Camptomelic Dysplasia in a 38 weeks neonate – A rare case report

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Abstract: Campomelic dysplasia (CMD) is a rare osteochondrodysplasia with skeletal and nonskeletal defects**.** This rare autosomal dominant syndrome is caused by heterozygous mutations in the *SRY-related gene SOX9* on chromosome *17q* causing sex reversal. In most of the cases, death occurs in the neonatal period due to breathing problems related to small chest size**. Case presentation:** We reported a 38 weeks female neonate with characteristic clinical and radiological findings of camptomelic dysplasia (CMD). The diagnosis was on the basis of clinical and radiological findings as well as inconsistent neonatal karyotype and phenotype**.** Unfortunately she had respiratory failure and passed away on the second day of her life. **Conclusion:** Due to high mortality rate of CMD, prenatal diagnosis using transabdominal ultrasonography is indispensable.
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Key words: Camptomelic Dysplasia, *SOX9*, Mesomelic Dwarfism, Sex Reversal, Bowing of Long Bones, Camptomelia, eleven pairs of ribs, *Mutation.*

Introduction

Campomelic dysplasia (CMD) is a rare osteochondrodysplasia with skeletal and nonskeletal defects, the name comes from the Greek words for "bent limb", due to shortness and bowing of the long bones (1, 2). Anterior femoral and tibial bowing, skin dimpling at the pretibial area, clubfoot or talipes equinovarus, small bladeless scapulae, small thoracic cavities and a finding of 11 pairs of ribs, short first metacarpals, non-mineralization of the pedicles of the thoracic vertebra, narrow iliac wings and incomplete ossification of pubis are all suggestive of *Campomelic dysplasia*. The major facial characteristics that set *CMD* apart from normal cases are a large head, flat nasal bridge, low set and malformation ears, small jaw and a cleft palate. From other frequent findings we can refer to congenital dislocation of the hip and talipes equinovarus that may affect one foot (unilateral) or both feet (bilateral) (3). About 75% of reported 46XY patients exhibit a complete sex reversal; ranging from ambiguous genitalia to normal female with external and internal female genitalia (4). This rare autosomal dominant syndrome is caused by heterozygous mutations in the *SRY-related gene SOX9* on chromosome *17q* causing sex reversal. Bearing in mind that *SOX9* is the only gene in charge of the disease. The incidence of the disorder is reported between 0.05 to 1.6 in 10000 live births (1, 5). A *milder* form of the condition, in which the limbs are not bowed and have less skeletal deformities is *referred to as* acamptomelic camptomelic dysplasia (ACD) and occurs in about 10% of cases. Bearing in mind that both CMD and ACD is followed by mutations in *SRY-related gene* SOX9(6). In most of the cases, death occurs in the neonatal period due to breathing problems related to small chest size(3). Some patients are expected to live until adolescence, however they will face frequent respiratory infections, kyphoscoliosis and spinal abnormalities, hip dislocation, learning disabilities, delay in the neurodevelopmental skills particularly gross motor, conductive hearing loss , height below the mean height for age and sex, tooth decay, irregular teeth alignment, and nearsightedness (1, 7).

Case Presentation

Our case was a 4 kg female neonate at 38 weeks to a third gravida mother delivered by caesarian section due to breech position. Apgar scores at 1 and 5 min were 5 and 8 respectively and the neonate was resuscitated with PPV. Right after birth the neonate was admitted to the neonatal intensive-care unit of Besat hospital, Sanandaj, Iran. After clinical examination, she was noted to have low set ears, flat nasal bridge, small jaw, short lower and upper extremities, bowed long bones of lower extremities and skin dimpling on anterior side of tibia [Figure 1], hypoplasia of scapula, small thoracic cavities, short stature (she was 43 cm high, below the

third percentile), a webbed short neck, club feet, short hand and foot phalanges [Figure 2]. Radiograph showed bowed femur and tibia, hypoplastic and bladeless scapulae [Figure 3], and only 11 pairs of ribs [Figure 4]. She had normal female genitalia with edema in labia major, however no mass was observed. Her septic screen was negative.

