CASE REPORT

A diagnostic and management odyssey of a rare case of rhizomelic chondrodysplasia punctata

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Abstract

Rhizomelic chondrodysplasia punctata (RCDP) is one of the rare inherited peroxisomal disorders that belongs to the heterogeneous group of chondrodysplasias presenting with proximal shortening of the limbs and distinctive punctate calcifications of bones and cartilages. This disorder occurs due to mutations in the genes responsible for peroxisomal biosynthesis inherited commonly as autosomal recessive, though a few are reported as x-linked dominant and recessive. The diagnosis can be made on clinical findings along with a skeletal survey; however, sonography and genetic analysis are crucial for a definitive prenatal diagnosis in cases where RCDP is inherited within a family as there is no definitive cure for RCDP and the treatment revolves around the management of its manifestations and complications.

We hereby report the case of a neonate with features of RCDP. Significant respiratory involvement in RCDP babies is linked with high mortality which was also observed in this case.

Key Words: Rhizomelia, Chondrodysplasia punctata, Peroxisomal disorder, Skeletal dysplasia.

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Introduction

Rhizomelic chondrodysplasia punctata (RCDP) is an extremely rare, commonly autosomal recessively inherited congenital skeletal dysplasia caused by defective plasmalogen biogenesis and impaired peroxisomal function with a reported prevalence of less than 1/100,000 live births. It is characterised by rhizomelic shortening of limbs along with ectopic punctate calcification of the axial and appendicular skeleton and distinctive facial features. It belongs to a group of congenital bone dysplasias termed chondrodysplasia calcificans punctate (CCP) recognised for the first time in 1914 by Eric Conradi.[1]

We present a case of RCDP in a neonate from Pakistan, highlighting the significance of timely prenatal diagnosis through genetic testing in conjunction with ultrasound findings and genetic counselling for planning future pregnancies given the positive family history.

Case report

A male neonate, born of a consanguineous marriage at 38 weeks of gestation via caesarean section to a 23-year-old G3P1+1 woman in May 2024 in Pakistan Air Force Hospital, Islamabad, Pakistan. Previously, the mother experienced one early miscarriage and one stillbirth due to hydrops foetalis at 32 weeks owing to gestational diabetes and polyhydramnios. The evolution of the currently investigated pregnancy was complicated by gestational diabetes and polyhydramnios (Amniotic fluid index: 30cm). There was no history of exposure to a teratogen, or any drug or medicine abuse during pregnancy. The mother had irregular antenatal visits and an antenatal scan at 33 weeks revealed dysmorphic facial features and proximal shortening of long bones with a two-week disparity.

The baby was born limp needing resuscitation, and had an APGAR score of 6 and 7 at 1 and 5 minutes. The baby developed a grimace but there was aphonia. His birth weight was 3,000g, head circumference was 34cm and length was 48.5cm (all at 50th centile). Upon physical examination, the baby had proximal shortening of both upper and lower limbs, with dysmorphic features including coarse facies, a depressed nasal bridge with upturned nostrils, a short neck, a narrow thorax, and thick velvety skin (Figure 1).

The baby had copious oral secretions and persistent respiratory distress, hence was put on ventilatory support. The supportive care started along with intravenous antibiotics, and a blood work-up including karyotyping. Chest radiographs were obtained shortly after delivery along with the skeletal survey revealing punctate calcifications of articular process ossification centres in the spine as well as tarsal ossification centres, suggestive

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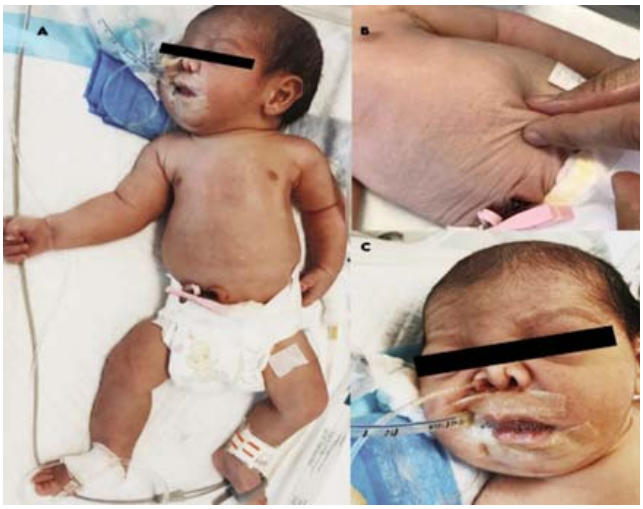

Figure-1: Showing rhizomelic shortening of limbs, thick skin, anteverted nares and coarse facies.

