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Case Report

Cytological findings of rhizomelic chondrodysplasia punctata: A rare skeletal dysplasia

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ABSTRACT

Chondrodysplasia punctata (CDP) is a rare, skeletal dysplasia characterized by stippled, punctuate calcifications around joints and within cartilages. A 4 months old female infant presented to us for aspiration cytology with clinical suspicion of sarcoma due to complaint of ankle swelling and failure to thrive. Fine needle aspiration (FNA) smears were acellular with only calcific deposits. On clinical co-relation depressed nose and frontal bossing were noted. We suspected it to be a case of congenital skeletal dysplasia. Plain X-ray of the lesion was ordered and it revealed stippled calcification in place of ankle bones consistent with chondrodysplasia punctata. The present case is an index case describing the cytology of chondrodysplasia punctata. CDP is mainly a radiologically diagnosed lesion, however the knowledge of its cytological picture through this case will make pathologists alike aware if they encounter such case. The management is basically supportive and rehabilitative.

1. Introduction

Chondrodysplasia punctata is one of the rare, congenital developmental disorder which have calcific stippling of cartilage and periarticular soft tissues. CDP is classified into four main types, the autosomal dominant (Conradi-Hu ñermann's type), autosomal recessive (rhizomelic type), the X-linked dominant form (Happle) and the X-linked recessive form. The prognosis of Conradi Hunermann type, referred to as Conradi's disease is good if the patient survives the first 3 months while in rhizomelic variety, survival past the ten year is poor.[1,2] Rhizomelic chondrodysplasia punctata is rare with reported incidence of 1 in 100,000 individuals. They are characterized by punctuate calcifications which may result in delayed endochondral ossification process, growth deficiency and deformity of the bones involved.[3] Chondrodysplasia punctata can be diagnosed by ultrasound during antenatal period.[4,5] An association with fetal ascitis and poly hydromnios has also been reported.[6]

Other causes of calcific epiphysial stippling include warfarin, phenytoin exposure in pregnancy, several peroxisomal disorders including Zellweger syndrome, Smith Lemli Opitz syndrome, trisomy 18 and 21.[7–9]

2. Case History

A 4 months old female infant presented to us for aspiration cytology with clinical suspicion of sarcoma due to complaint of ankle swelling and failure to thrive. Fine needle aspiration smears showed only calcific deposits and were acellular [Figure 1a and b]. On the basis of FNAC we considered calcinosis cutis but as this condition is rare in infancy. Clinical co-relation with thorough proper history and examination was repeated. It revealed that the child was born from a 3rd degree consanguineous marriage at

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full term gestation from the second pregnancy of a healthy 26-year-old mother. The mother was under routine prenatal follow-up during pregnancy. There was no history of intake of toxic drugs or any chronic medications. The mother had one previous delivery of a female child who is healthy.

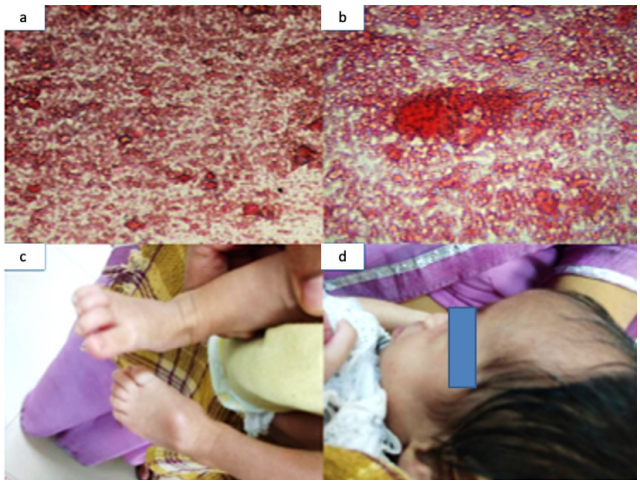

Fig. 1: Aspiration smear shows dispersedamorphic eosinophilic calcific deposits (H&E x40 in a and X200 in b). Clinical image of the patient shows ankle swelling in bilateral foot in c along with flat nasal bridge and frontal bossing in d.

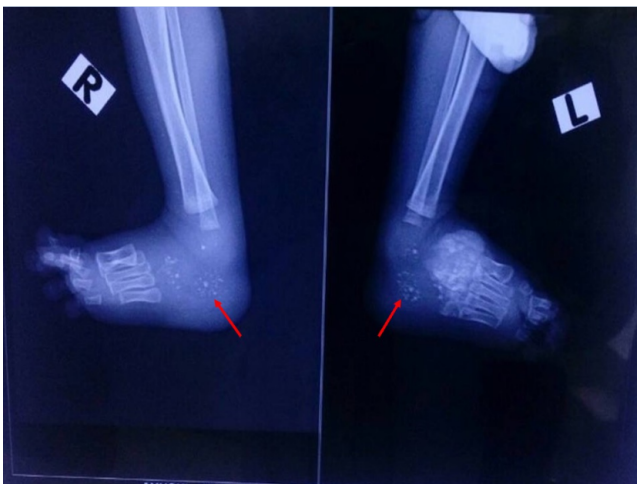

Fig. 2: Plain radiograph of bilateral ankle shows punctuate calcific deposits in bilateral ankle joints.

