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Case Report

A Case Report of Rhizomelic Chondrodysplasia Punctata

Prashant Bhadane, Sanjay Joshi, Jagdish Pakhare, Mahesh Ahirrao, Parikshit Deore

Department of Pediatrics, ACPM Medical College, Dhule, Maharashtra, India

Corresponding Author: Prashant Bhadane

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ABSTRACT

The authors present a case of a 5 year old, male child born out of 3rd degree consanguineous marriage affected by the recessive form of chondrodysplasia punctata, a rare condition radiologically characterized by severe proximal shortening and anomalous ossification (epiphyseal stippling) of limbs. Clinical and radiological findings as well as main differential diagnoses are emphasized on the basis of data originating from a brief literature review.

Keywords: Chondrodysplasia punctata; Bone dysplasia; Peroxisomal disorders; Anti Ro/SSA; Punctate epiphyseal calcification

INTRODUCTION

Rhizomelic chondrodysplasia punctata is a rare, autosomal recessive peroxisomal disorder that impairs the normal development of many parts of the body. [1] The major features of this disorder include skeletal abnormalities, distinctive facial features, intellectual disability, and respiratory problems. [1]

Rhizomelic chondrodysplasia punctata is characterized by shortening of the bones in the upper arms and thighs (rhizomelia), which affects the growth of the long bones. People with Rhizomelic chondrodysplasia punctata often develop joint deformities (contractures) that make the joints stiff and painful. [3,4]

Distinctive facial features of prominent forehead, widely set eyes (hypertelorism), a sunken appearance of the middle of the face (midface hypoplasia), a small nose with upturned nostrils, and full cheeks. Birth history of prematurity. [5] Additionally, almost all affected individuals have clouding of the lenses of the eyes (cataracts).

Rhizomelic chondrodysplasia punctata (RDP) is associated with significantly delayed development and severe intellectual disability. Affected infants grow much more slowly than other children their age, and many also have seizures. Recurrent respiratory infections and life-threatening breathing problems are common. [6] It is rare for affected children to live past age 10. [7]

Researchers have described three types of Rhizomelic chondrodysplasia punctata: type 1 (RCDP1), type 2 (RCDP2), and type 3 (RCDP3). The types have similar features and are distinguished by their genetic cause. [8]

CASE REPORT

A 5 year old, 3rd, male child born out of 3rd degree consanguineous marriage came to us with respiratory complaints and noted to have short limbs.

