Case Report

Chondrodysplasia Punctata with Severe Airway Stenosis

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Abstract

Chondrodysplasia punctata (CDP) is a group of skeletal dysplasias characterized primarily by punctate calcifications in cartilage. It is a rare disease with an incidence of 1:100,000 live births. Extensive airway involvement with calcification of tracheal, bronchial, and thyroid cartilage in CDP is an infrequent finding. We aim to report a case of CDP with characteristic radiological features and severe airway involvement.

Keywords: Airway stenosis, chondrodysplasia punctata, Conradi disease, tracheal calcifications

Introduction

Chondrodysplasia punctata (CDP) is a rare heterogeneous skeletal dysplasia characterized by punctate stippling of cartilaginous structures and periarticular soft tissues due to abnormal deposition of calcium during endochondral bone formation. Underlying disorders for CDP include inborn errors of metabolism (peroxisomal and cholesterol biosynthesis disorders), disorders of Vitamin K metabolism, chromosomal abnormalities (Trisomies 18 and 21 and Turner syndrome), and idiopathic in a large majority.[1,2] CDP is essentially a radiological diagnosis; the cartilage stippling commonly involves epiphyseal end plates with subsequent resolution in first year of life.[2] However, it may also involve noncalcifying regions such as costal cartilage and tracheal rings. Involvement of tracheal cartilage may interfere with *in utero* tracheal development and cause critical airway narrowing in the postnatal period. We hereby report a young infant with severe fatal airway stenosis associated with extensive calcification of thyroid, tracheal, and bronchial cartilage.

Case Report

A 40-day-old male infant presented to the emergency department with complaints of noisy breathing since birth exacerbated by a recent history of cough, cold, and fast breathing for the last 4 days. The noisy breathing, noticed by parents since 4 h of life, worsened in intensity with crying and decreased while sleeping. There was no associated history of cyanosis, fever, poor feeding, or past hospital admissions. He was born out of nonconsanguineous marriage with uneventful antenatal history, except maternal polyhydramnios on antenatal ultrasound at 30 weeks of gestation. The baby was a full term, normal vaginal delivery, birth weight 3.5 kg, not requiring resuscitation at birth, and exclusively breastfed. Family history revealed phenotypically normal parents and two elder siblings (female and male) with no known syndromic or heritable disease.

On examination, the baby looked toxic with heart rate 162/min, respiratory rate 68/min, temperature 37°C, and oxygen saturation 84% in room air and 96% on oxygen hood. There was audible inspiratory stridor with severe respiratory distress requiring admission to PICU. General physical examination revealed craniofacial dysmorphism in the form of frontal bossing, hypertelorism, midfacial hypoplasia, depressed nasal bridge, and bilateral low set ears [Figure 1]. On respiratory system examination, normal breath sounds were heard with no additional sounds. The rest of the systemic examination including ophthalmological and skin assessment was normal. The presence of inspiratory stridor and craniofacial dysmorphism predicted a possibility of the difficult airway, and a formal airway assessment was planned. Otolaryngologist's consultation showed normal findings on anterior rhinoscopy

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Access this article online

Quick Response Code:

Website: www.ijccm.org

DOI: 10.4103/ijccm.IJCCM_105_18

How to cite this article: Deepthi B, Chhapola V, Kanwal SK, Sharma AG, Kumar V. Chondrodysplasia punctata with severe airway stenosis. Indian J Crit Care Med 2018;22:552-4.

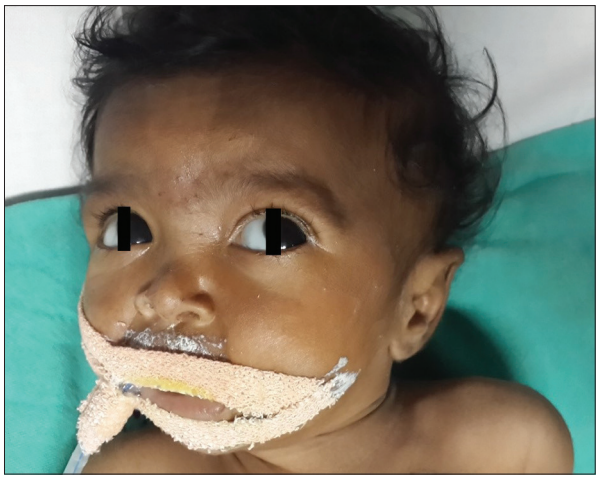

Figure 1: Facial profile of patient demonstrating low set ears, hypertelorism, depressed nasal bridge, and midfacial hypoplasia

and direct laryngoscopy vocal cord evaluation. Chest X-ray and lateral X-ray neck were obtained. Airway evaluation by fibro-optic flexible bronchoscopy was planned, but could not be performed due to persistent severe respiratory distress. The baby was started on humidified oxygen, intravenous fluids, adrenaline nebulization, dexamethasone, and empirical antibiotic therapy. His blood investigations were unremarkable.

