Journal of Morphological Sciences
J Morphol Sci
Brazilian Society of Anatomy

Review Article
J Morphol Sci 2023;40:533-353

An Overview of Clinical Manifestations in Chondrodysplasia Punctata

Jessy JP[1], Rajesh Kumar[2], Neerja Rani[1], Kanchan Kapoor[3], Mahesh Sharma[3], Anupriya Kaur[4], Chetan Sahni[5]

[1]Department Of Anatomy, All India Institute of Medical Sciences, New Delhi, India
[2]Department Of Anatomy, All India Institute of Medical Sciences, Patna, India
[3]Department of Anatomy, Government Medical College, Chandigarh, India
[4]Department of Pediatrics, Postgraduate institute of medical research and education, Chandigarh, India
[5]Department of anatomy, Institute of medical sciences, Banaras Hindu University, Varanasi, India

Disclose and conflicts of interest: none to be declared by all authors

ABSTRACT

Introduction: chondrodysplasia punctata (CDP) is a rare, autosomal recessive disorder characterized by the punctuate calcifications of long bones epiphyses, cataract, and developmental delay. CDP is associated with inborn errors of metabolism, chromosomal abnormalities, and teratogens. The routine fetal autopsy was performed in 23+1 weeks abortus fetus showed dysmorphic facies, bilateral brachydactyly, and overriding of the toes, and X-ray examination suggested stippling of the epiphysis of long bones. Coronal clefts were seen in the region of the lumbar vertebrae. In this case, genetic counseling was offered to the couple. The diagnosis of CDP on autopsy was made after the radiological examination; hence this case also illustrates the importance of radiology in fetal autopsies. Molecular analysis is required for final diagnosis in such cases. **Keywords:** Chondrodysplasia punctata; Rhizomelic chondrodysplasia punctata.

Introduction

Chondrodysplasia punctata (CDP) is a condition characterized by punctate calcifications, stippled epiphysis, and other skeletal changes such as defects of the vertebral bodies, microcephaly, facial dysmorphism including depressed nasal bridge, hypertelorism, hypoplastic midface, anteverted nostrils[1]. It can be inherited as X-linked dominant, X-linked recessive, and autosomal recessive forms. More recently, the biochemical and molecular basis of many CDP syndromes has recently been elucidated and a new aetiological classification has emerged. CDP is classified into 3 major subtypes: autosomal dominant Conradi-Hunerman type, X-linked recessive type, and autosomal recessive rhizomelic type 2[2]. Rhizomelic chondrodysplasia punctata (RCDP) is a rare, autosomal recessive disorder characterized by proximal shortening of the limbs due to the punctuate calcifications of the epiphyses of long bones, cataracts, developmental delay, and early lethality[3]. Some cases were found to be secondary to teratogen exposure or maternal conditions such as mothers with connective tissue disorders. Incidence is found to be one in 100,000 live births[1]. Three genetic subtypes of rhizomelic chondrodysplasia punctate are described. RCDP type 1 is the commonest and is caused by mutations in the PEX7 gene[4]. RCDP type 2 and type 3 are single enzyme deficiencies in the plas-malogen biosynthesis pathway[1]. CDP is associated with several disorders, including inborn errors of metabolism, disruption of vitamin K metabolism, chromosomal abnormalities involving peroxisomal and cholesterol pathways, embryopathy, and chromosomal abnormalities[1]. The abnormality of cholesterol metabolism is also considered a cause of CDP2. CDP is seen in associated with chromosomal abnormalities like Turner syndrome, Down syndrome, trisomy 18 (Edwards's syndrome), and maternal exposure to cytomegalovirus or rubella viruses[2]. Some cases were found to be secondary to teratogen exposure or maternal conditions such as mothers with connective tissue disorders.Incidence is found to be one in 100,000 live births[1]. Three genetic subtypes of rhizomelic chondrodysplasia punctate are described. RCDP type 1 is the commonest type and is caused by mutations in the PEX7 gene[4]. RCDP type 2 and types 3 are single enzyme deficiencies in the plas- malogen biosynthesis pathway[1].

Materials and Methods

A 23+1 week fetus was brought to the Department of Anatomy for conducting the routine fetal autopsy. Informed and written consent was taken from the parents before performing the autopsy. A radiological examination was also done before fetal autopsy to analyze the bony deformities associated with chondrodysplasia punctata. In fetal autopsy, internal as well as external gross morphology was analyzed in detail. Maternal history revealed that mother was 30 years old, fifth gravida with previous four abortions. Medical history of the mother was not significant and there was no history suggestive of Systemic lupus erythematosus (SLE) or intake of drugs like warfarin or phenytoin. Antenatal scan was not suggestive of any fetal malformation.

