Case 12388

Eurorad

Rhizomelic chondrodysplasia punctata

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Section: Paediatric radiology
Area of Interest: Bones
Procedure: Diagnostic procedure
Imaging Technique: Conventional radiography
Special Focus: Dysplasias Case Type: Clinical Cases
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Patient: 1 days, female

Clinical History:

A female infant weighing 2.8 kg was born to non-consanguineous parents at 38+6 weeks gestation. On examination, the infant was hypotonic with bilateral fixed talipes and radial deviation of both wrists. The upper limbs were noted to be short. A referral to Medical Genetics and a skeletal survey were requested.

Imaging Findings:

There is rhizomelic shortening of the limbs affecting predominantly the humeri and to a lesser extent the femora. Pronounced metaphyseal flaring and epiphyseal stippling are seen in relation to the humeri; these abnormalities are again less marked in the femora. Stippled calcific foci are seen within the cartilage at the insertion of the patellar tendon and surrounding the patella itself. Similar stippled foci of calcification are seen in relation to the anterior pelvis and around the SI joints, and in the anterior neck.

In addition, there are coronal cleft vertebrae visible on the spine radiographs.

The survey showed the forearms, lower legs bones and the extremities to be spared.

Discussion:

Chrondroplasia punctata describes the spotted calcifications visible on plain radiographs that result from abnormal calcium deposition in areas of enchondral bone formation [1].

Rhizomelic chondrodysplasia punctata—rhizomelia refers to shortening of the proximal limb segment—is rare, having an incidence of approximately 1:100, 000. Inheritance is via an autosomal recessive mechanism, with the disorder being due to an abnormality in the metabolism of subcellular organelles known as peroxisomes, which are essential in many human metabolic pathways [2, 3].

At a genetic level, three subtypes of rhizomelic chondrodysplasia punctata are recognised, though clinically they are indistinguishable. Type I is the most common, arising due to mutations in the PEX7 gene located on chromosome 6q23. Our patient was typed as a compound heterozygote with additional p.G217R and p.L292 mutations. The 'Online Mendelian Inheritance of Man' (syn. OMIM) directory numerically classifies rhizomelic chondrodysplasia punctata type I as #215100 and gives further detail of the genetic and enzyme defects of this condition.

Subtypes II and III are likewise inherited in an autosomal recessive fashion. GNPAT and AGPS gene mutations respectively lead to separate peroxisomal enzyme defects [4, 5].

Phenotypically, involved infants have a characteristic facies, with a prominent forehead, mid-face hypoplasia and

cataracts. Anteversion of the nares and a long philtrum may also be observed. Severe neurodisability, with spastic tetraplegia, seizures, intellectual impairment and failure to reach developmental milestones is present too [2, 6]. Together with immobility and restricted expansion of a physically small thorax, the neurological complications predispose to aspiration and pneumonia; life expectancy is consequently reduced, with death usually occurring within the first decade of life [3].

The radiographic findings in the presented case are classical for (sub-type I) rhizomelic chondrodysplasia punctata and include: rhizomelic limb shortening, which is most striking in the humeri, pronounced coronal cleft vertebrae, and the eponymous stippled epiphyseal cartilage, which involves the knee, hip, elbow and shoulder joints. The costo-chondral junctions, vertebrae, larynx and hyoid are similarly involved. Metaphyseal modelling anomalies have also been documented [3]. The stippling seen in the epiphyses occurs as a result of heterogeneous ossification of the cartilage. Residual cartilage in the vertebral bodies results in the striking radiological appearance of coronal cleft vertebrae.