On examination, she had frontal bossing, flat facial features with depressed nasal bridge, micrognathia, high arched palate and proximal shortening of upper and lower limbs along with flexion contractures [Figure 1 c and d]. She had swelling of the joints for which the child was referred to our OPD. The swelling was non- tender, bony hard and did not show any effusion. She had no organomegaly. On the basis of cytology and clinical signs we suspected it to be a case of congenital skeletal dysplasia so we advised for radiological investigation. X-ray revealed symmetrical bilateral proximal shortening of upper and lower limbs (rhizomelic pattern), multiple stippled calcifications in the epiphyseal cartilage of long bones and ankles, metaphyseal splaying, punctuate calcification in vertebral bodies, pedicles including the sacrum [Figure 2]. Based on clinical and radiological findings, a diagnosis of chondrodysplasia punctata was made. Biochemical tests and genetic assay to identify the mutated gene was not undertaken. Genetic counselling was given to the parents. Child is receiving regular physiotherapy and is currently under follow up.

3. Discussion

Chondrodysplasia punctata (CDP) is a rare skeletal dysplasia characterized by stippled, punctate calcifications around joints and within cartilages.[3] It is associated with a number of disorders, including inborn errors of metabolism, involving peroxisomal and cholesterol pathways, embryopathy, and chromosomal abnormalities. Rhizomelic chondrodysplasia punctata (RCDP) is a peroxisome biogenesis disorder characterized by rhizomelic proximal shortening of the humerus and femur, ichthyosis, cataracts, restricted joint mobility, micrognathia, flattened nasal bridge, bulbous nose and flattened face appearance.[10] Patients may subsequently develop seizures and severe psychomotor delay. Radiological features include epiphyseal stippling, metaphyseal abnormalities and clefts in vertebral bodies.[11] These patients do not present as swelling in the affected area, which was quite unusual in the present case. Hence the cytological examination of swelling was ordered. To best of our knowledge of published English literature this is an index case where child with CDP was cytologically sampled. All these classical radiological findings were present in our case with added depressed nasal bridge and frontal bossing. Though we did not observe any cataract, it has been reported to present either congenitally or may develop in later infancy.[12] Cytological findings were of diffuse presence of calcific material with no intermixed osteoclast or osteoblastic cells.

Further RCDP is distinguished in three types on basis of involved genes and effected enzymes. Phenotypically all of them are similar. RCDP type 1 involves PEX7 gene and enzyme linked with peroxisome function while both RDCP 2 and 3 result from deficiency of dihydroxyacetone phosphate acyltransferase and alkyl dihydroxyacetone phosphate synthase respectively.[12]

Calcifications also can be observed in other cartilaginous namely ribs, sternum, larynx, vertebrae, and ischiopubic bones. Usually, these calcifications disappear towards the end of the first year of life, making the definitive diagnosis of this disease difficult after the first year.[13] Pathologically they are postulated to be the defects seen due to variations in

bone formation during endochondral ossification. Through clinical examination, drug history, maternal history is of crucial importance in definitive diagnosis as punctate radiological calcifications may be seen in few other conditions as well.[7–9,14] There was no history of maternal drug or alcohol use and any symptoms or positive laboratory test that indicated autoimmune disease in the mother of affected child. Interestingly the mother attended all her antenatal visits and still the disease was not picked up during antenatal ultrasounds.

Management is mainly supportive and limited by the multiple anomalies present at birth and poor outcome. Cataract extraction may restore vision in some cases. Physiotherapy is recommended to improve contractures and orthopaedic procedures may improve function in some cases. Genetic counselling may be necessary for individuals who have been determined to be carriers. Monitoring growth and development, regular assessment for vision, hearing, contractures, and orthopaedic complications are required in these children on follow up. Her height, weight, and cognitive development were age appropriate. Genetic counselling was given to parents of our case. She is on continuous follow up and is undergoing physiotherapy. After making the diagnosis, we feared any complication or impediment due to aspiration of the affected area. However, no deterrent effect of the procedure was identified. Mild to moderately affected individuals usually survive to adulthood and retain their reproductive capacity. Severely affected individuals usually die early in infancy.[13]

4. Source of Funding

None.

5. Conflict of Interest

None.

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