One Health Journal of Nepal

Case Report Open Access

Chondrodysplasia Punctata: A Case Report

Saurav Khetan,[1*] Rohit Gahlawat,[2] Prerana Kansakar[3]

[1]Department of Paediatrics, Sumeru Dhapakhel, Kathmandu, Nepal.

[2]Department of Paediatrics, Aagyapal Advanced Care Hospital, Panipat, India.

[3]Department of Paediatrics, Patan Academy of Health Sciences, Kathmandu, Nepal.

ABSTRACT

Chondrodysplasia Punctata (CDP) is a genetic disorder with skeletal and developmental abnormalities. This case report describes the clinical features, diagnostic evaluation, management, and genetic counselling of patients with CDP. This report aimed to increase awareness about this condition and importance of early diagnosis, multidisciplinary management care, and genetic counselling for better patient outcomes.

Keywords: *Chondrodysplasia Punctata, Genetic Disorder, Skeletal Abnormalities, Developmental Anomalies, Genetic Counselling*

INTRODUCTION

Chondrodysplasia Punctata (CDP) is a group of disorders causing bone and cartilage dysplasia with characteristic findings seen in X-ray. These disorders present in the neonatal or early infancy period.

CDP are broadly divided in three groups on the basis of mode of inheritance. The autosomal recessive known as Rhizomelic Chondrodysplasia Puncata (RCP) is a group of disorders caused by homozygous or compound heterozygous mutations in the PEX7 gene. This is the most severe form and only 50% of children survive by 6 years of age(1). The second group is X linked form which is caused by mutation in the Aryl-sulfatase L (ARSL) gene and Aryl-sulfatase E (ARSE) gene. This can be X linked dominant also known as Conradi–Hunermann disease or X linked recessive known as CDPX1 or Brachytelephalangic Chondrodysplasia Punctata (BCDP) (2). The X linked Dominant condition mainly affects girls and is lethal in homozygous males, they generally present with short stature, extra-epiphyseal punctate calcifications, sparse hair with patchy alopecia, cataracts, and variable joint contractures(2). The BCDP form is characterised by short stature, deafness, depressed nasal bridge, frontal bossing, and distal phalangeal hypoplasia.(3)

CASE REPORT

A male term baby was born via Lower Segment Cesarean Section (LSCS) in view of previous LSCS to a mother of gravida 2, para 1 and live birth 1. Mother had no history of consanguinity, autoimmune disease, intake of warfarin, hydantoin, drugs, and alcohol during pregnancy. No history of poly or oligohydramnios. Her first girl baby was born by LSCS, did not require NICU admission and is healthy with no known morbidity. Mother had regular antenatal visits and she regularly took iron, calcium, and folic acid tablets.

As the baby was born by LSCS and the birth weight of the baby was 2400 grams. Baby had features of facial dysmorphism (Binders Facies) in the form of midfacial hypoplasia, right sided choanal atresia and nasal bone hypoplasia (Figure 1). After birth the baby cried immediately but soon developed respiratory distress thus the baby was admitted to NICU and kept on CPAP. As respiratory persisted and FiO2 requirements increased, the baby was intubated and kept on a ventilator.

In view of the dysmorphism skeletal survey and CT scan of head and upper thorax was done. Skeletal survey showed midface hypoplasia with flattening of nasal bridge, epiphyseal stippling in the spinal

***Correspondence:** drsauravkhetan@gmail.com
Department of Paediatrics, Sumeru Hospital, Dhapakhel, Kathmandu, Nepal

and paraspinal region and characteristic triangular hypoplastic distal phalanges in the hands and feet (Figure 2,3,4). Femoral length was within normal. CT scan was suggestive of Binder's syndrome with features of abnormal calcification of trachea, main bronchi, nasal septum, and stippled calcification of the vertebrae (figure 5). Screening for congenital infection was done which was negative. As above findings was suggestive of brachytelephalangic CDP, genetic review was taken and gene analysis for CDP i.e. ARSE gene was sent which came out to be positive. With the help of above findings and investigations the baby was diagnosed with CDPX1.

As the baby had persistent respiratory distress and ventilatory requirements ENT opinion was taken and tracheostomy was done and the baby was continued on a ventilator. As the requirements decreased, the baby was weaned to CPAP and later to room air. During this time USG cranium and abdomen was done which were normal. Echocardiography, eye, and fundal examinations were also normal.

At the time of writing the baby was 40 days old on paladai feeds, room air and tracheostomy tube in situ.

DISCUSSION

Chondrodysplasia Punctata 1 (CDPX1), is a X linked recessive genetic disorder that presents from birth and mainly affects the development of bone and cartilage. The hallmark finding is punctate epiphyseal stippling which generally disappears by early childhood(4,5). Other common findings such as short stature, short fingertips and end of toes can be seen. These patients have a distinctive facial feature with flattened midface and nasal bridge(3,5). Babies may have choanal stenosis, spinal cord abnormality, hearing loss, vision abnormalities, and heart defects. Patients generally have normal intelligence and normal life expectancy in milder variants. Presentation highly variable ranging from early lethality to milder forms with facial dysmorphism being only the presentation(4).

Histological findings that are seen in the epiphyseal cartilage are fibrosis, calcification, cyst formation, neovascularization, and mucoid degeneration. Radiological findings include stippled epiphyses on skeletal x-rays usually of the ankle, feet, distal phalanges, long bones, vertebrae, and hips. The distal phalanges have a characteristic inverted triangular shape with lateral stippling. Calcification has also been seen in the upper airway i.e. larynx, trachea, and bronchi which later causes stenosis and respiratory distress. Vertebral abnormalities such as dysplastic or hypoplastic vertebrae, cervical kyphosis, and atlantoaxial instability are commonly associated with CDP.

