18 Chondrodysplasia Punctata, Rhizomelic Type

CDPR

Symmetrical rhizomelic dwarfism, koala bear facies, hypoplastic distal phalanges, cataracts, contractures, calcific stippling of hyaline cartilage

Frequency: 1 in 84,000 live births; both sexes equally affected.

Genetics

Autosomal recessive (OMIM 215100); peroxisomal disorder, mutation in the *PEX7* gene, mapped to 6q22-q24; complementation analysis after somatic cell fusion suggests that mutations in several genes can produce either rhizomelic or nonrhizomelic chondrodysplasia punctata; type 2 rhizomelic chondrodysplasia punctata caused by deficiency of DHAPAT, which maps to chromosome 1, and type 3, by mutations in the *AGPS* gene at chromosome 2q31.

Prenatal Diagnosis

Biochemical analysis of cultured amniotic cells or chorionic trophoblasts is possible and may yield the diagnosis prenatally.

Clinical Features

- Early lethality for most children
- Growth deficiency identifiable at birth
- Sparse, coarse hair
- Koala bear facies due to nasal bone hypoplasia, saddle nose
- Bilateral congenital cataracts (2/3 of cases)
- Symmetrical proximal limb shortening, humeri most severely involved
- Spasticity and seizures
- Microcaphaly
- Severe mental retardation

Differential Diagnosis

- Chondrodysplasia punctata X-linked
- Fetal warfarin syndrome
- Phytanic acid oxidase deficiency, infantile type
- Rhizomelic syndrome, Urbach type
- Cerebro-hepato-renal syndrome

Radiographic Features

Extremities

- Calcific stippling of hyaline cartilage (ends of humeri and femurs), epiphyseal centers, and extracartilaginous tissues
- Symmetrical rhizomelic shortening of the limbs (humeri and femurs)
- Marked metaphyseal changes (splaying, irregularities, calcific stippling)
- Severely retarded and distorted epiphyseal ossification
- Brachymetacarpalia (4th metacarpals most frequently involved)
- Hypoplastic distal phalanges
- Progressive disappearance of stippling during the first 3 years of life in the (few) surviving children

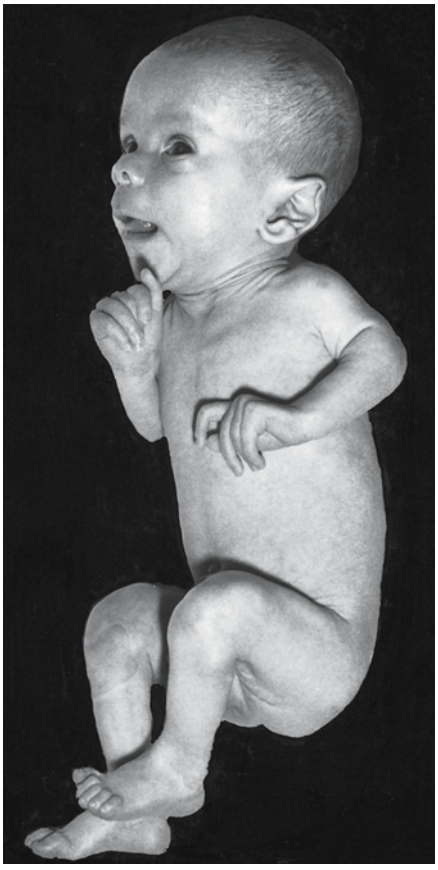

Fig. 18.1. Patient 1, 2 months. Koala bear facies owing to nasal bone hypoplasia and saddle nose. Symmetrical shortening of proximal portions of the limbs, with humeri most severely involved. (Reprinted, with permission, from Canepa et al. 1996)

