A Case Report of Camptomelic Dysplasia

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Abstract

Camptomelic Dysplasia (CMD) is a rare autosomal dominant congenital dwarfism characterized by shortness and bowing of long bones (camptomelia) and other severe skeletal and extra skeletal malformations. CMD is generally considered to be lethal and the majority of cases die in the neonatal period due to respiratory insufficiency.

We hereunder report a term male neonate with characteristic clinical and radiological findings of CMD, hydrocephaly, no sex reversal, and a negative family history of skeletal problems who was born to non-consanguineous healthy parents and was admitted to Shahid Sadoughi Hospital, Yazd, Iran, immediately after birth due to respiratory distress.

The patient required continuous mechanical ventilation support and all attempts to reduce respiratory support failed and the patient died on the 21th day of his life.

Camptomelic Dysplasia is a terrible experience for parents; thus, prenatal diagnosis of CMD by ultrasound is essential and mandatory for a better therapeutic intervention.

Keywords: Camptomelic dysplasia; dwarfism/congenital; bowing of long bones; sex-reversal

Introduction

Camptomelic Dysplasia (CMD) is a malformation syndrome and its name is derived from characteristic shortness and bowing of the long bones (camptomelia) (1).

This rare autosomal dominant syndrome (2) is caused by heterozygous mutations (as well as chromosomal aberrations: translocations, inversions or deletions) in SOX9 on chromosome 17q, an SRY-related gene regulating testis and chondrocyte development (1,3). The incidence of the disorder is reported between 0.05 to 1.6 in 10,000 live births (4).

This syndrome is usually lethal in the first year of life due to airway malformations and respiratory distress. Some patients may live up to childhood and adolescence, but survivors suffer from recurrent chest infections, progressive kyphoscoliosis and spinal deformity, dislocation of hips, mild to moderate learning difficulties, neurodevelopmental delay (especially gross motor), conductive hearing loss, short stature, dental caries with irregular teeth and myopia (1,2,5).

Male to female sex reversal occurs in most of the patients with an XY karyotype. A mild form of CMD characterized by the absence of camptomelia itself has been described as acamptomelic camptomelic dysplasia in which sex-reversal may be also absent (1).

Diagnostic criteria of CMD are as follows: (4)

A) Radiological:

Hypoplastic scapulae, bowed femurs (marked or mild), bowed tibias (marked or mild)

non-mineralized thoracic pedicles, vertically narrow iliac wings

B) Clinical (Seven or more of the following):

Macrocephaly, micrognathia, cleft palate, a flat nasal bridge, low set ears, talipes equinovarus,

congenital dislocation of the hip, bowed femurs, bowed tibias, Pretibial skin dimples, and respiratory distress

C) or sex reversal and bowed lower limbs

In this article, a neonate with camptomelic dysplasia and hydrocephaly is presented from Yazd, Iran. Another Iranian case has been reported from Mazandaran (6).

Case presentation

The neonate was transferred and admitted to the neonatal intensive-care unit of Shahid Sadoughi Hospital, Yazd, Iran, immediately after birth in view of severe respiratory distress.

The patient was the product of the third pregnancy of non-consanguineous parents, born by cesarean section for maternal pregnancy-induced hypertension at 38 weeks.

The routine antenatal ultrasound scan performed at seven months gestation had shown polyhydramnious. Two previous pregnancies had yielded two healthy children.

Family history was negative for skeletal abnormality or congenital malformation.

Birth weight was 2550 g (third percentile), length was 43 cm (< third percentile), and head circumference was 39 cm (>97th percentile).

Physical examination showed a high arch palate, cleft palate, hypertelorism, low set ears, micrognathia, a small face and oral orifice, a webbed short neck, a belly narrowed chest, bilateral anterior tibial and femoral midshaft bowing with skin dimpling at the apex of the tibial angulations (Fig.1), hip dislocation, club feet, cryptorchidism, hypospadias and a bifid scrotum.

Roentgenograms (Fig.2) revealed thoracic hypoplastic vertebras, thoracic scoliosis, absence of eleven ribs, scapula hypoplasia, absence of sternal ossification, bilateral tibia and humerus angulation, absence of fibula and bilateral dislocated hips.

Abdominal and pelvic ultrasonography showed a normal urinary tract system and no female internal genitalia.

Brain ultrasonography revealed hydrocephaly, as evident by lateral ventricles enlargement, and a prominent intrahemispheric fissure and cortical sulcus. Other neuroimaging studies (CT scan or MRI) were not performed in view of the serious condition of the patient and the need for ventilator support.

Karyotype study of the patient was 46 XY and his parents' karyotypes were normal. Laboratory equipment for DNA analysis was not available in our city.

