Approach to skeletal dysplasia in the newborn

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Definition and prevalence

- Skeletal/ osteochondrodysplasias are heterogeneous disorders of generalized abnormalities of the bones and cartilage altering growth, shape and development of the skeleton
- Individually rare but not uncommon as a group: estimated prevalence of 2.4/ 10,000 live births and for lethal skeletal dysplasia: 1-1.5/ 10,000 births
- About 40% of skeletal dysplasias can be diagnosed perinatally that contribute to 9/1000 deaths

Role of neonatologist

- As a part of perinatal team: in prenatally suspected lethal skeletal dysplasia to discuss possible outcome with the family
- NICU management mainly respiratory and feeding

Fetal Skeletal Dysplasia:

- Fetal appendicular and axial skeleton undergo a patterned endochondral ossification while the calvarium and parts of clavicle and pubis ossify via membranous ossification
- Fetal skeleton is visualised by ultrasound around 14 weeks. It is important to remember that not all fetuses with short long bones carry a diagnosis of skeletal dysplasia.
- Fetal femur/ humerus <5thcentile or -2SD from the mean, Femur: foot ratio<1 in the second trimester should be evaluated further for a possible skeletal dysplasia
- Following fetal parameters and their comparison helps in predicting the pattern of abnormal skeletal growth: fetal cranium, abdominal circumference, mandible, clavicle, scapula, chest circumference and all long bones

    - Facial profile, presence and shape of vertebral bodies
    - Relative appearance of hands and feet with digits
    - Shape and mineralization pattern
- Ultrasound pointers to lethality
    - Short narrow chest with large head
    - Long bones<3SD below the mean with HC >75% ile
    - Chest: abdominal circumference< 0.6
    - Femur length: abdominal circumference< 0.16
    - Altered bone mineral density with fractures
    - Presence of hydrops fetalis and severe polyhydramnios
- Fetal MRI
    - Mainly for evaluation of fetal spine: scoliosis, stenosis, diastematomyelia or vertebral anomalies
- Molecular diagnosis possible only when there is family history of skeletal dysplasia and exact genetic mutation is known
- Prenatally diagnosed skeletal dysplasias are more likely to be lethal mainly because of
    - Respiratory insufficiency due to pulmonary hypoplasia
    - Concomitant visceral anomalies
- While prenatal imaging may point to a skeletal dysplasia it may not confirm a precise diagnosis given presence of variable phenotypes, overlapping features, rarity of the condition and lack of family history. Precise diagnosis is important for molecular studies and prenatal diagnosis in a future pregnancy
- Pre-delivery multi-disciplinary consultation (neonatologist, geneticist, obstetrician)
    - Genetic counseling regarding what could be expected and need of further evaluation, in utero transfer to a higher center with facilities

- Mode of delivery in view of relative macrocephaly and if the mother herself has a skeletal dysplasia with altered spine and pelvis anatomy
- Resuscitation and neonatal management for respiratory concerns
- Appropriate X-rays and sampling for genetic studies

- Common lethal skeletal dysplasias
  - Thanatophoric dysplasia
  - Osteogenesis imperfecta type II
  - Achondrogenesis

Skeletal dysplasia: postnatal management

- **Lethal skeletal dysplasia:**
  - Newborns with lethal skeletal dysplasia may also survive for a few days and sometimes for many months with significant morbidity
    - Minimal handling and mainly supportive/ palliative care as per discussion with the parents
    - Mortality is often secondary to respiratory failure (pulmonary hypoplasia, rib fractures, unstable thoracic cage, pneumonia), CNS hemorrhage and associated visceral anomalies etc
  - Descriptive documentation, clinical photographs depicting face, limbs and the body proportions and skeletal survey, especially to aid prenatal diagnosis in a future pregnancy
  - Genetic counseling and molecular diagnosis (DNA banking at the least)
  - Post mortem: Autopsy including bone and cartilage histopathology if necessary
- **Non-lethal skeletal dysplasia**

