osteogenesis imperfecta, lethal IIA

**Eponyms:**
- COL1A1
- COL1A2
- osteogenesis imperfecta, lethal type IIA
- osteogenesis imperfecta, neonatal lethal form IIA
- Vrolik osteogenesis imperfecta with rib fractures

**Inheritance:**
- autosomal dominant
- autosomal recessive
- genetic heterogeneity
- supposed germinal mosaicism

**Semiological Synthesis:**
Facio-skeletal disorder. Extreme bone fragility, intrauterine fractures, broad cupped femora, continuous rib beading, marked reduction in collagen I synthesis.

**LABORATORY DATA**

- chromosomal assignment
- chromosome 17q localization
- chromosome 7q localization

- gene, structural-functional anomalies
  - COL1A1 collagen I, alpha-1 polypeptide,
    gene chr.17q21.31-q22
  - gene analysis-DNA analysis

- tissue, biochemical changes
  - chondrocytes/articular-periarticular tissue,
    changes
  - COL1A2 collagen type I, alpha-2 polypeptide,
    gene chr.7q22.1
  - collagen biosynthesis/structure disorders
  - collagen gene defects

**MUSCULAR DISEASES**

- muscular defects, distrectual
  - hernia, inguinal

- systemic muscular defects
  - hypotonia, muscular weakness, muscular hypoplasia, myastenia, not including atrophy

**NEUROLOGICAL DISORDERS**

- brain anomalies
  - hydrocephalus not including: aquaeductal stenosis and Dandy Walker

**OCULAR DISORDERS**

- orbital changes
  - orbit, shallow, including: orbital ridges flat,
    hypoplastic supraorbital ridges

- sclera, changes
  - sclerae blue

**OROCRANIOFACIAL ANOMALIES**

- facies, modified appearance
  - dysmorphic face

- maxilla-cheek changes
  - midface hypoplasia, malar hypoplasia,
    hypoplastic zygomata

- neck, modified appearance
  - neck, short

- nose, modified appearance
  - nose, hooked’ parrot, beaked
  - nose, small, nose tiny, nose short, not including very small

**OTHERS**
inheritance
- inheritance, autosomal dominant
- inheritance, autosomal recessive
- inheritance, genetic heterogeneity

PRENATAL-NEONATAL MODIFIED DATA
foetal changes
- birth length, decreased; low birth length
- birth weight, low; foetal growth decreased, intrauterine growth retardation, intrauterine growth restriction, IUGR
- foetal changes, recognized by laboratory data
- foetal changes, recognized by ultrasound techniques
- foetal fractures, fractures in utero
- foetal movements decreased, foetal akinesia, foetal hypokinesia
- hydrops foetalis, foetal hydrops, including foetal ascites

prenatal diagnosis
- prenatal diagnosis, echographic
- prenatal diagnosis, metabolic
- prenatal diagnosis, molecular

SKELETAL DISORDERS
bones, lesions, structural changes
- bone, fractures not including: fractures in utero
- bone, twisted
- bones, crumpled
chest, changes
- chest, narrow, narrow thorax
fontanelles-sutures, changes
- fontanelles, cranial sutures, closure delayed
limb anomalies, limb defects
- bone, bowing, limbs bowed, camptomelia
- lethality, constant in osteochondrodysplasias
- osteogenesis imperfecta
ossification, changes
- osteopenia, bone hypodensity, demineralization of the bones, deficient ossification
- wormian bones
pelvis, changes
- pelvis, dysplasia
ribs, anomalies
- ribs, short, hypoplastic
skull, lesions, mineralization changes
- calvarium thin, poorly mineralized
spine, changes
- platyspondily, including short spine
stature, growth, modified habitus
- stature, short, including micromelia, including short limbs
vertebral changes
- vertebral anomalies, unspecified type

Super group:

Super aggreg. COLLAGEN, BIOSYNTHESIS/STRUCTURE DISORDERS
Aggregations: osteogenesis imperfecta

FOETAL CHANGES
foetal changes, recognized by laboratory data
foetal changes, recognized by ultrasound techniques
hydrops foetalis

LETHALITY
lethality, constant in osteochondrodysplasias
osteochondrodysplasias and other severe skeletal defects

**OTHER**
- craniofacial dysmorphism due to cranial changes, including microcephaly
- dysmorphic face

### Differential diagnosis:

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<th>ID</th>
<th>Condition</th>
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<tr>
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<td>acrania</td>
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<td>Caffey disease</td>
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<td>camptomelic dysplasia, dominant type</td>
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<td>dyssegmental dwarfism, Rolland type</td>
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<td>Knowles-Winter syndrome</td>
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<td>thanatophoric dwarfism</td>
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**Aggregation(s) [in differential diagnosis]:**
- osteogenesis imperfecta
- hydrops foetalis
- lethality, constant in osteochondrodysplasias

### Bibliography

- OMIM ID: 166210
  - Smith’s Recognizable Patterns of Human Malformation. 6th Edition pag. 565-567
  - Prenat.Diagn.17(6),559-570,1997
  - OMIM ID: 120160
  - OMIM ID: 120150
  - Annuario Orphanet-Italia delle Malattie Rare 2005, pag. 635
  - OMIM ID: 259400