DOI: 10.51929/jms.40.533.2023
ISSN 2177-0298

Results

External Examination:

Gross examination of the fetus showed dysmorphicfacies showing hypertelorism, depressed nasal bridge and ridge, bilateral brachydactyly of hands, bilateral overriding of the 4th toe over 3rd toe (Fig 1). There was no rhizomeliaas shown by the proximal and distal limb measurements, which corresponded to approximately 21-22 weeks.

Internal Examination:

No suggestive malformations could be detected on internal examination after the autopsy. All the internal organs appeared normal on gross examination.

Radiological Finding:

The X-ray examination of the fetus was performed before the autopsy suggested stippling of epiphysis at the upper end of femur, sacral vertebrae, and pelvis and also of the tarsal bones. Coronal clefts were seen in the region of lumbar vertebrae (Fig 2).

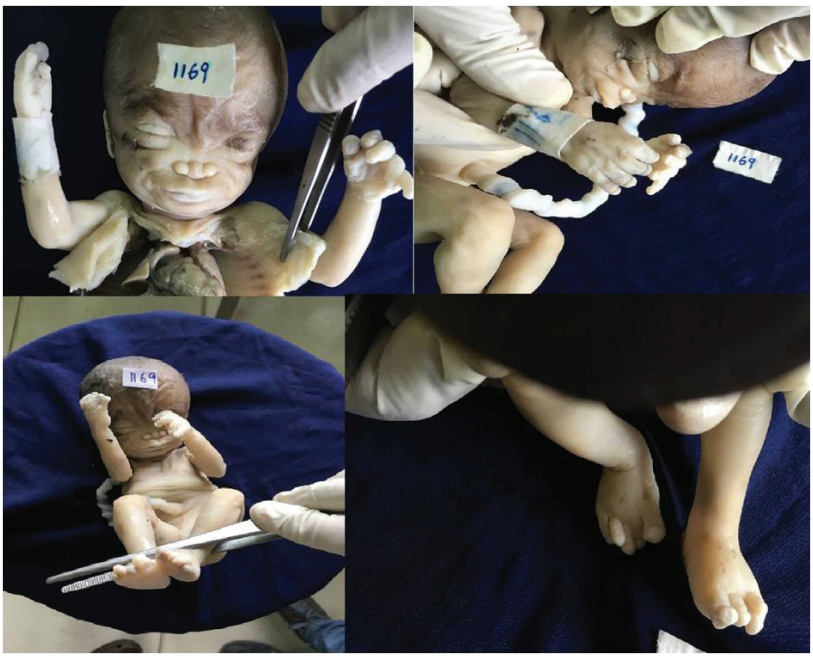

Figure 1. Dysmorphicfacies, hypertelorism, depressed nasal bridge and ridge, bilateral brachydactyly of hands, bilateral overriding of the 4th toe over 3rd toe.

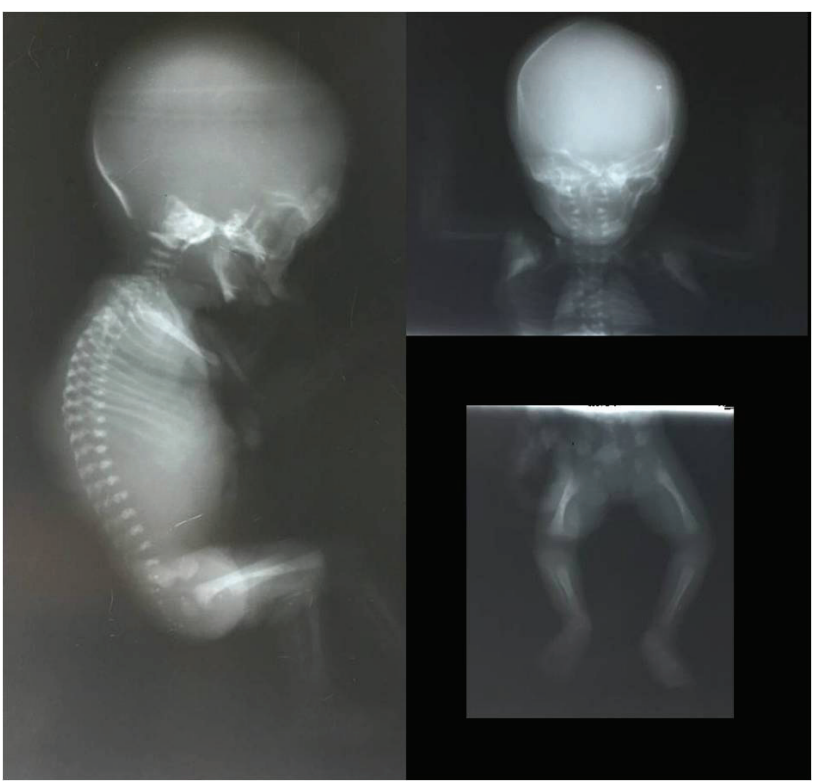

Figure 2. Stippling of epiphysis at the upper end of femur, sacral vertebrae, pelvis and tarsal bones.