Microcephaly, with delayed myelination, increased ventricular size and prominent subarachnoid spaces is shown by MR imaging. Supra-tentorial myelination abnormalities, progressive cerebellar atrophy, and cervical stenosis and subsequent cord compression are also recorded. [7, 8]. To date, our patient has not undergone neuroimaging.
Differential Diagnosis List: Rhizomelic chondrodysplasia punctata Type I. Compound heterozygous PEX7 gene mutation, Zellweger\'s syndrome, Non-rhizomelic chondrodysplasia punctata (Conradi Hunerman Syndrome), Trisomy 18, Vitamin K reductase deficiency, Drug and teratogen exposure: warfarin, Phenytoin or phenacetin, Fetal alcohol syndrome

Final Diagnosis: Rhizomelic chondrodysplasia punctata Type I. Compound heterozygous PEX7 gene mutation

References:

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Figure 1

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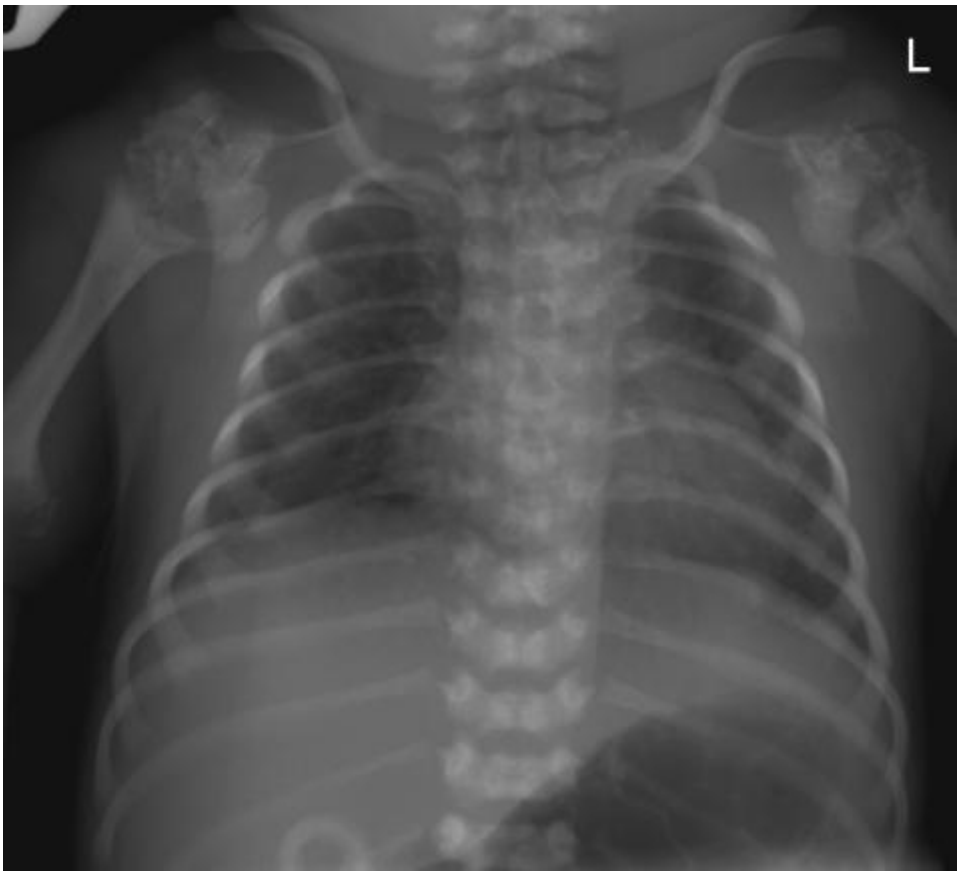
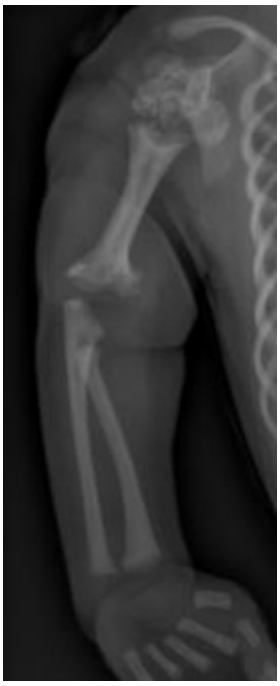