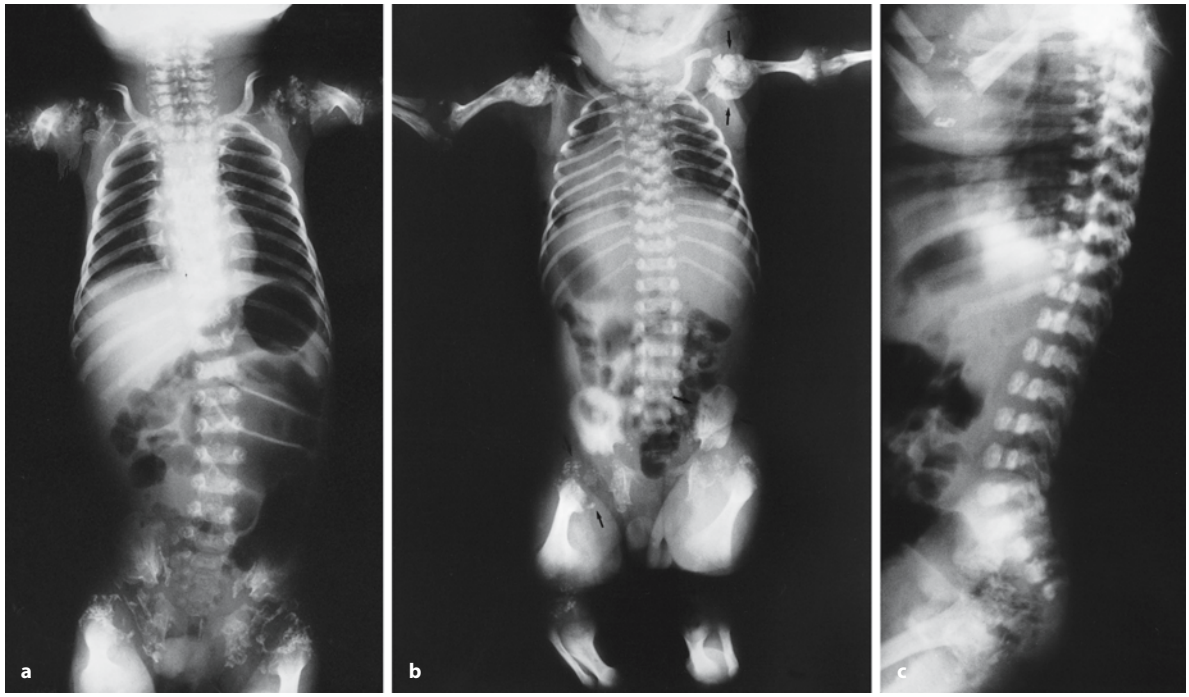

Fig. 18.2. **a** Patient 1, 2 months. Stippling is seen at proximal ends of humeri and femurs and in the pelvic region. Metaphyses of humeri and femurs are irregular and splayed. Vertebrae are flat with widened intervertebral spaces. (Reprinted, with permission, from Canepa et al. 1996). **b** Patient 2, 3 days after birth. The humeri and femurs are short and broad, with splayed metaphyses and extensive epiphyseal calcific stippling. There is mild platyspondyly. **c** Patient 2, 3 days after birth. Vertebral bodies at dorsal and lumbar levels are each split into a ventral and a dorsal segment (coronal clefts). Stippling is seen at hips and elbows

Spine

- Coronal cleft vertebrae
- Vertebral abnormalities (platyspondyly, vertebral plate irregularities)
- Absent stippling of axial skeleton

Pelvis

- Trapezoid shape of iliac bones (iliac crests and basilar portions of iliac bones of similar width)