- These may not be suspected prenatally or may be suspected very late in gestation often leading to parental anxiety about "misdiagnosis." There are concerns about immediate survival and eventual "height/appearance" which need to be sensitively handled
- It is important to note family history, check parents' heights, facial features and body proportions while evaluating a newborn for skeletal dysplasia
    - A complete skeletal survey typically consists of the following radiographs and given the small size of the newborn can be combined as AP and lateral babygram/ kidogram
        - Skull: AP, LAT
        - Cervical spine: LAT
        - Thoracolumbar spine: AP, LAT
        - Chest: AP
        - Pelvis: AP
        - Both hands and wrists: PA
        - Extremities with feet: AP

Table 1: Reading a skeletal survey

Region	Features to look for
Skull	Sutures: craniosynostosis, Wormian bones in the lambdoid suture Mineralization, thickness of calvarium Craniofacial proportions: frontal bossing, midface hypoplasia, mandibular hypoplasia, retrognathia Shape of sella turcica
Chest	Ribs: number, shape, morphology, fusion Scapular hypoplasia Cardiac and lung
Spine	Alignment, vertebral shape, fusion/ segmentation anomalies, coronal clefting, beaking, scalloping / wedging of vertebral bodies

	Vertebral pedical ossification and interpedicular distance in lumbar spine Sidewise lateral convex curvature-scoliosis and dorsal convex curvature- kyphosis/gibbus, accentuated lordosis Cervical: shape and ossification of dens
Pelvis	Ossification: pubic bones ossified at birth Iliac bones shape, sacro-sciatic notches, acetabular roof Hip subluxation and dislocation Sacral fusion/segmentation anomalies
Extremities	Shortening: general/segmental Epiphyseal flattening, irregularity, delayed ossification Metaphyseal irregularity, widening Diaphyseal thinning/ thickening, shape Phalanges: shape, proximal pointing Accessary bones: polydactyly

- Apart from the structural variations generalized abnormalities of diffusely increased/decreased mineralization, epiphyseal/ metaphyseal abnormalities, diffuse platyspondyly may be noted
- 3D CT/MRI might be of additional help for further assessment of airways and help surgical intervention
- Airway fluoroscopy and laryngo-bronchoscopy with caution to assess airway anatomy and function

Issues in neonatal management

- Respiratory difficulties may be acute and/or chronic and may require prolonged mechanical ventilation or tracheostomy. Airway clearance and pulmonary toileting are important; however routine chest physiotherapy can be detrimental in view of rib fractures/ chest cage anomalies. Following risk factors need to be considered in managing newborns with skeletal dysplasia