The patient required continuous mechanical ventilation support and all attempts to reduce respiratory support failed. He finally died on the 21th day of his life.

Discussion

For the first time, a combination of malformations including micrognathia, hypoplastic fibula and scapula, long bones bowing and other skeletal abnormalities was delineated as Camptomelic Dysplasia by Maroteaux et al(7).

CMD is characterized by bowing of long bones and a variety of other skeletal and extra skeletal defects with or without XY disorders of sexual development. The majority of the cases are caused by mutations in SOX9 coding region. Unbalanced translocation involving the 17q24 region has been reported in some patients. (3,8) Camptomelia is absent in 10% of the patients (acamtpomelic CMD) (8).

Today, ultrasound prenatal diagnosis is made in many of the affected fetuses since transabdominal ultrasonography may be diagnostic at 12-32 weeks gestation with a more definite yield at around 24 weeks gestation(9,10).

This disorder is generally considered to be lethal, and the majority of cases die in the neonatal period (4,5,11); however, a 26-year-old patient with chromosomal translocation has been reported (12).

In the neonatal period, respiratory manifestations (recurrent apnea, chest infections, and stridor sometimes requiring tracheostomy) are the main clinical problems (4,5).

Our reported case had camptomelia, no sex reversal and hydrocephaly in brain sonography.

Male to female sex reversal occurs in the majority of XY karyotype patients (1,4,5). In 36 patients with camptomelic dysplasia whose data were collected from genetic, radiology and pathology centers in the United Kingdom, 75% of the chromosomal males were sex reversed or had ambiguous genitalia (4,5).

Two patients have been reported to have the mild non-lethal form of CMD, in which camptomelia and sex reversal may be absent (1).

A patient with acamptomelic CMD, sex reversal with male karyotype, muscular hypotonia, craniofacial dysmorphism, cleft palate, brachydactyly, malformations of thoracic spine, and gonadal dysgenesis has been reported from Germany (3).

Kos et al reported a female neonate with normal karyotype (46XX) and characteristic signs of CMD, macrocephaly, dolichocephaly, hydrocephalus, nail hypoplasia and skin dimpling on the anterior side of tibia. Parents were non – consanguineous. Respiratory distress, which was present since birth, exacerbated and led to death on the second day of life (13).

Congenital spinal deformity (14) and neonatal cervical instability (15) are reported in CMD patients.

A CMD patient with a normal 46 XX karyotype and female phenotype with frameshift mutation in C-terminal region of SOX9 has been reported from Canada (16).

Camptomelic dysplasia has been reported in a twin pregnancy from Greece (17). A CMD patient with cleft in the mandible has been reported from Turkey(18).

Rebage Moisés et al reported a camptomelic dysplasia patient associated with anorectal atresia (19).

In conclusion, camptomelic dysplasia is a terrible experience for parents; thus, prenatal diagnosis of CMD by transabdominal ultrasonography is essential and mandatory for a better therapeutic intervention.

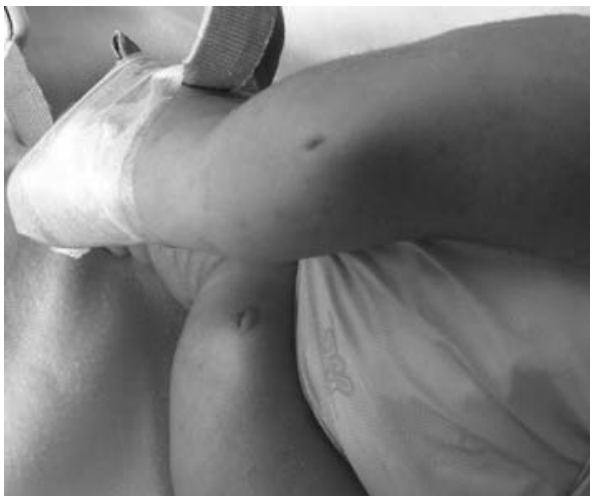

Fig 1. Skin dimpling over the bowed tibial area and anterior bowing of the tibia

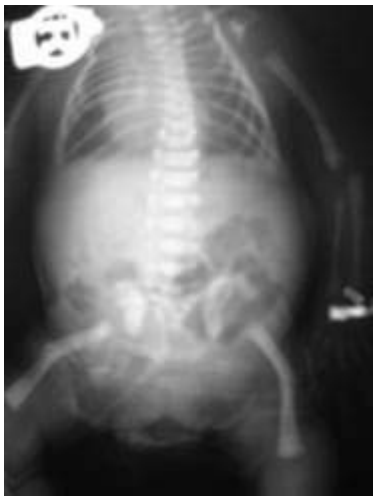

Fig 2. Missing ribs (eleven pairs of ribs), slender ribs, femoral bowing, and hypoplasia of the scapula and sternum

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