Description: Coronal cleft vertebrae and epiphyseal stippling involving the humeral heads is evident, with flaring of the adjacent metaphyses. **Origin:** Paterson A, Dept of Radiology, Royal Belfast Hospital for Sick Children

Figure 2

a



Description: There is rhizomelic shortening of the limb with flaring of the humeral metaphyses and stippling of the epiphyses around the shoulder and elbow. The forearm bones and hand are spared.
Origin: Paterson A, Radiology Dept, Royal Belfast Hospital for Sick Children, UK

Figure 3

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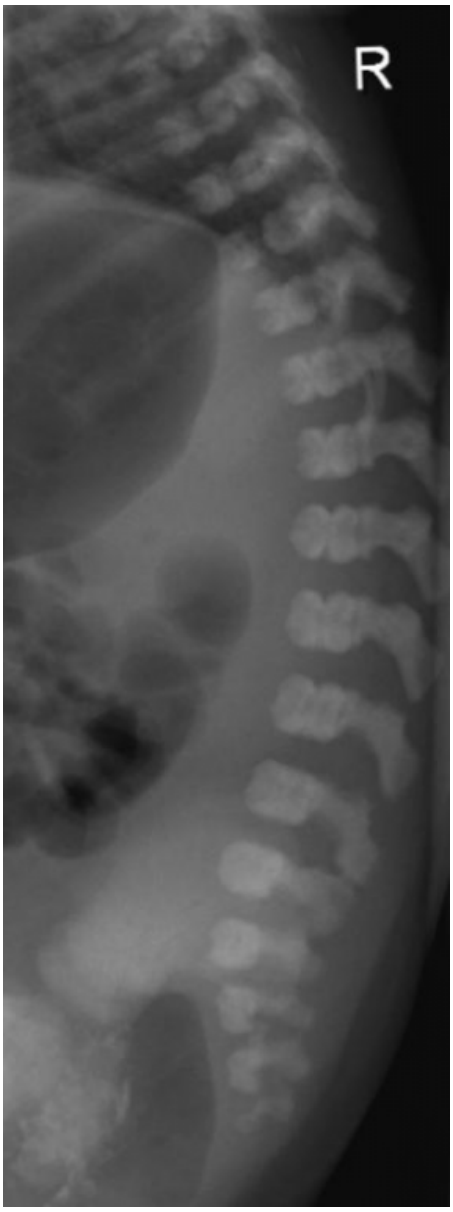

Description: Prominent coronal cleft vertebrae are seen in the lower thoracic and lumbar region. The pedicles are broader than normal. **Origin:** Paterson A, Radiology Dept, Royal Belfast Hospital for Sick Children, UK