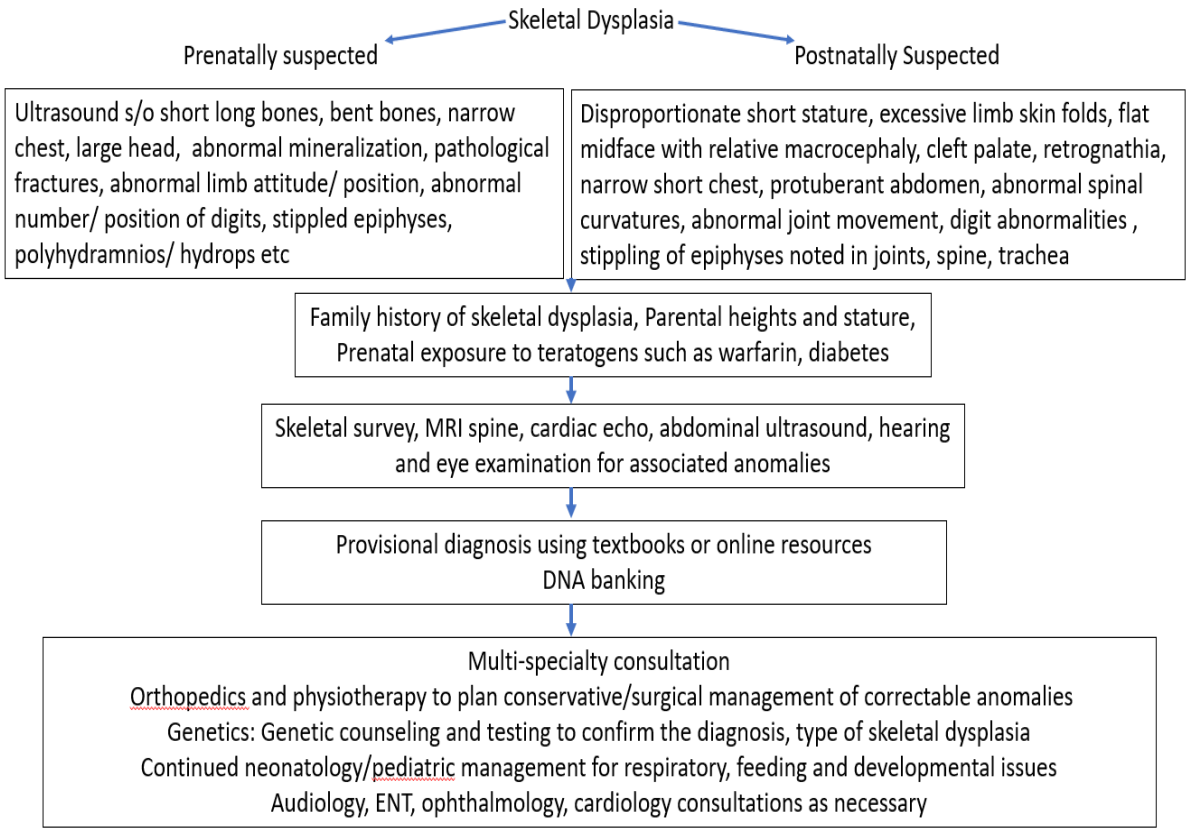
        - Airway anomalies due to narrow respiratory passages due to altered craniofacial structure, copious secretions, large tongue with relative micrognathia, altered airway tone: floppy and collapsing or rigid
        - Chest wall anomalies and restrictive lung disease: over-compliant or rigid chest wall leading to decreased functional residual capacity, narrow chest with reduced total lung capacity and increased work of breathing, tachypnea and increased risk of aspiration
        - Pulmonary hypoplasia
        - Central apnea secondary to brainstem and central nerve compression due to atlantoaxial instability
        - Associated congenital heart disease and secondary cor pulmonale
        - Iatrogenic: drug induced: bisphosphonate used to prevent bone resorption and fractures is pro-inflammatory and may lead to respiratory distress, pulmonary edema and acute exacerbation of pre-existing respiratory failure
    - Bethanechol: a cholinergic muscarinic agonist is being tried to increase tracheal smooth muscle tone and maintain airway patency and stability. This may help in reducing positive pressure ventilation and associated lung injury
    - Intrapulmonary percussive ventilation for better airway clearance by delivering low volumes of positive pressure to the airway at high frequencies creating an internal percussion effect and might help mobilization of mucus
- Anaesthetic issues secondary to respiratory complications and cervical anomalies contributing to difficult intubation. Fiber-optic intubation may be of choice and extreme flexion or extension of neck must be avoided
- Feeding difficulties secondary to respiratory issues which may require feeding gastrotomy

- Poor weight gain and growth in addition to underlying bone disorder

Post-NICU follow up

- Most infants with skeletal dysplasia need growth and development monitoring
- Orthopedic assessment and follow up as necessary for corrective and preventive measures
- Genetic work up for diagnosis of the index case and carrier testing/ prenatal diagnosis in a future pregnancy
- Social agencies and support groups may be of help as resources and advocacy groups

Fig 1: Approach to skeletal dysplasia



References and Further Reading

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