CASE REPORT

Rhizomelic chondrodysplasia punctata - case report

Gilberto Pascolat,1 José L. Zindeluk,2 Karen C. Abrão,3 Fabiana M. Rodrigues,3 Carolina I.M. Guedes3

Abstract

Objective: To report a case of rhizomelic chondrodysplasia punctata and present a brief literature review.

Description: The authors report the case of a 52-day-old child presenting the main findings of the syndrome: rhizomelic micromelia, characteristic facies, suction difficulty and anthropometric measures below the expected indexes for his age. Skeletal radiographies showed humeri and femora shortening and calcifications stippling on shoulders, hips and knees joints. The patient also presented heart malformation, a less common manifestation of the syndrome.

Comments: The rhizomelic form of chondrodysplasia punctata is rare, with only 72 cases reported until 1995. The prognosis is bad and death usually occurs within the first year of age. The case presented here was diagnosed based on clinical and radiological criteria, due to the impossibility of searching for the peculiar biochemical markers.


Introduction

Chondrodysplasia punctata denotes a group of heterogeneous bone dysplasia characterized by punctate calcifications of the cartilage, frequently associated with a shortening of the limbs, cataracts, ichthyosis and alopecia, alterations of the nervous system, mental and growth deficiencies.1-4 The chondrodysplasia punctata family includes a dominant autosomal form (Conradi-Hünermann disease), a recessive autosomal form (rhizomelic), forms linked to X recessive (chondrodysplasiaX1) and dominant (chondrodysplasiaX2 or Conradi-Hünermann-Happle). During the nineties two milder forms were described, tibial-metacarpal and brachytelephalangic.4,5

The rhizomelic form of chondrodysplasia punctata is a disease of the peroxisomes, structures present in every cell in the organism, which explains the great variation between clinical manifestations presented by the syndrome. The principle characteristics as described in literature are severe and symmetrical rhizomelic micromelia (proximal shortening of the limbs); punctate calcifications and alterations to the ossification in metaphyses and epiphyses of the long bones; punctate calcifications and coronal fissures in thoracic and lumbar vertebrae; microcephaly and delayed growth; psychomotor retardation, spasticity and early death.5 Other characteristics have been described with variable frequency, including ichthyosis, cataracts, restricted joint mobility, suction and deglutition difficulties, alopecia, hearing loss and visual impairment, convulsions,
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During the first month of life there was a weight loss of 400 g, without ever having recovered birth weight in the meantime.

The patient was born by caesarian delivery, at full term, weighing 3,110 grams, in good condition (it was not possible to obtain an Apgar score). The mother attended 6 prenatal consultations and there were no intercurrent conditions during gestation, except for the fact that she is a carrier of the hepatitis B virus. Hyperimmune immunoglobulin was administered at birth. The mother used amoxicillin during the pregnancy and denies having used other medication. She describes a first trimester miscarriage, of which the cause is not known, a child of the same father, a year before the patient’s birth.

The father and mother of the patient are both healthy, being 23 and 24 years old respectively and non-consanguineous. The patient has three siblings, all healthy, but children of a different father. There is family history of congenital cardiopathy in a paternal cousin (female), who does not present any other abnormalities.

On admission to hospital the patient presented in a regular general state of health, pallid, without jaundice, acyanotic, eupneic and without fever. Anthropometric evaluation: weight of 3,090 g, stature of 52 cm, cephalic perimeter of 35 cm and thoracic perimeter of 30 cm (all below the fifth percentile). There is a flattened bridge and bulbous point of the nose, and additionally micrognathia. Anterior fontanelle 2x2 cm, under normal tension with juxtaposed sutures. Cardiopulmonary auscultation revealed a rough and intense systolic heart murmur, pleuropulmonary fields clear. Abdomen unaltered. Superior and inferior limbs presented with rhizomelic micromelia in addition to the restricted joint mobility in fingers and knees (Figures 1 and 2). Discrete spasticity is present in all four limbs and newborn reflexes are normal. Integument is unaltered.

