Skeletal dysplasia. A guide to the orthopaedic surgeon

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Abstract

Skeletal dysplasias encapsulate a wide variety of rare musculoskeletal diseases, predominantly of genetic origin. Recognition of these diseases and their natural history is crucial to the management of patients presenting with these conditions. We describe here some of the more common conditions in this category, with important orthopaedic aspects being highlighted.

Keywords deformity; guided growth; osteochondrodysplasias; osteotomy

Introduction

Skeletal dysplasias comprise a very large group of rare, complex, heterogeneous disorders that involve the bone and cartilage. Each can present on a spectrum of varying severity. The 2015 revision of the comprehensive '*Nosology and classification of genetic skeletal disorders*' lists 436 such disorders in 42 phenotypically related groups.[1] It is beyond the scope of this article to list these. The following is a guide the most common among these rare disorders presenting to the orthopaedic surgeon and appearing in orthopaedic postgraduate examinations.

Classification

The nosology is a comprehensive classification and is less useful for day-to-day use in the clinical setting. A simpler categorization, used by The Skeletal Dysplasia Group, more conveniently classifies the disorders into:

1. Spondylo-epiphyseal disorders (predominantly epiphyseal)
   Examples – multiple epiphyseal dysplasia, Stickler syndrome, chondrodysplasia punctata
2. Spondylo-epiphyseal disorders
   Examples – spondylo-epiphyseal dysplasia congenita and tarda, spondylo-epiphyseal dysplasia with progressive arthropathy (pseudorheumatoid type)
3. Metaphyseal and spondylo-metaphyseal disorders
   Examples – metaphyseal chondrodysplasia (Schmid/McKusick/Jansen), spondylo-metaphyseal chondrodysplasia
4. Short limbs normal trunk
   Examples – achondroplasia, hypochondroplasia, dyschondrosteosis, acrodysostosis
5. Short limbs and trunk
   Examples – pseudoachondroplasia, diastrophic dysplasia, metatropic dysplasia, Kniest disease
6. Perinatal lethal dysplasias
   Examples – thanatophoric dysplasia, short rib polydactyly, campomelic dysplasia
7. Storage disorders
   Examples – mucopolysaccharidoses (Hurler, Scheie, Hunter, Morquio, Maroteaux–Lamy, Sanfilippo)
8. Metabolic bone disease and decreased bone density
   Examples – hypophosphatasia, hypophosphataemic rickets, osteogenesis imperfecta, pseudohypoparathyroidism
9. Increased bone density
   Examples – osteopetrosis, pycnodysostosis
10. Tumour like disorders
    Examples – melorheostosis, hereditary multiple exostosis, Ollier's disease, neurofibromatosis, polyostotic fibrous dysplasia

Though not as comprehensive as the previously mentioned classification, this captures most disorders based on the phenotype, making it a clinically useful system.

An alternative classification, which helps us to understand the anatomic basis of the conditions, is the dynamic classification of bone dysplasia by Rubin (Table 1).[2]

Clinical approach

A thorough history is essential and includes enquiry about the age at which the condition first manifests, a detailed family history over three generations, consanguinity in the family tree, maternal and paternal ages and obstetric and perinatal history, in addition to the presence of any systemic problems.[3]

A clinical assessment of height and body proportions is important. Children have a longer upper segment (trunk and head), but this proportionally changes with growth and adults have an upper segment equal in length to the lower segment. Trunk: extremity ratios, sitting and standing heights as well as limb segment ratios (using radiographs) are noted. Note is made of dysmorphism as well as evidence of any major systems involvement. Segmental measurement of the limb is generally not assessed.[4] Proportion can be easily assessed visually. Limb proportions may show shortening in different segments as follows

- rhizomelic (proximal, i.e. humerus/femur)
- mesomelic (middle, i.e. forearm and leg)
- acromelic (distal, i.e. hands and feet).

Particular note is made of the ranges of joint movement, joint laxity and any evidence of deformity in the limbs and spine.

Radiological evaluation involves a skeletal survey that includes the skull, spine, chest, hands and at least one upper and one lower limb. Increasingly, ultrasound is being used as part of routine antenatal tests to screen and diagnose anomalies.[5] Further follow-up tests in at-risk groups may include amniocentesis and chorionic villus sampling.

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Rubin's classification of bone dysplasia

Location	Failure of		Excess of	
Epiphyseal	Cartilage	Spondylo-epiphyseal dysplasia congenita and tarda (SEDc/SEDt)	Articular cartilage	Dysplasia epiphysealis hemimelica
	Bone	Multiple epiphyseal dysplasia (MED)		
Physeal	Proliferating cartilage	Achondroplasia	Proliferating cartilage	Hyperchondroplasia
	Hypertrophic cartilage layer	Metaphyseal dysostosis/chondrodysplasia	Hypertrophic cartilage layer	Enchondromatosis
Metaphyseal	Primary spongiosa formation	Hyposphosphatasia	Spongiosa	Hereditary multiple exostosis (HME)
	Primary spongiosa absorption	Osteopetrosis		
	Secondary spongiosa absorption	Craniometaphyseal dysplasia		
Diaphyseal	Periosteal bone formation	Osteogenesis imperfecta	Periosteal bone formation	Hyperphosphataemia
	Endosteal bone formation	Idiopathic osteoporosis	Periosteal bone formation	Englemann's disease

Table 1

Appropriate blood tests to narrow the differential diagnosis include bone profile for hypophosphatasia, Jansen and PHP, and a bone marrow examination in storage disorders. Chromosome and genetic studies involving the family are done in order to study the genetic basis and help confirm and counsel for the condition.

Specific conditions

Tables 2–5 list the commonest skeletal dysplasias that may present to the orthopaedic surgeon. We have endeavoured to give a brief snapshot of each of these conditions, with particular emphasis on the orthopaedic manifestations and their management.

Epiphyseal conditions (part 1)

	Multiple epiphyseal dysplasia (MED)	Spondylo-epiphyseal dysplasia congenita (SEDc)	Spondylo-epiphyseal dysplasia tarda (SEDt)
Phenotype	Mild short stature with delayed formation of epiphyses, which are irregular	Very short – short trunk and limbs	Mild short stature
Inheritance	Autosomal Dominant (AD) due to mutations of COMP/COL9A/Matrilin 3 Autosomal Recessive (AR) due to DTDST gene mutation	AD – COL2A1 gene	X linked Recessive SEDt gene
Presentation	Adolescence	Birth	Late childhood
Orthopaedic manifestation	Joint stiffness Short digits Genu varum/valgum Hips similar to Perthes but symmetrical	Short limbs – rhizo and mesomelic Flat face/Cervical spine instability Talipes equino varus Coxa vara Premature OA	Early OA in second/third decade Spondylosis
Radiologic features	"double layer" patella Coxa Vara Early OA Mild irregularity end plates	Coxa vara Platyspondyly Metaphyseal involvement (less than SEMD)	Perthes-like but with synchronous lesions Atlanto-axial instability
Management	Guided growth to correct deformities before maturity Osteotomies for correction after maturity Joint replacement for osteoarthritis (OA)	Guided growth around hip and knee Osteotomies for coxa vara Joint replacement	Spinal stabilization Corrective osteotomies Joint replacement

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