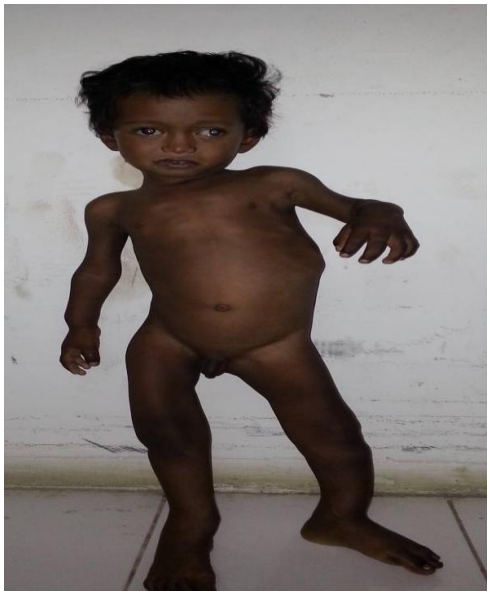

Figure 1: Clinical photograph

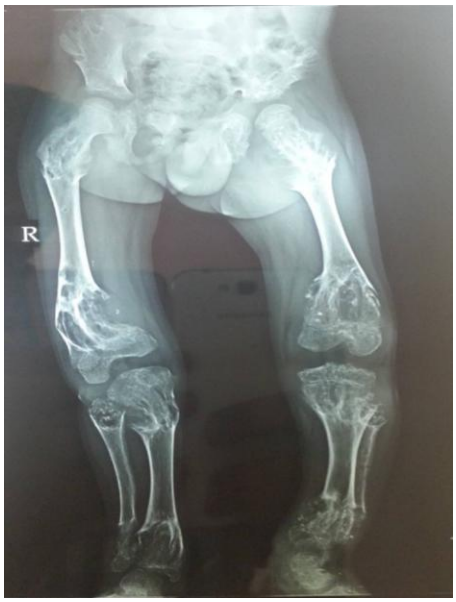

Figure 2: X-ray of lower limb

He presented with congenital cataract, joint contractures, and developmental delay. There was no history of any drug exposure or maternal disease and no family history of a child with similar problem. Antenatal ultrasound was not done. His weight was below < 3rd percentile. [5] He had a flat face, thin upper lip, bilateral congenital cataract, right sided hydrocele, symmetrical rhizomelic shortening of all 4 limbs and joint contractures at elbows and knee. Hepatomegaly was present. Other clinical features were normal. A skeletal survey showed rhizomelic shortening, epiphyseal stippling and metaphyseal flaring. In regards to a diagnosis, blood was sent for biochemical analysis of peroxisome metabolites showed high phytanic acid, 6.80mcg/ml. The plasma C 26:0/C 22:0 fatty acid ratio and pipecolic acid were normal. Skin fibroblast phytanic acid oxidase, dihydroxyacetone phosphate acyltransferase and alkyl dihydroxyacetone phosphate-synthase activities were reduced. Glyceryl-ether lipid levels were also greatly reduced. DNA amplification and sequence of the PEX7 gene showed that the patient was homozygous for 540_541 insT (exon 6). [8-11] Parental DNA was not evaluated.

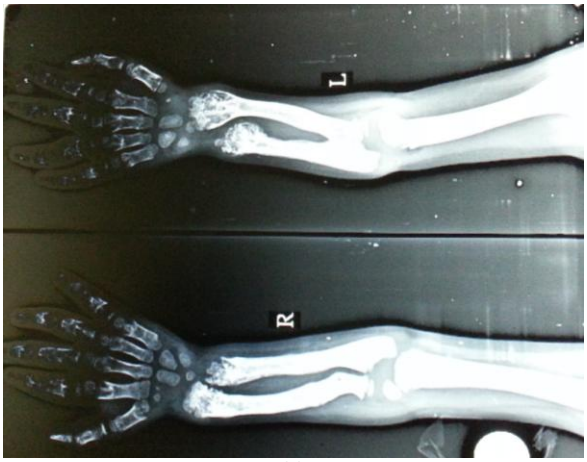

Figure 3: X-ray of forearm and hand

DISCUSSION

Chondrodysplasia punctata (CDP) is characterized by punctuate calcification of cartilage. It includes peroxisome biogenesis disorders (Zellweger syndrome, neonatal adrenoleukodystrophy, infantile Refsum

disease, and RCDP Type1), maternal conditions and teratogen exposure. CDP has four main types, the autosomal dominant (Conradi-Hunermann's type), autosomal recessive (rhizomelic type), the X-linked dominant form (Happle) and the X-linked recessive form.

There are three types of RCDP. RCDP Type 1 involves mutations in the PEX7 gene. [3] RCDP Types 2 and 3 are phenotypically similar to RCDP Type 1, but result from deficiencies of dihydroxyacetone phosphate acyltransferase and alkyl-dihydroxyacetone phosphate synthase, respectively. [11]

Though our patient presented with many characteristic features of RCDP but he differed from other patients in that there was no abnormality of red blood cell plasmalogens and phytanic acid levels. Antenatal history of teratogens like rubella infection, and warfarin or dilantin use was negative. There was no association of maternal conditions like SLE. [12]

The proposed mechanism for stippling in CDP-associated maternal lupus is immune mediated by maternal autoantibodies crossing the placenta in early to midgestation. These antibodies inhibit a high-affinity calcium-binding protein of endoplasmic reticulum, calreticulin. Anti Ro/SSA is an autoantigen complex that may include calreticulin. Auto-antibodies to calreticulin and Ro/SSA are involved in the pathogenesis of congenital heart block and the cutaneous lesions of SLE and may be responsible for the skeletal changes by inhibiting calcium binding. Animal model studies showed that immunization of mice with Ro resulted in the production of anti-Ro, anti-La, and anti-calreticulin antibodies. [14] Our patient's mother was positive for Ro/SSA. Alternatively maternal autoantibodies affect the infant's vitamin K metabolism resulting in bleeding into the epiphyseal cartilage, which produces the stippled appearance. [15]

Autoantibodies may be the largest single risk factor for the development of CDP in the neonate but the presence of autoantibodies cannot be the only determining factor to predict the occurrence of CDP. Management of these babies is mainly supportive. Cataract extraction and physiotherapy may help. Genetic counseling is necessary. Monitoring growth and development, seizure control, vision, hearing, contractures and orthopedic complications need regular assessment on follow up.

CONCLUSION

The knowledge of various associations of Chondrodysplasia punctata (CDP) can be helpful in establishing diagnosis. Clinical features of Chondrodysplasia punctata were consistent with the case findings. Atypical features were also studied. No history of maternal conditions and organomegaly were observed. Molecular diagnosis may be helpful in prevention of the disease.

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