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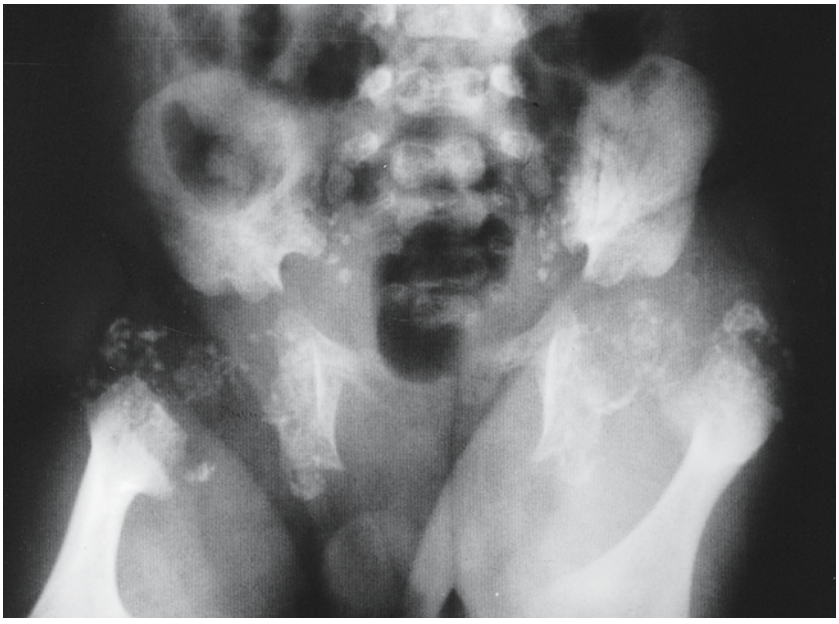

Fig. 18.3. Patient 2, 3 days after birth. Iliac bones are trapezoid. Extensive stippling is seen in area of femoral heads, necks, greater trochanters, ischia, and sacroiliac joints. Ossification of pubic bones is retarded

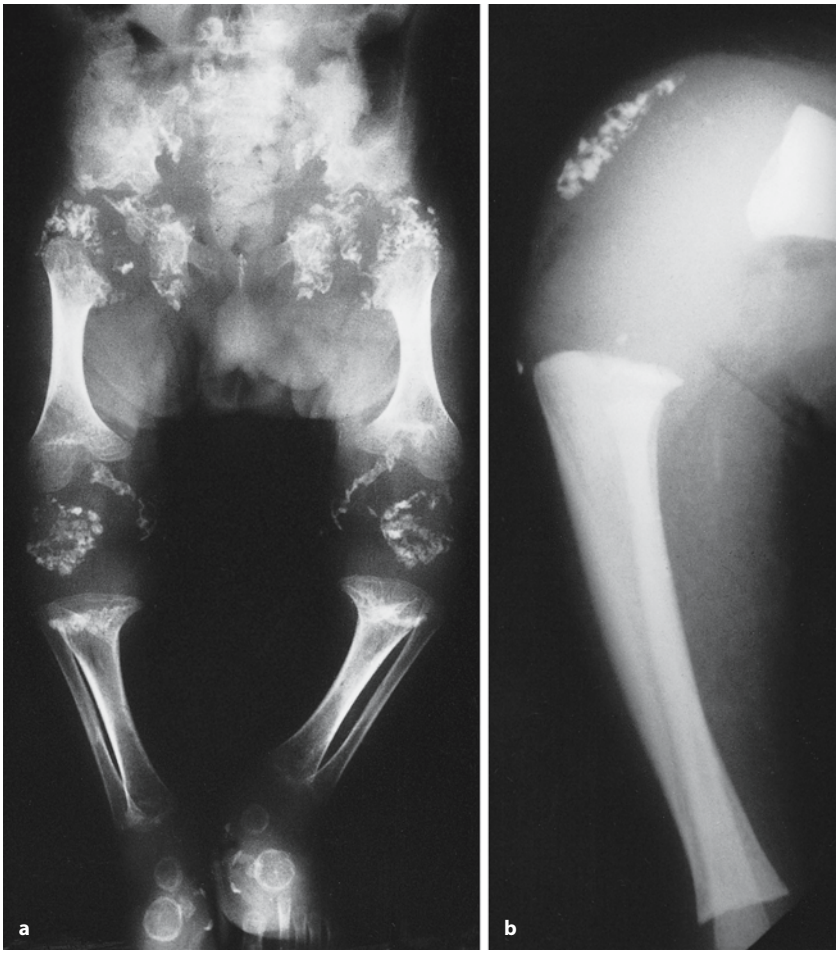

Fig. 18.4. **a** Patient 1, 2 months. Femurs are symmetrically shortened, with wide and irregular metaphyses. Tibias are more fully developed. Pelvis is trapezoid. Stippling is seen at pelvis and hips, knees, and heels. (Reprinted, with permission, from Canepa et al. 1996). **b** Patient 2, 3 days after birth. Tibia and fibula are well developed