Skiagram of chest and neck showed features of the calcified thyroid, hyoid cartilage, and tracheal ring calcification up to proximal main bronchus giving a "zipper-" like appearance [Figure 2]. Skeletal survey showed the presence of generalized punctate calcification involving long bone epiphyses (bilateral humerus and femur), epiphysis of both scapulae, costal cartilages, vertebrae, and tarsal bones. No significant shortening of long tubular bones was noted. There was bilateral hypoplasia of terminal phalanges in all digits. These characteristic radiological features combined with clinical manifestations suggested the diagnosis of CDP (brachytelephalangic type). Ultrasonography of the abdomen and cranium and echocardiography were normal. The baby was electively intubated over next 48 h due to increased work of breathing and hypoxemia. As a backup plan, otolaryngologists were present during the time of intubation to perform a tracheostomy in case of failed intubation. As anticipated, we faced difficulty in endotracheal intubation when age appropriate endotracheal tube size was selected. Attempts were made with 3.5 mm and 3 mm and ultimately airway was secured with a small 2.5 mm size endotracheal tube with difficulty. Airway stenosis was assumed to be the cause. Despite symptomatic treatment, the child required continued ventilator support, developed ventilator-associated pneumonia with an increase in ventilator requirements, and eventually succumbed to severe sepsis and septic shock after 7 days.

Discussion

Calcification of airways in children is very rare and may be physiological, idiopathic, associated with congenital

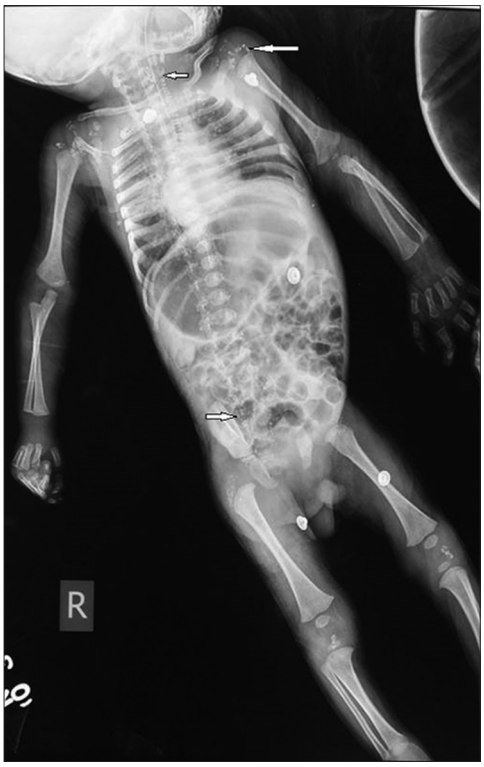

Figure 2: Whole-body X-ray showing calcification of thyroid cartilage and tracheal rings (small arrow pointing right), punctate calcification at shoulder joint (large arrow), vertebra, and sacrum (small arrow pointing left)

cardiac disease, warfarin embryopathy, or known syndromes such as Keutel syndrome or CDP.[3] The presence of (1) radiographic findings of stippled calcification around long bones, vertebral stippling, and airway involvement, (2) characteristic phenotypic findings of midfacial hypoplasia with depressed nasal bridge, (3) brachytelephalangy and (4) absence of maternal history of warfarin/phenytoin/alcohol abuse or lupus suggested the diagnosis of brachytelephalangic CDP in our case.

CDP, first described by Conradi in 1914, involves diffuse calcific stippling with varying severity of phenotypic features (craniofacial dysmorphism like prominent forehead, flat midface, depressed nasal bridge; limb shortening; congenital heart disease; hearing impairment; cataract; skin lesions and arthropathies).[2,4] The occurrence of CDP itself does not constitute a diagnosis, rather than it represents a common observation seen in a complex group of disorders with different etiological factors and congenital abnormalities.[5] The inheritance pattern in genetic causes of CDP is variable, and the mutations have variable penetrance and expressivity. CDP can be broadly divided into rhizomelic and nonrhizomelic forms. Symmetrical shortening of proximal fragments of long bones with punctate calcifications of axial skeleton cartilage characterizes rhizomelic forms; diffuse punctate calcifications around proximal epiphysis of the femur, soft tissue of joints, vertebral stippling, and tracheal cartilage calcifications suggest

nonrhizomelic forms.[6-8] Hypoplasia of distal phalanges of hands and feet and triangular distal phalanges are seen in brachytelephalangic type CDP.[7]

There are very few reported cases of CDP with extensive airway involvement.[3,9-13] Most of the CDP cases with airway involvement had a fatal outcome, as surgical intervention is yet to be defined. Schweiger *et al.* described a successful treatment of CDP with tracheal stenosis using balloon dilation of the trachea.[9]

Diagnostic imaging allows visualization of punctate calcifications together with other radiological features, providing a classic spot diagnosis of CDP. In our case, calcification of airway cartilages was very characteristic. These features should alert the treating physician to plan a targeted workup for underlying causes. Treatment essentially involves supportive care, treating specific complications and a multidisciplinary approach. An important aspect to be addressed in such disorders deals with genetic counseling and providing an early prenatal diagnosis.

Conclusion

Radiological imaging is the key to demonstrate airway complications in an infant with respiratory distress as it can help in the correct and early diagnosis of this rare entity aiding in the management of complications and for future genetic counseling. Diagnostic workup of CDP is an integration of appropriate history taking, family history, general physical examination, radiological features, and molecular and biochemical testing, most important of which is radiological findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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