CASE REPORT

Brachytelephalangic Type Chondrodysplasia Punctata - An Under Diagnosed Entity

Anupama Thanka[a], Kamala Swarnam[b], Mili Thomas[b], P Madhava Chandran Nair[b]

a. DNB Resident, Ananthapuri Hospitals and Research Institute, Thiruvananthapuram, Kerala, India;
b. Department of Pediatrics, Fellowship in Neonatalogy, Ananthapuri Hospitals and Research Institute, Thiruvananthapuram, Kerala, India*

ARTICLE INFO

KEYWORDS

Brachytelephalangic, Chondrodysplasia Punctata
ARSE, Binder Phenotype, Developmental Delay, Spasticity

CORRESPONDING AUTHOR

Dr. Anupama Thanka, MBBS,DNB Resident,
Ananthapuri Hospitals and Research Institute
Thiruvananthapuram, Kerala, India. Phone – 8248708577
Email: anupamathanka27@gmail.com

PUBLISHED ON

23rd May 2022

DOI

https://doi.org/10.52314/fnb.2022.v2i1.25

CITE THIS ARTICLE AS

Thanka A, Swarnam K, Thomas M, Nair PMC. Brachytelephalangic Type Chondrodysplasia Punctata - An Under Diagnosed Entity. Fetus and Newborn. 2022 May 23;2(1):12–4.

AUTHOR INFORMATION

1. Dr. Anupama Thanka, MBBS, DNB Resident, Ananthapuri Hospitals and Research Institute, Thiruvananthapuram, Kerala
2. Dr. Kamala Swarnam, MBBS, MD (Pediatrics), Fellowship in Neonatalogy (Canada), Senior Consultant, Ananthapuri Hospitals and Research Institute, Thiruvananthapuram, Kerala
3. Dr. Mili Thomas, MBBS, DCH, DNB Pediatrics, Consultant, Ananthapuri Hospitals and Research Institute Thiruvananthapuram, Kerala
4. Dr P.Madhava Chandran Nair. MD, DNB, DM (Neonatology), FIMSA, FRCP, Fellowship in Neonatology (Australia). Hon: Consultant, Ananthapuri Hospital and Research Institute, Thiruvananthapuram, Kerala, India

CONFLICT OF INTEREST

None

FINANCIAL SUPPORT

Nil

Access this Article Online

Scan this QR Code

ABSTRACT

Brachytelephalangic type chondrodysplasia punctata is a rareX linked recessive type of congenital disorder affecting cartilage and bone development with typical findings of binder phenotype, stippled epiphysis and short distal phalanges in male child.[1]

This occurs due to loss of arylsulfatase E (ARSE) activity. Hypoplastic midface is an important prenatal clue for the diagnosis of chondrodysplasia punctata. Genetic confirmation can be done by detection of deletion of ARSE gene. Even though prevalence of this condition is stated as 1 in 500000, only 55 patients with genetically confirmed disease has been reported so far.[2] According to latest literature, genetically confirmed cases were not reported from India so far.

We report the case of a newborn baby in our hospital, resident of South Kerala, with typical clinical findings of brachytelephalangic type of chondrodysplasia punctata and genetically confirmed later.

INTRODUCTION

Brachytelephalangic type chondrodysplasia punctata is a rare X linked recessive type of congenital disorder affecting cartilage and bone development with typical findings of binder phenotype, stippled epiphysis and short distal phalanges in male child.[1] Here we report the case of a newborn baby in our hospital, resident of South Kerala, with typical clinical findings of brachytelephalangic type of chondrodysplasia punctata.

CASE REPORT

26 year old G4P1L1A1E1 mother delivered a male baby of normal weight via elective LSCS. There was no specific antenatal issue. Soon after birth baby was noted to have nasal dysplasia and respiratory distress. Hence baby was shifted to NICU for further monitoring and evaluation.