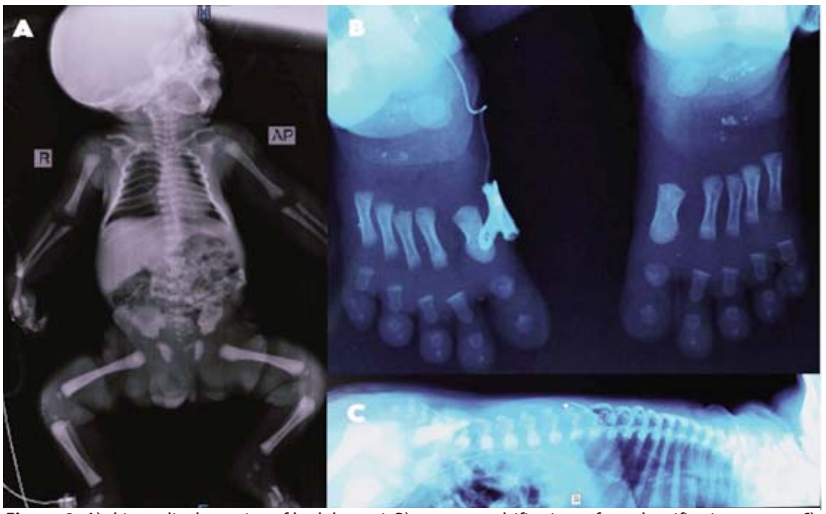

Figure-2: A) rhizomelic shortening of both humeri; B) punctate calcifications of tarsal ossification centres; C) extensive punctate calcifications.

of chondrodysplasia punctata (Figure 2).

Thereafter, a blood sample was sent for genetic analysis. The child maintained normal saturations on minimal ventilatory settings. His ophthalmologic examination and cranial ultrasound were unremarkable while a horseshoe kidney was demonstrated on ultrasound of the kidneys, ureters, and bladder (KUB) and echocardiography revealed a small Patent Ductus Arteriosus (PDA). His initial blood workup including inflammatory markers, metabolic screen, and thyroid stimulating hormone (TSH)was unremarkable. Blood cultures were negative. Multiple trials of weaning off were carried out but failed despite maintaining normal saturations on minimal ventilatory settings. On the 11th DOL (day of life), the baby had an episode of desaturation, and cyanosis with decreased air entry on the left side of the chest for which needle thoracotomy was done followed by chest drain insertion after the CXR confirmed tension pneumothorax. Due to the prolonged ventilator dependency low dose Dexamethasone therapy was started for weaning.

Echocardiography was repeated to look for pulmonary hypertension which came out to be unremarkable. Karyotyping exhibited a normal male genotype. The baby remained on ventilatory support for 35 days and our team had a detailed discussion with both parents regarding the disease, associated complications, and the poor outcome of the baby. Considering the exhaustion of financial support and the poor prognosis of the baby, the parents opted for extubation and keeping the baby on non-invasive ventilation (NIV). The baby suddenly collapsed and expired on the 38th DOL on NIV. Genetic analysis report confirmed RCDP having a homozygous mutation in the Arylsulfatase E (ARSE) gene which in the index case came out to be x-linked recessive; however, it is more commonly inherited as autosomal recessive.

