Rhizomelic Chondrodysplasia Punctata: A case Report and Brief Review of Literature

Goyal V K, Jora R, Sharma P, Sundarajan S
Department of Pediatrics, Dr Sampurnanand Medical College Medical College, Jodhpur, Rajasthan, India


INTRODUCTION

Rhizomelic chondrodysplasia punctate (RCDP) is a rare peroxisomal disorder with an estimated incidence of 1: 100000 live births. Classical form is characterized by proximal shortening of the limbs, punctate epiphyseal calcifications, facial dysmorphism, cataracts, cardiac malformations, growth failure, and psychomotor retardation.1

We are reporting a 3½-month-old male child who presented to us with growth failure, but on evaluation, also had developmental delay, facial dysmorphism, symmetric proximal shortening of limbs, multiple joint contractures, and cataracts. X-ray limbs revealed punctate calcifications at epiphyseal regions. Based on the clinicoradiological picture, we inferred the diagnosis as RCDP. Though biochemical and genetic tests are confirmatory, the diagnosis can be emphasized with a compatible clinicoradiological picture.2,3 Through this case report, we want to highlight the importance of simple investigations like X-ray in clinching the rare diagnosis. In addition, clinical presentation of RCDP has been briefly reviewed.

CASE REPORT

A 3½-month-old male infant, the first issue of second-degree consanguineous marriage parents, presented to us with impairment of growth. He was delivered at 36 weeks of gestational age with a birth weight of 2.2 kg via lower segment cesarean section in view of decreased fetal movements, oligohydramnios, and poor progression of labor. Antenatal history revealed delayed quickening and decreased the perception of the fetal movements to the mother. There was no history of fever, rash, or lymphadenopathy during the antenatal period. History of teratogen or radiation exposure was also absent. Birth history was uneventful. Since birth, he received exclusive breastfeeding but failed to grow.

Anthropometry revealed weight 2.25 kg (3rd centile - 5.4 kg), length 47 cm (3rd centile - 59 cm), head circumference 32 cm (3rd centile 38 cm), US/LS ratio 1.95:1 (normal - 1.7:1). All four limbs had symmetric shortening of proximal parts. He had multiple contractures over ankle, knee, and elbow joints. Facial features included depressed nasal bridge and flattened facies. Eye examination showed both eye cataracts.

ABSTRACT

We are reporting a 3½-month-old male child who presented to us with growth failure, but detailed evaluation revealed clinicoradiological picture compatible with rhizomelic chondrodysplasia punctata; a rare autosomal recessive peroxisomal disorder.

Keywords: Epiphyseal calcifications, Growth failure, Rhizomelic chondrodysplasia punctata
The bilateral reducible inguinal hernia was also present. X-ray limbs revealed short humerus of both upper limbs and short femur of both lower limbs with epiphyseal calcifications at the bilateral shoulder, elbow, knee, and ankle joints (Figures 1 and 2). Echocardiography showed ostium secundum atrial septal defect of 7 mm size, and tricuspid regurgitation, with no evidence of pulmonary artery hypertension or right outflow tract obstruction. Brain stem evoked response audiometry revealed bilateral cessation of activity of around 50 dB.

Routine biochemical tests and thyroid function tests were normal. Based on these features, diagnosis of RCDP was entertained. Biochemical and genetic tests for RCDP could not be performed due to financial constraints. Parents were counseled about the nature and prognosis of the disease.

**DISCUSSION**

Chondrodysplasia punctata (CDP) is the name given to a collection of skeletal dysplasias characterized by punctate epiphysis. This entity was first described by Conradi in 1914. Previously, it was also known as chondrodystrophy calcificans congenital or congenital stippled epiphyses and was broadly divided into two forms; non-rhizomelic and rhizomelic.

Etiological classification of CDP includes: peroxisomal disorders (zellweger syndrome, neonatal adrenoleukodystrophy, infantile refsum disease, and RCDP), chromosomal disorders (trisomy 18 or 21), maternal disorders (like SLE), congenital infections, and teratogenic drugs (like alcohol, warfarin). Based on inheritance pattern, CDP can classified into four types; autosomal dominant (Conradi-Hunermann’s type), autosomal recessive (rhizomelic type), the X-linked dominant form (Happle syndrome), and the X-linked recessive form. 

RCDP is a rare form of CDP. It includes clinically indistinguishable 3 genetic subtypes; RCDP I, II, and III. Type I is the most common, and results from disorder of peroxisomal biogenesis, whereas Type II and III are caused by a single peroxisomal enzyme deficiency. Mutations in PEX7, acyl-CoA: dihydroxyacetone phosphate acyltransferase and alkyl-dihydroxyacetone phosphate synthase genes result into RCDP I, II, and III, respectively.

Clinical presentation of RCDP varies from mild to severe form. At the severe end of the spectrum, the disease is characterized by a distinct facial appearance, congenital cataracts, symmetric shortening of the proximal long bones, transient periartricular calcifications, arthrogeneous contractures, somatic growth impairment (microcephaly, short height, and underweight), psychomotor retardation, seizures, and cardiac defects. Facial features include micrognathia, malar hypoplasia, flattened nasal bridge, and bulbous nose, with flattened face appearance. In addition skin changes like, ichthyosis and alopecia, and variable deficiency of audition and vision may be associated. On the other hand, mild RCDP may present only with congenital cataracts and developmental delay.

Common radiological features are punctate epiphyseal calcifications, metaphyseal abnormalities, and coronal clefts in vertebral bodies of thoracic and lumbar spine. Kyphoscoliosis and spina bifida may be seen with variable frequency. The punctate radiological lesions result from the degeneration of cartilage, represented by chondrocytes with pyknotic nuclei and eosinophilic cytoplasm, followed by ossification.

MRI shows delayed myelination, dilated ventricles, progressive cerebellar atrophy, and cervical stenosis. Cardiac defects are seen in 52% of cases; atrial septal defects (80%) are the most common followed by patent ductus arteriosus, pulmonary artery hypoplasia, Tetralogy of Fallot, and mitral valve prolapse.
All the three sub-types of RCPDs are biochemically characterized by low levels of plasmalogens in erythrocytes. Normal to high level of phytanic acid seen in Type I may help in differentiating it from other two subtypes as Type II and III are associated with normal phytic acid levels.\textsuperscript{15} RCDP can be suspected antenatally also based on characteristic bone deformities seen during second-trimester sonography. Prenatal diagnosis can be established by demonstration of peroxisomal dysfunction in cultured chorionic villous or amniotic fluid cells.\textsuperscript{16}

Treatment is mainly supportive. Dietary phytanic restriction acid to avoid the consequences of phytanic acid accumulation over time may benefit individuals with milder forms. Genetic counseling should be provided to the affected family.\textsuperscript{6,11}

Prognosis depends on clinical severity, which in turn, is determined by the erythrocyte plasmalogen levels; lower the level more severe the disease. Classical form is lethal with 60% of deaths occurring by 1 year of age.\textsuperscript{6,13}

CONCLUSION

Organic failure to thrive, a disease of diverse etiology usually requires an extensive evaluation to unearth the underlying cause. But sometimes, even basic investigations like X-ray can pinpoint the etiology and thereby help in reducing the unnecessary investigations.

REFERENCES