On examination, baby was found to have depressed nasal bridge, crescent nares and hypertelorism, an acute nasolabial angle, a short columella and a convex upper lip (Binder phenotype). Limbs were apparently normal in length with

short stout extremities suggestive of brachytelephalangy.

Chest Xray was suggestive of TTN. Even though lung parenchyma was normal, stippling at the vertebral bodies was noted. In view of binder phenotype and stippling, baby was evaluated for the possibility of chondrodysplasia punctata type 1 (CDPXI).

On skeletal survey, stippling at epiphysis of posterior arches of vertebrae, humeral head, femoral head, acetabulum were noted. Xray hand was suggestive of triangle shaped terminal phalangeal stippling and shortening. Xray lateral skull showed absent nasal bone and septum.

ECHO showed atrial septum aneurysm with mild PDA. Initially baby had feeding difficulties, but later oral feeds were tolerated. Respiratory distress settled within 24 hours. In view of suspecting brachytelephalngic type of CDPXI, genetic work up was done. Chromosomal microarray was normal. Next Generation Sequencing confirmed X-linked recessive pattern of mutation in ARSE gene [Exon9]. Hearing evaluation was done. Both Oto-Acoustic Emissions (OAE) and Brain stem evoked response audiometry (BERA) were normal. USG head was also normal.

Baby was lost to follow up till 6 months of age due to Covid pandemic. At 6 months follow up, baby had developmental delay with normal growth. Baby was noted to have increased spasticity with adductor spasms and hyperreflexia. Baby also had torticollis left side. MRI Brain and spine were taken. Both were normal. Repeat X-rays showed persistent metaphyseal stippling. Repeat ECHO was normal.

Developmental therapy and physiotherapy interventions were started. Now baby is under regular follow up.

DISCUSSION

Chondrodysplasia punctata is a congenital skeletal dysplasia with multiple syndromic types and characterized by aberrant epiphyseal bone mineralization. Brachy-telephalangic type of chondrodysplasia punctata is an X linked recessive rare form; which was first described by Moroteaux in 1989 and has a prevalence of 1 in 500000. But literatures showed only 55 genetically confirmed diagnosis all over the world.[2] In most of affected children, it is usually associated with good prognosis, but in some it may cause cervical spinal instability and airway stenosis leading to death.

Defect in calcium deposition is associated with mutation in vitamin K dependent arylsulfatase enzyme gene or deletion in X chromosome carrying the gene. The pathophysiological mechanism behind radiological and phenotypical variation have not been clearly established.

Facial dysmorphism including Binder phenotype [depressed nasal bridge, crescent nares and hypertelorism, an acute nasolabial angle, a short columella and a convex upper lip] and chondrodysplasia involving tracheobronchial cartilage, vertebrae and tarsal bones are consistent with brachytelephalangic type. All these findings were clearly observed in this patient **(Figures 1,2,3).**

Hypoplastic midface is considered as an important prenatal clue in the diagnosis of chondrodysplasia punctata. Abnormal