Figure 4

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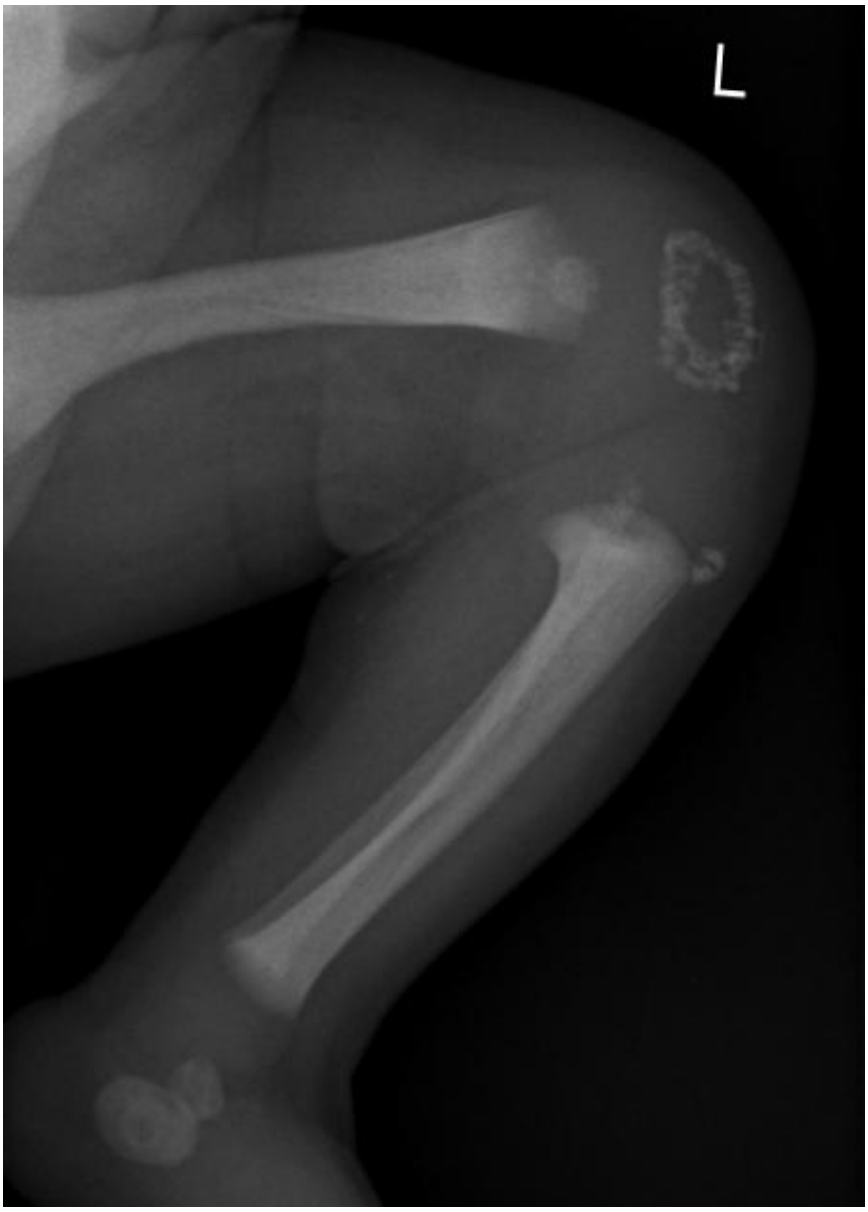

Description: Epiphyseal stippling involves the femur and the proximal tibia. Stippling is also apparent at the insertion of the patellar tendon and surrounding the patella itself. **Origin:** Paterson A, Dept of Radiology, Royal Belfast Hospital for Sick Children, UK

Figure 5

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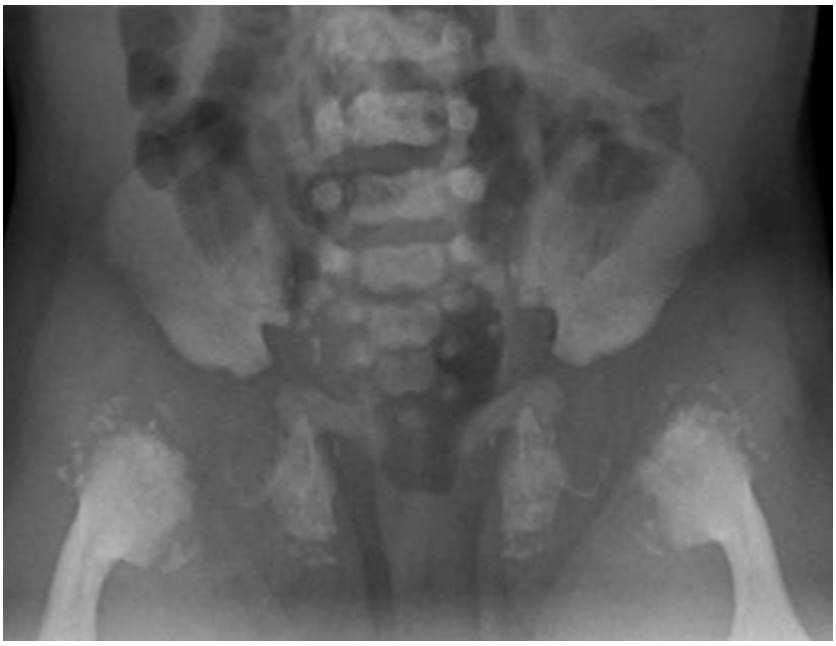