During internment, echocardiography was performed, revealing subaortic perimembranous intraventricular communication (IVC) with moderate repercussion and interatrial communication (IAC), ophthalmological
evaluation revealed bilateral microcephaly and a decrease in the red reflex. Abdominal ultrasound and a test of otoacoustic emissions did not reveal alterations.

Further x-rays of the skeleton showed bilateral cartilage calcifications, most evident at knees and shoulders. Alterations of the cranium and spinal column were absent (Figure 3).

The patient was discharged with a clinical diagnosis of rhizomelic chondrodysplasia punctata, prescribed digoxin and instructions were given. Sudden death occurred while asleep at four months.

Discussion

Punctate calcifications that are symptomatic, i.e. manifesting with limited joint mobility and pain, have been described not only with have been described not only with chondrodysplasia, but also in children with congenital infections, chromosomal anomalies, neonatal lupus and embryopathies caused by the use of anticoagulants or phenytoin, among others. These calcifications are commonly visible with radiography during the first months of life and, as with chondrodysplasia, tend to disappear after one or two years of age.

Currently, RCP diagnosis is made based on clinical characteristics which are compatible with the syndrome, associated with biochemical findings which include serum phytanic acid assay and investigation of plasmalogen synthesis in a fibroblast culture. Chromosome study denotes a mutation in the PEX7 gene, 50% of which are in the L292ter allele. More than twenty mutations have been described which result in abnormalities of the peroxisomes. A DHAPAT deficiency (acyl-CoA: dihydroxyacetone phosphate acyltransferase) results in RCP subtype 1. Subtypes 2 and 3 are caused by a reduction in DHAPAT activity and alkyl-DHAP synthesis, respectively.

The diagnosis of the subtypes of chondrodysplasia is difficult due to the large number of manifestations which they all have in common. With the discovery of specific genetic and biochemical markers, cases previously described have been reclassified and new subtypes have surfaced.

There are descriptions of cases which have been diagnosed purely by radiological and clinical criteria, one of which does not have the biochemical alterations which are peculiar to the disease. The case described here presents with a face characteristic of RCP, further to the symmetrical proximal shortening of the limbs and punctate cartilage calcifications. At seven weeks of life the child presented feeding difficulties and anthropometric measurements below the values expected for that age, including of the head circumference. The diagnosis of RCP was based on the clinical criteria observed.

One common characteristic of RCP is the presence of coronal fissures in vertebral bodies. Coronal fissures of thoracic and lumbar vertebral bodies is a result of deficient ossification, at around four months of gestation, which results in an incomplete fusion between the anterior and posterior halves of the vertebrae. The punctate lesions diagnosed radiologically are resultant upon the degeneration of cartilage, represented by chondrocytes with picnotic nuclei and eosinophilic cytoplasm, followed by ossification.

Rhizomelic cases exist in which, as with this patient, no coronal vertebral fissures are presented. Despite being cited by many authors as a characteristic which is invariably found with this syndrome, a review of previously published cases shows that this characteristic is common, but not necessarily present.
Cardiac lesions are not cited as common characteristics of the rhizomelic form, being more often found among patients with Conradi-Hünermann syndrome. Nevertheless, a review performed in 1995 found nine patients with congenital cardiac lesions out of 72 with RCP. The most frequent types were: patent oval foramen, persistent arteriosus ductus, atrial and ventricular septal defects, associated or not with each other. The patient described here presented subaortic perimembranous IAC and IVC.

It is important to observe that patients who are diagnosed with RCP should be accompanied at clinics, because despite the current non-existence of any specific treatment, many of the clinical manifestations may not be present at the time of diagnosis, but appear as the case evolves, such as alopecia, ichthyosis and cataracts. Others tend to disappear with age such as punctate calcifications, without leaving bone deformities. Despite this motor development is compromised, as is cognitive development, which becomes evident in patients who survive longer.

The treatment of the principal complications which lead to death, repeated infections of the respiratory system, is merely supportive.

References