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Case Report

Campomelic Dysplasia, Not So Much Frequent Not So Much Rare Diagnostic Dysmorphic Syndrome

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Abstract

Campomelic dysplasia is a clinical picture characterized by symmetrical curvature and shortening of the lower extremities, peculiar and generally fatal facies due to respiratory failure. This disease is associated in 50% of the cases with gonadal dysgenesis with a female phenotype and an XY karyotype. It is a genetically determined process linked to mutations in the SOX9 gene.

We present the clinical case of a newborn woman, 37 weeks of gestational age, diagnosed prenatally with bone dysplasia, with a phenotype and radiological study compatible with the characteristics of this disease. The concordance between the female phenotype and its XX chromosomal formula stands out. During her stay, she presented progressive respiratory distress, dying at 27 days of age due to multiple organ failure.

Keywords: *Campomelia; Dysplasia; Karyotype*

Introduction

Campomelic Dysplasia (CD) is a dysmorphic condition characterized by deformations of the long bones together with other extra skeletal defects. The term campomelic was proposed by Maroteaux in reference to the bending of the limbs that appears as a characteristic sign [1].

The frequency is difficult to determine, although it seems to be in the range of 1 per 100,000 new-borns (alive and dead), but it must be taken into account that other bone dysplasias whose predominant sign is the bending of long bones, could have been reported with the name of Campomelic [2].

The set of malformations is enormously wide and present from birth. In all cases the shortening of the height is constant, at the expense of the bend of the lower extremities together with the presence of pretibial pits. Craniofacial dysmorphia with megadolicocephaly, a prominent occiput and a broad forehead is also common; set back ears, anteverted nostrils, broad philtrum, micrognathia, and small mouth and inverted V, with cleft palate in a significant percentage of cases. Other characteristics are the existence of thoracic dysplasia, renal malformations, generalized hypotony, and redundant skin on the neck and club feet. All of this constitutes the broad spectrum that allows the neonatal diagnosis of this disease.

Survival is generally short and they usually die in the course of respiratory distress secondary to thoracic hypoplasia [1-4].

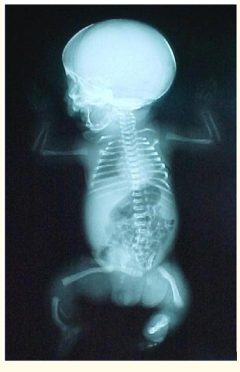
Clinical Case

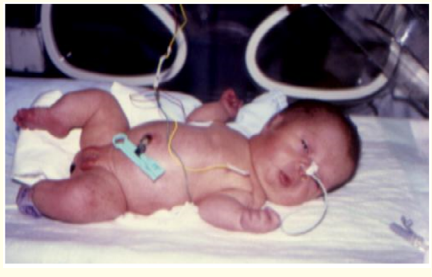
Female new-born, born of a well-controlled first pregnancy, with a gestational age of 37 weeks and of non-consanguineous parents. She was diagnosed in the prenatal period with unspecified bone dysplasia. Delivery: artificial amniorrhexis, clear amniotic fluid and polyhydramnios; emergency caesarean delivery due to fetal distress, cephalic presentation, Apgar 5/7 (1′, 5′). Somatometry: Weight 2020g. (P3), length 36 cm. (< P3), head circumference 34.5 cm. and thoracic circumference 26 cm.

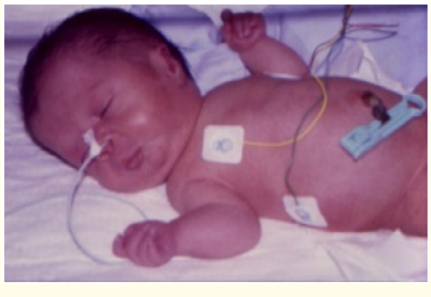
Physical examination: At birth she had moderate vitality, weak crying with subcyanotic coloration and generalized hypotonic. Relative megacephaly, olympic forehead, wide anterior fontanelle, dysmorphic facies with hypertelorism, epicanthus, antimongoloid obliquity, micrognathia, microstomic and cleft palate. Short neck, bell-shaped chest with mild respiratory distress. Extremities: Single bilateral transverse fold, shortening of upper and lower extremities with curving of both femurs and tibiae, pretibial skin pits and clubfoot. Cardio circulatory system and abdomen normal. Normal female genitalia.