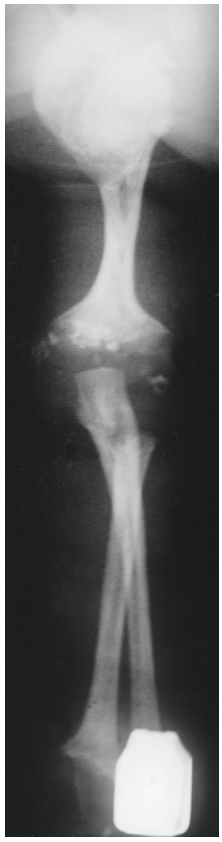

Fig. 18.5. Patient 2, 3 days after birth. The humerus is short and broad relative to radius and ulna

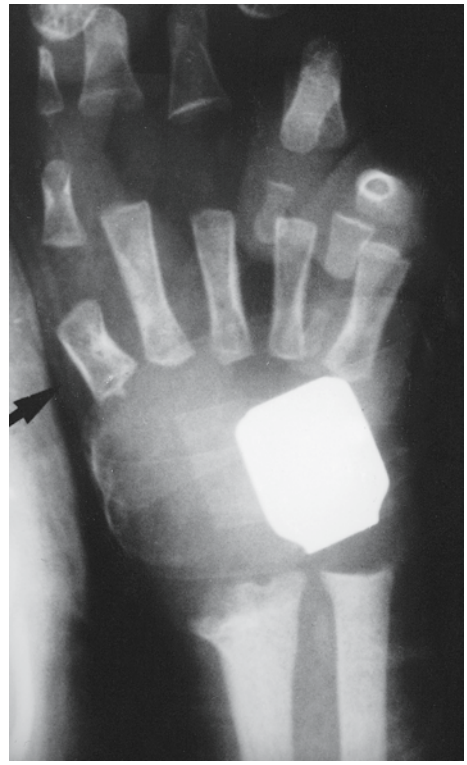

Fig. 18.6. Patient 2, 3 days after birth. There is irregular shortening of the metacarpals. Metaphysis of radius is widened and irregular

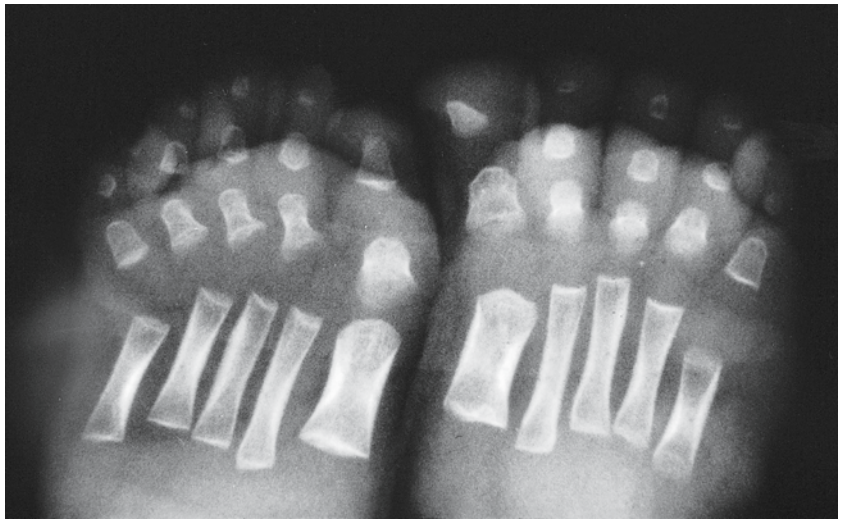

Fig. 18.7. Patient 2, 3 days after birth. Distal phalanges are hypoplastic. Mild metaphyseal irregularities and length discrepancies of the metatarsals are also apparent