Campomelic Dysplasia:
Medical Treatment, Musculoskeletal Management, and Mistakes Not to Make

12\textsuperscript{th} International Congress on Early Onset Scoliosis

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DISCLOSURES

• No financial disclosures
• No conflicts of interest related to this talk
WHAT DOES IT MEAN – “CAMPOMELIC”

• Campto
  • Greek
  • Kamptos – flexible, base of “kamp-” meaning to bend of curve

• Melia
  • Greek
  • Denotes a condition of the limb

• Campomelic
  • “Bent limb”
CLINICAL DIAGNOSIS

• Based on clinical features
  - No single clinical finding is obligatory
  - Short, bowed limbs are classic (LE>UE)

Respiratory Distress

Large Head
Pierre Robin Sequence

Flat Face
Laryngotracheomalaica

Unambiguous genitalia

Dislocatable hips

Clubfeet

Bowed limbs
CLINICAL DIAGNOSIS

- Based on clinical features
  - No single clinical finding is obligatory
  - Short, bowed limbs are classic (LE>UE)
FACIAL DYSMORPHOLOGY

• Triangular long face, prominent nose, microstomia, and retrognathia

RADIOGRAPHIC FINDINGS

Scapular Hypoplasia

Vertically oriented Iliac wings

11 Ribs

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RADIOGRAPHIC FINDINGS

Limbs
- Bent - Not Always!
- Pre-tibial dimpling

Acamptomelic
Campomelic Dysplasia
RADIOGRAPHIC FINDINGS

Spine

- Cervical spine deformity
- Kyphoscoliosis
• Genetic Variation in the SOX9 gene
  • Found on Chromosome 17, q arm

• Encodes for SOX9 protein
  • Binds to DNA and regulates skeletal development and sex determination

• Genetic Variations
  • ~90% sequence variations (missence, splice variations)
  • ~5% chromosomal translocations
  • ~2% whole/partial gene deletion
LOCATION OF MUTATION LEADS TO PHENOTYPE

- Coding vs regulatory regions
GENETIC PATHOLOGY

• Prevalence
  • 1:40,000-80,000
  • ~15 case reports of living patients in the literature

• Penetrance
  • 100%

• Inheritance
  • Autosomal dominant
  • Most cases are *de novo* genetic variants
  • Some cases of mosaicism – can affect inheritance
DIFFERENTIAL DIAGNOSIS

• Severe OI – type 2,3
• Hypophosphatasia
• Cartilage Hair Hypoplasia
• Thanatophoric Dysplasia
• SED, congenita
• Stickler’s Syndrome (similar facial features)
DIFFERENTIAL DIAGNOSIS – PRENATAL BENT FEMURS

- > 40 disorders can be associated with bent femurs
- 459 cases reviewed

GENETIC COUNSELING

- AD - 50% chance of inheritance
- *De novo* case
  - *Test parents for mosaicism*
- Many newborns die in neonate period
  - Respiratory compromise
- Variably affected intelligence
- Short stature
- Hearing loss, aggressive scoliosis

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TREATMENT

• Airway Considerations
  1. Cleft Palate
  2. Laryngotracheomalacia / Pierre Robin Sequence

• Genitourinary
  1. Can have XY karyotype and female genitalia
  2. Recommend gonadectomy due to risk of gonadoblastoma

• General Orthopaedics
  1. Clubfoot casting
  2. Hip dysplasia per routine
TREATMENT

• Cervical Spine
  1. Early assessment necessary
  2. Bracing/early fusion may be needed

• Spinal deformity
  1. Progressive kyphoscoliosis – cervico-thoracic apex
  2. Bracing difficult
  3. Variable congenital abnormalities

• Respiratory Compromise
  1. Chest typically ok
  2. Airway instability
  3. Neurologic – c-spine instability/deformity
WHAT NOT TO MISS – CONGENITAL SPINAL DEFORMITIES

- 10 yo girl with CD and severe progressive scoliosis
- Congenital absence of pedicles C5-T9
WHAT NOT TO MISS – SEVERE CERVICAL ABNORMALITY

- Intubated after birth for apnea
- CTO brace attempted, but support withdrawn

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WHAT NOT TO MISS – MALIGNANT HYPERTHERMIA

• 16 month old boy with CD and significant medical issues
  • CHD, lung hypoplasia, skeletal pattern c/w CD
• Presented with severe respiratory compromise c/w malignant hyperthermia (prolonged fever, hypercarbia, elevated CK)
• Delayed diagnosis → cardiopulmonary arrest
CLEFT PALATE REPAIR – C SPINE ABNL

- 18 mn old – evaluated for cleft palate repair
- Xray and MRI showed dysplastic upper c spine and stenosis
- Intubated with little neck flexion, head stabilized during surgery
  neck extension avoided
# The phenotype of survivors of campomelic dysplasia

S Mansour, A C Offiah, S McDowall, P Sim, J Tolmie, C Hall

<table>
<thead>
<tr>
<th>Facial features</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flat face</td>
<td>5/5</td>
<td>5/5</td>
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</tr>
<tr>
<td>Hypertelorism</td>
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<tr>
<td>Long philtrum</td>
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<td>5/5</td>
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</tr>
<tr>
<td>Depressed nasal bridge</td>
<td>5/5</td>
<td>5/5</td>
<td>5/5</td>
<td>5/5</td>
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<tr>
<td>Micrognathia</td>
<td>5/5</td>
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<tr>
<td>Relative macrocephaly</td>
<td>5/5</td>
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<td>5/5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyphoscoliosis</td>
<td>Mild thoracic scoliosis</td>
<td>Yes, moderate, progressive</td>
<td>Yes, severe and progressive</td>
<td>Yes, severe and progressive</td>
<td>Yes, severe and progressive</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>No</td>
<td>Moderate</td>
<td>Gross motor delay only</td>
<td>Mild to moderate, global</td>
<td>Mild to moderate, global</td>
</tr>
<tr>
<td>Short stature</td>
<td>&lt;3rd centile</td>
<td>&lt;3rd centile</td>
<td>&lt;3rd centile</td>
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<td>&lt;3rd centile</td>
</tr>
<tr>
<td>Recurrent apnoea and respiratory problems</td>
<td>No</td>
<td>Yes, required tracheostomy</td>
<td>Yes</td>
<td>Mild</td>
<td>Yes</td>
</tr>
<tr>
<td>Conductive hearing loss</td>
<td>Yes (left side)</td>
<td>Yes</td>
<td>Yes</td>
<td>?</td>
<td>Yes</td>
</tr>
<tr>
<td>Dislocation of hips</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

+ = feature present, ? = not known.
CASE - 7 YEAR OLD FEMALE WITH C2/3 KYPHOSIS AND STENOSIS AT C2/3 WITH CORD COMPRESSION
CONCLUSIONS

1. Rare disease – but can test for genetic abnl in SOX9 gene

2. Clinical diagnosis
   - Bent limbs, 11 ribs, scapular hypoplasia, facial dysmorphism
   - No single feature is necessary for diagnosis

3. Genetic counseling → bent limb finding

4. Know what “not to miss”
   - C spine deformity
   - Airway issues
   - Progressive scoliosis with congenital issues
   - Malignant hyperthermia risk