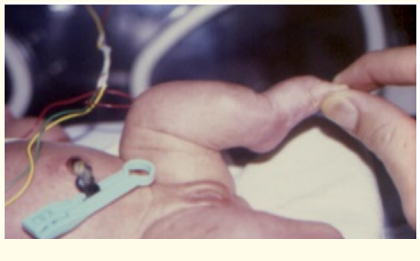
Complementary tests: Hemogram, biochemistry, blood gas and complete urine, normal. Cardiology study, transfontanellar ultrasound and fundus, normal. Abdominal ultrasound: Right hydro nephrosis. Radiological study: campaniform thoracic hypoplasia with chondro-costal dehiscence, raised and hypo plastic scapulae, dysplastic pelvis, curvature at the level of the femurs and tibiae with hypo plastic fibulae and club feet. Chromosomal formula 46 XX.

Evolution: During her stay, she presented progressive respiratory distress and died at 27 days of life due to multiple organ failure.









Comments

In the newborn, the clinical diagnosis is usually not difficult because of an appearance so striking that it does not go unnoticed; however, this diagnosis must be confirmed with the corresponding radiographic study. In this sense, Khajavi., *et al*. [5] based mainly on the radiographic pattern, they propose to classify campomelic syndromes into 3 varieties:

1. Long bone campomelic syndrome, in which the curved bones retain their normal caliber and are only shortened.
2. Campomelic syndrome of short limbs, normocephalic type; conspicuously short and broad curved bones.
3. Short limb campomelic syndrome with craniostenosis, similar to the previous one and with a cloverleaf skull.

Differential diagnosis should be made with other congenital curving of the long bones, especially with Stuve and Wiedemann Syndrome (kyphomelic dysplasia); lethal dysplasias that present with limb deformity, such as thanatophoric; antenatal forms of osteogenesis imperfecta; hypophosphatasia and diastrophic dysplasia [2].

Rodríguez [6] found striking abnormalities, particularly the absence or marked deficiency of the anterior tibia artery. For these authors, the long bone curves would be explained by an alteration of the balance of forces that would occur due to an abnormal vascularization of the muscular group in the area.

Regarding inheritance, this disease was generally considered autosomal recessive transmission due to the presence of consanguinity and involvement of other siblings. Other authors have proposed autosomal dominant inheritance as a transmission mechanism, suggesting the presence of minimal defects in the parents [7]. Molecular genetic studies have shown that the SOX9 gene, located on chromosome 17, is a primary factor in the etiologic and manifestations of this disease [8,9].

Another interesting aspect is the descriptions made of genetic variants with discordance between the apparent sex and the chromosomal formula. These would generally be female neonates with 46XY karyotypes [10,11]. The phenotype of DC is sensitive to the level of expression of the SOX9 gene, which has an important influence during bone formation and sexual differentiation; thus, the analysis of mutations of the SOX9 gene demonstrate its involvement in chondrogenesis and development of the testis [12].

Although there are published cases of more or less prolonged survival, this bone dysplasia is considered lethal and it is the insufficient development of the rib cage together with tracheobronchial hypoplasia, the defects that determine the appearance of severe respiratory distress that conditions the death of these patients in the neonatal period.

Conclusion

Campomelic dysplasia is a clinical entity whose diagnosis is based on the combination of specific somatic features and characteristic radiological findings. The most important evidence is that campomelic dysplasia is an autosomal dominant transmission disease, although it can sometimes present genetic heterogeneity. Thus, patients who show a genetic rearrangement manifest a milder phenotype with a better long-term prognosis.

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