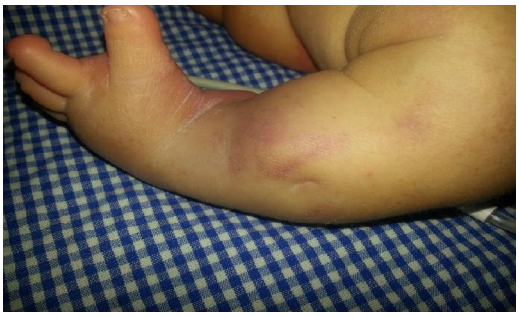

Figure 1- Skin dimpling on tibial anterior side

Figure 2- Low set ears, flat nasal bridge, small jaw, short lower and upper extremities, bowed long bones of lower extremities, small thoracic cavities and normal female genitalia, a webbed short neck, club feet, short hand and foot phalanges

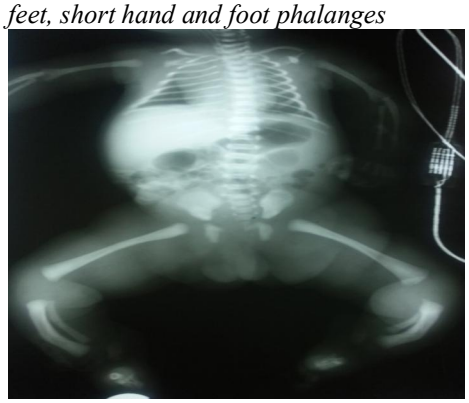

Figure 3- Radiograph shows bowed femur and tibia, hypoplastic and bladeless scapulae

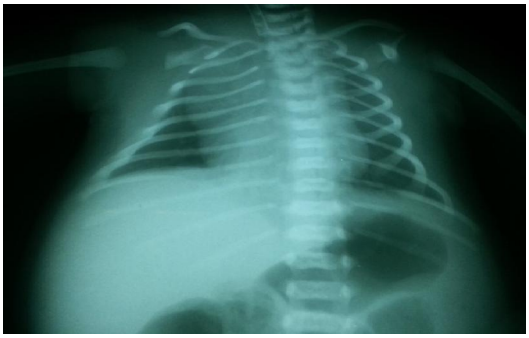

Figure 4-Missing ribs (11 pairs of ribs)

Mother was not exposed to medications or radiations during pregnancy and there were no known family histories of skeletal abnormalities or congenital malformations. The two elder siblings were normal. Triple Screen Test was conducted due to mother's age (40 year), to rule out any chromosomal abnormalities, resulting in detection of high AFP. In spite of normal female phenotype, amniocentesis showed male karyotype 46, XY. Our reported case had camptomelic dysplasia on the basis of clinical and radiological findings as well as different neonatal karyotype and phenotype. Unfortunately genetic studies were not done due to parent disagreement but according to diagnosis, the gene responsible for the condition was SOX9. Consequently, the patient went under continuous ventilatory support due to respiratory failure and despite medical team efforts she passed away on the second day of her life.

Discussion

Maroteaux et al described camtomelic dysplasia for the first time as deformities including microgonathia, hypoplastic fibula and scapulae, long bones bowing and other skeletal abnormalities(8). The incidence of camtomelic dysplasia is about 2 per million live births.(9) Bowing of long bones plus skeletal and extra skeletal malformations are signs of CMD which may or may not go along XY disorders of sexual development, which are mainly due to SOX9 coding-region mutations (4, 10).

Antenatal finding of long bone angulations may be a differential diagnosis for osteogenesis imperfecta (11) however in our case, findings like hypoplastic scapula, and unfractured ribs ruled out osteogenesis imperfecta. Another significant differential diagnosis to be noted is Kyphomelic dysplasia due to its good prognosis and no need for termination of the pregnancy, however it is often involves the femora(12).

In view of the fact that most of the skeletal dysplasias are fatal, making an accurate prenatal

diagnosis is very important in order to timely termination of pregnancy. CMD is often fatal due to neonatal death related to respiratory conditions (3, 7). Nowadays prenatal screening using ultrasound is conducted frequently at 12-32 weeks gestation (7). In high-risk mothers frequent ultrasound is supportive of the diagnosis and Three-dimensional ultrasound may facilitate an exact diagnosis (13).

Conclusion

Owing to high mortality rate of CMD, prenatal diagnosis using transabdominal ultrasonography is indispensable.

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Consent

Written informed consent was obtained from the patient's parents for publication of this study.

Competing interests

The authors declare that there is no conflict of interest.

Authors' contributions

All authors contributed to the writing of the manuscript. All authors read and approved the final manuscript.

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