Description: Stippling is apparent around the anterior pelvis and the sacro-iliac joints. The proximal femoral epiphyses are also stippled. **Origin:** Paterson A, Dept of Radiology, Royal Belfast Hospital for Sick Children, UK

Figure 6

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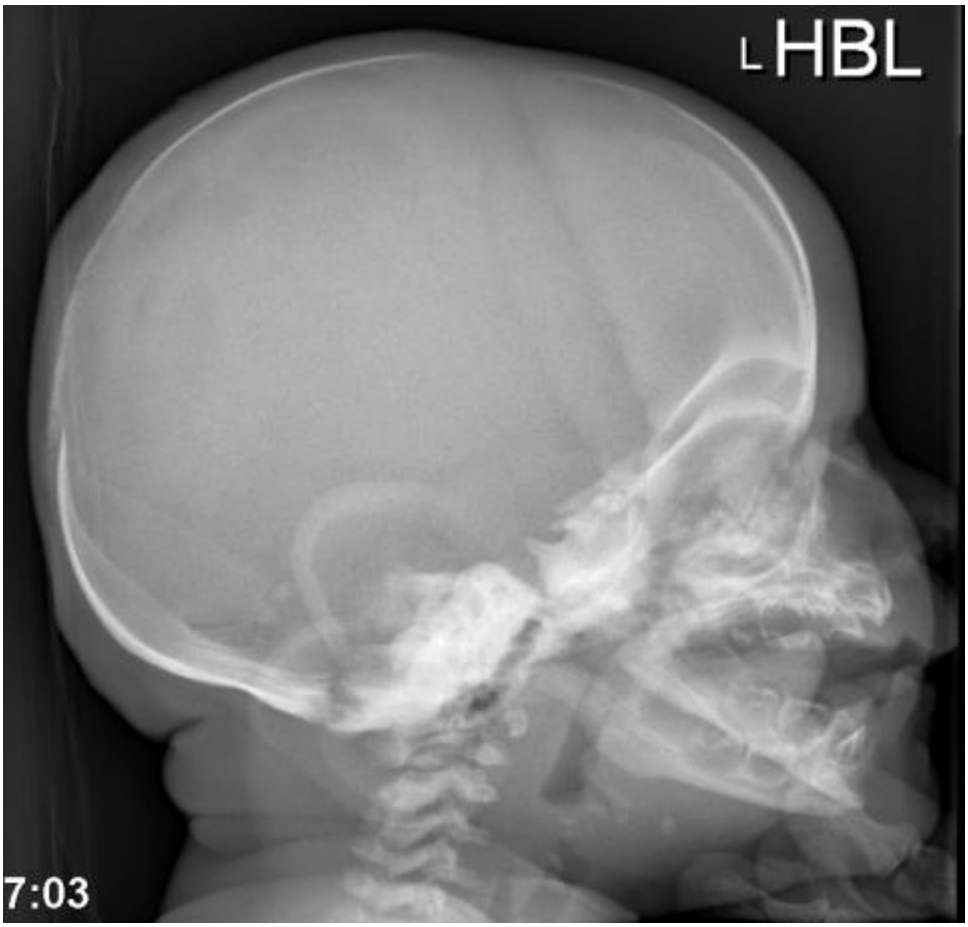

Description: There is maxillary hypoplasia. The cervical vertebrae show platyspondyly. Foci of calcification are seen in the soft tissues of the neck inferior to the hyoid bone. **Origin:** Paterson A, Dept of Radiology, Royal Belfast Hospital for Sick Children, UK