Figure 1. Showing Binder phenotype

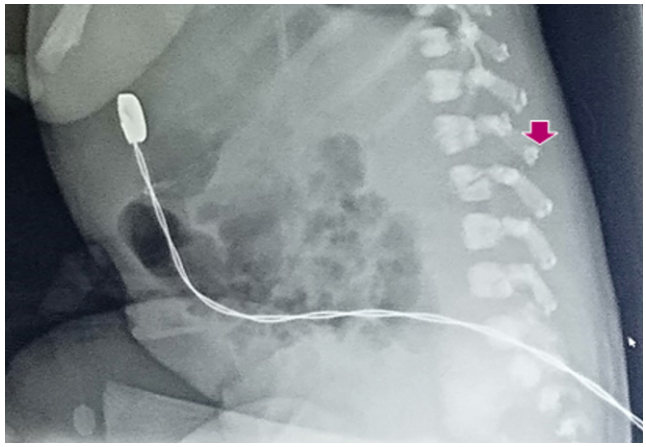

Figure 2. Showing vertebral stippling

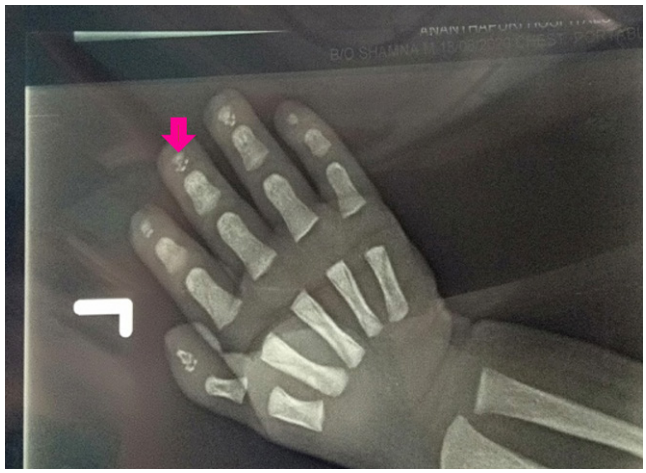

Figure 3. Showing brachytelephalangic type of hand with epiphyseal stippling

stippling should be looked for in such cases. Prenatal 3D ultrasonography of spine will detect vertebral stippling.[3] So we retrospectively checked antenatal ultrasound films which failed to report the nasomaxillary dysplasia which was an important prenatal clue.

Triangle shaped distal phalangeal hypoplasia is the most characteristic finding in this case. Punctate calcifications observed in neonatal period usually disappear by infancy and childhood. Usually, cognition will be spared. Developmental delay, cardiac abnormalities, cataract, sensory neural hearing loss, coloboma were reported in some cases.[4] Rarely, airway narrowing due to cervical stenosis is also noted. Therefore timely follow up is important to assess all these complications. Most of the time, binder phenotype is associated with CDP. Hence all suspicious binder phenotype in antenatal scan should be evaluated for CDP. Prenatal diagnosis is important for timely management of this condition. Cervical stenosis should also be considered prenatally.

ARSE gene study is the only way to confirm the diagnosis. Most of the times Binder phenotype is associated with CDPXI type. Rarely investigated long lasting specific sign is brachytelephalangy.

CONCLUSION

Binder phenotype is often treated as an isolated one and CDPXI is under diagnosed. Prenatal diagnosis will help to anticipate respiratory distress soon after the delivery in most of the cases. Regular follow up is needed as early detection of related abnormalities is an indication for good prognosis.

Abbreviations

ARSE - Aryl Sulfatase E
CDPXI - Chondrodysplasia punctata type 1
NICU - Neonatal intensive care
TTN - Transient tachypnea of newborn
PDA - Patent ductus arteriosus
CDP - Chondrodysplasia Punctata
OAE - Oto-acoustic emissions
BERA - Brain stem evoked response audiometry

REFERENCES

1. Koç U, Karakaş P. Radiological picture of premature baby with manifestation of brachytelephalangic type chondrodysplasia punctata, myelomalacia. TurkJPediatr. 2017;59(5):604.
2. Vrečar I, Rudolf G, Peterlin B, Lovrecic L. Brachytelephalangic chondrodysplasia punctata caused by new small hemizygous deletion in a boy presenting with hearing loss. Molecular cytogenetics. 2015 Oct 31;8:83.
3. Benaicha A, Dommergues M, Jouannic JM, Jacquette A, Alexandre M, Le Merrer M, et al. Prenatal diagnosis of brachytelephalangic chondrodysplasia punctata: case report. Ultrasound Obstet Gynecol. 2009 Dec;34(6):724–6.
4. Sanfilippo A, Bartoletti S. Brachytelephalangic chondrodysplasia punctata: A difficult diagnosis. Radiol Case Rep. 2010;5(1):308.