD: milder

- Decreased/absent ossification of calvaria
- Poor ossification of vertebrae or islands of deficient bone
- Abnormal metaphyses
11 month old - pancytopaenic

- **Infantile osteopetrosis**

- Diffuse osteosclerosis with a "bone-in-bone" appearance in the iliac bones and the femora

- Irregular femoral metaphyseal ossification

- Comment: The bone-in-bone appearance reflects fluctuating disease activity. The innermost bone is the size and shape of a neonatal bone. The metaphyseal appearances may resemble rickets ('osteopetrorickets')
2 day old with short limbs

- **Achondroplasia**
- Rounded iliac wings with horizontal acetabula and narrow sacrosciatic notches
- Narrowing of the lower lumbar interpedicular distance
- Upper femoral metaphyses are broad and lucent

The pelvic appearances (‘trident’ acetabulum) are seen in other conditions, but the combination, with the spinal changes indicates achondroplasia.
Neonate with severe respiratory distress and short limbs

- **Thanatophoric dysplasia (type 1)**
- Small iliac bones with small sacrosciatic notches
- Broad ischial and pubic bones
- Severe platyspondyly
- Short curved femora

- The pelvic appearances are similar to, but more severe than those seen in achondroplasia, as well as those in asphyxiating thoracic dystrophy and related disorders.
1 year old with short limbs and large joints

- **Metatropic dysplasia**
- Crescent shaped iliac crests with short inferior portions of the iliac bones
- Low anterior iliac spines and horizontal acetabula
- The proximal femora show metaphyseal broadening (‘battle-axe’ appearance)
- Small femoral epiphyses
- Lumbar platyspondyly

- Affected individuals may have a tail-like appendage of the sacrum.
3 year old with short stature and facial dysmorphism

- Mucopolysaccharidosis type IV (Morquio disease)
- Narrowing of the inferior portions of the iliac bones, with shallow acetabula
- Irregular ossification of the femoral epiphyses
- Lumbar platyspondyly

- The iliac and acetabular morphology is common to all mucopolysaccharidoses. The platyspondyly and epiphseal changes suggest Morquio disease
11 yr old with painful hips

- **Diagnosis:** Multiple epiphyseal dysplasia
- Femoral capital epiphyses are symmetrically flattened
- The acetabula are mildly shallow
- Normal metaphyses and tubular bones
- Varying degrees of platyspondyly and end-plate irregularity
- MED results in progressive joint deformities and early degenerative changes. The phenotype may be due to >5 different gene mutations
Skeletal dysplasia

- Daunting task!

- “there are known knowns. These are things we know that we know. There are known unknowns, that is to say, there are things that we know we don’t know. But there are also unknown unknowns. These are things we don’t know we don’t know”
  - Donald Rumsfeld, US Ex-Secretary of Defence
Thank you