Discussion

Rhizomelic chondrodysplasia punctata (RCDP) is commonly inherited as an autosomal recessive, exceptionally rare type of inherited skeletal dysplasia caused by impaired genes responsible for the peroxisomal functioning and biogenesis of plasmalogens that are essential for preserving the cellular membrane's structure and functionality. The insufficiency of plasmalogens leads to defective mental and physical development. Rhizomelic chondrodysplasia puntata has five different forms, type 1 being the most prevalent as a result of variants of the PEX7 gene. The genes that account for the other four respective types of RCDP are GNPAT, AGPS, FAR1, and PEX5.[1]

The life expectancy of children born with RCDP is expected to be less than third decade with the majority of the patient population being under the age of 15, while children with classic RCDP1 do not survive beyond infancy and mostly die as a consequence of infections and respiratory insufficiency. Currently, there is no definitive cure for RCDP and the main focus of care is managing its manifestations and complications which involves multidisciplinary approaches.[1,2]

The most prevalent type, i.e. RCDP1, is further subdivided into classic (severe) and non-classic (mild) types subject to the plasmalogen levels. The classic RCDP1 type is characterised by rhizomelic limb shortening, contractures, frequent chest infections secondary to lung disease, spinal stenosis, growth retardation, intellectual disability, feeding difficulties, heart defects, and eczema. Additionally, there is impaired vision and cataracts in the initial six months of life. Facial features include mid-facial hypoplasia, hypertelorism, and an upturned nose. However, the non-classical type of RCDP1 is characterised by skeletal deformities, intellectual disability, and cataracts but they are usually milder and/or develop later in life.[2]

Post-natal diagnosis is done by skeletal survey with characteristic findings including rhizomelia, metaphyseal splaying, punctate cartilaginous calcifications, and coronal clefting of the vertebral column, of which rhizomelic shortening and discrete punctate calcifications are the most consistent findings as depicted in previous case reports.[3-6]

Prenatal diagnosis is vital in cases with a family history of chondrodysplasia via genetic analysis coupled with distinctive sonographic findings as early as the second trimester.[6, 7]

Conclusion

This case report emphasises that early prenatal diagnosis and genetic counselling are crucial given the family history of RCDP for family planning and future pregnancies.

Consent: Consent to publish was obtained in writing from the father of the neonate.

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References

1. Luisman T, Smith T, Ritchie S, Malone KE. Genetic epidemiology approach to estimating birth incidence and current disease prevalence for rhizomelic chondrodysplasia punctata. Orphanet J Rare Dis 2021; 16:300. doi: 10.1186/s13023-021-01889-z.
2. Rijn R van. Rhizomelic chondrodysplasia punctata | Radiology Case | Radiopaedia.org. [Online] [Cited 2024 July 7]. Available from: URL: https://radiopaedia.org/cases/rhizomelic-chondrodysplasia-punctata-2
3. Kumar A, Singh A, Singh S, Agarwal P, Parihar A. Cytological findings of rhizomelic chondrodysplasia punctata: A rare skeletal dysplasia. IP J Diagnostic Pathol Oncol. 2022; 7:204–6. doi.org/10.18231/j.jdpo.2022.049
4. Javaid HA, Fawzy NA, Mostafa R, Shehata N, Javaid HA, Fawzy NA, et al. A Case of Rhizomelic Chondrodysplasia Punctata in a Neonate. Cureus. 2022; 14:e31702. doi: 10.7759/cureus.31702.
5. Qadir A, Nousheen A, Jamil M, Abbas H, Naz S, Khan MA. Rhizomelic Chondrodysplasia Punctata in a New-born: A Case Report. Pak Paediatr J. 2024; 48:22-7.
6. Erdogdu E, Dilek N, Arisoy R, Tahaoglu AE, Karacor T, Andan C. Prenatal Diagnosis of Rhizomelic Chondrodysplasia Punctata. Genet Couns. 2016; 27:533–5.
7. Gerami R, Barkhordari S. Antenatal Ultrasonographic Diagnosis of Rhizomelic Chondrodysplasia Punctata. Journal of Ultrasound. 2022; 26:539–42. doi: 10.1007/s40477-022-00737-5.

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QUA: Concept, drafting, data collection, literature review, writing and revision.
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