Discussion

Chondrodysplasiapunctata (CDP) is characterised by punctiform calcification of bones, especially the epiphysis of the long bones, patellae and carpal and tarsal bones. The sites to look on the radiograph are spine, knee joint and shoulder. CDP is a heterogeneous condition and can be caused by both genetic and acquired defects. The acquired causes includematernal use of warfarin or phenytoin, maternal SLE, maternal malabsorption of Vit K[5]. The negative maternal case history for above ruled out acquired causes of CDP in the present case. The genetic causes of CDP aredefect in peroxisomal metabolism (Zellweger syndrome), defect in cholesterol metabolism (Smith- Lemli- Opitz syndrome), Rhizomelicchondrodysplasiapunctate, X-linked recessive chondrodysplasiapunctata, Conradi-Hunermann syndrome and Autosomal dominant chondrodysplasia punctata[6].

In the present case genetic counselling was offered to the couple depending upon the final diagnosis which requires molecular analysis of fetal DNA. In the present case diagnosis of CDP was made after the radiological examination of the fetus, hence this case also illustrates the importance of radiology in fetal autopsies.

Acknowledgement

We are very thankful to the parents who had given us permission to use radiographic and photographic images of their fetus in publishing the article.

References

1. Karabayır N, Keskindemirci G, Adal E, Korkmaz O. A case of rhizomelicchondrodysplasiapunctata in newborn. Case Rep Med. 2014;2014:879679. doi: 10.1155/2014/879679. Epub 2014 Mar 9. PMID: 24715923; PMCID: PMC3970257.
2. Alrukban H, Chitayat D. Fetalchondrodysplasiapunctata associated with maternal autoimmune diseases: a review. ApplClin Genet. 2018 Apr 20;11:31-44. doi: 10.2147/TACG.S150982. PMID: 29720879; PMCID: PMC5918624.
3. Heymans HS, Oorthuys JW, Nelck G, Wanders RJ, Schutgens RB. Rhizomelicchondrodysplasiapunctata: another peroxisomal disorder. N Engl J Med. 1985 Jul 18;313(3):187-8. PMID: 4010717.
4. Wanders RJ, Waterham HR. Peroxisomal disorders I: biochemistry and genetics of peroxisome biogenesis disorders. Clin Genet. 2005 Feb;67(2):107-33. doi: 10.1111/j.1399-0004.2004.00329.x. PMID: 15679822.
5. Landino J, Jnah AJ, Newberry DM, Iben SC. Neonatal RhizomelicChondrodysplasiaPunctata Type 1: Weaving Evidence Into Clinical Practice. J Perinat Neonatal Nurs. 2017 Oct/Dec;31(4):350-357. doi: 10.1097/JPN.0000000000000282. PMID: 29068853.
6. Poulos A, Sheffield L, Sharp P, Sherwood G, Johnson D, Beckman K, Fellenberg AJ, Wraith JE, Chow CW, Usher S, *et al*. Rhizomelicchondrodysplasiapunctata: clinical, pathologic, and biochemical findings in two patients. J Pediatr. 1988 Oct;113(4):685-90. doi: 10.1016/s0022-3476(88)80378-0. PMID: 3171792.

Mini Curriculum and Author's Contribution

1. Jessy JP - MBBS, MD; Contribution- Dissection and making Prosected Specimen for Case Report, Writing the Manuscript.

2. Rajesh Kumar – MBBS, MD; Contribution-Writing manuscript. ORCID- 0000-0002-8743-7541

3. Neerja Rani - MBBS, MD; Contribution-

4. Kanchan Kapoor - MBBS, MD; Contribution- Fetal Autopsy

5. Mahesh Sharma - MBBS, MD; Contribution- Fetal Autopsy

6. Anupriya Kaur - MBBS, MD; Contribution- Fetal Collection and collection of radiological images

7. Chetan Sahni – MBBS, MD; Contribution- Collecting References & Editing the manuscript. ORCID- 0000-0002-4301-4643

Received: November 10, 2023
Accepted: November 27, 2023

Corresponding author
Chetan Sahni
E-mail: chetansahni@bhu.ac.in