The exact prevalence of CDPX1 is not known but in some studies it has been shown that the birth prevalence is 1/500,000 newborns (6). CDPX1 is caused by genetic changes in the ARSE gene. This gene is important for normal skeletal development and participates in chemical pathways involving vitamin K. Mutation, insertion or deletion of the ARSE gene leads to reduction or absence of function of arylsulfatase E thus leading to signs and symptoms (4,7). Some patients with phenotypic features of BCDP lack mutation in ARSE thus suggesting unidentified genetic mutation or environmental factors (4,7). Sporadic mutations have also been seen where both males and females have been affected and typical X linked pedigree may not be present (5,7,8).

This suggests that BCDP does not behave as a classic X linked recessive disorder and there is no correlation between the mutation type of deletion size of ARSE gene thus in a patient with absence of mutation BCDP cannot be ruled out completely. Once ARSE gene mutation or deletion has been diagnosed in a family member prenatal or preimplantation testing for a pregnancy should be done (4,9). Antenatal ultrasonographic evaluation should be done routinely in high risk pregnancy which might show hypoplastic nose nasal bone, epiphyseal stippling, and abnormal spinal curvature (9,10).

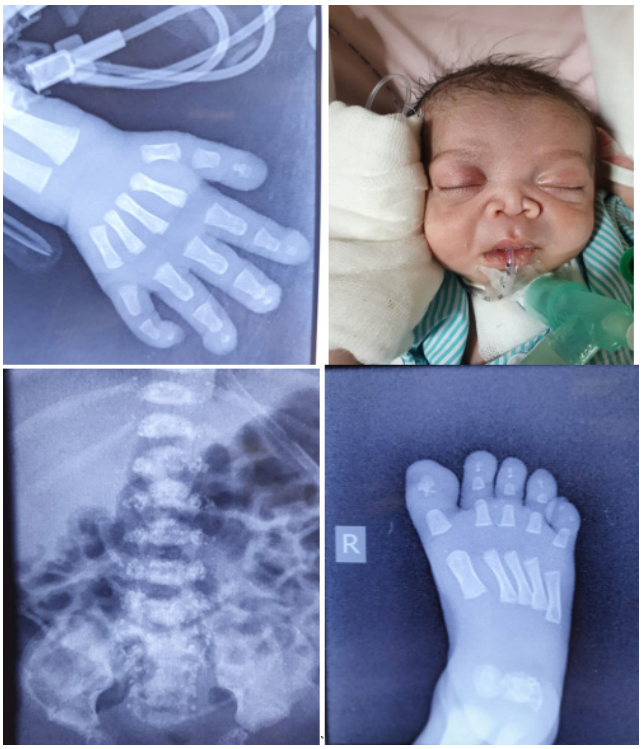

Figure 1 Fig A: *Picture of neonate showing midfacial and nasal bone hypoplasia*

Fig B, Fig C, Fig D : *X Ray showing epiphyseal stippling in the spinal and paraspinal region and characteristic triangular hypoplastic distal phalanges in the hands and feet.*

CONSENT

Case Report Consent Form was signed by the patient.

CONFLICT OF INTEREST

None

REFERENCES

1. White AL, Modaff P, Holland-Morris F, Pauli RM. Natural history of rhizomelic chondrodysplasia punctata. Am J Med Genet. 2003 May 1;118 A(4):332–42.
2. Kumble S, Savarirayan R;, Adam MP, Mirzaa GM, Pagon RA. Chondrodysplasia Punctata 2, X-Linked. 2011.
3. Brunetti-Pierri N, Andreucci MV, Tuzzi R, Vega GR, Gray G, McKeown C, et al. X-linked recessive chondrodysplasia punctata: Spectrum of arylsulfatase E gene mutations and expanded clinical variability. Am J Med Genet. 2003 Mar 1;117 A(2):164–8.
4. Casarin A, Rusalen F, Doimo M, Trevisson E, Carraro S, Clementi M, et al. X-linked brachytelephalangic chondrodysplasia punctata: A simple trait that is not so simple. Am J Med Genet A. 2009 Nov;149(11):2464–8.
5. Sheffield LJ, Danks DM, Mayne V, Hutchinson LA. Chondrodysplasia punctata-23 relatively common variety cases of a mild and. 1976.
6. Malou E, Gekas J, Troucelier-Lucas V, Mornet E, Razafimanantsoa L, Cuvelier B, et al. Chondrodysplasie ponctuée récessive liée à l'X. Étude cytogénétique et place de la biologie moléculaire. 2001.
7. Murdin L, Sirimanna T, Hartley BE, Holder SE. Chondrodysplasia punctata: Case report and review of audiological and ENT features. Journal of Laryngology and Otology. 2006 Mar;120(3):233–6.
8. Alrukban H, Chitayat D. Fetal chondrodysplasia punctata associated with maternal autoimmune diseases: A review. Vol. 11, Application of Clinical Genetics. Dove Medical Press Ltd.; 2018. p. 31–44.
9. He G, Yin Y, Zhao J, Wang X, Yang J, Chen X, et al. Prenatal findings in a fetus with X-linked recessive type of chondrodysplasia punctata (CDPX1): A case report with novel mutation. BMC Pediatr. 2019 Jul 23;19(1).
10. Matos-Miranda C, Nimmo G, Williams B, Tysoe C, Owens M, Bale S, et al. A prospective study of brachytelephalangic chondrodysplasia punctata: Identification of arylsulfatase e mutations, functional analysis of novel missense alleles, and determination of potential phenocopies. Vol. 15, Genetics in Medicine. 2013. p. 650–7.