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Campomelic Dysplasia: 2 Cases

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Abstract: Campomelic dysplasia (CD; OMIM #114290) is an osteochondrodysplasia associated with skeletal malformations and sex reversal. It occurs due to de novo mutations in SOX9 gene in the 17q24 chromosome. It is associated with bent lower limbs, micrognathia, cleft palate, hypoplastic scapulae, congenital hip dislocation and a high rate of neonatal mortality. We evaluated 2 neonates diagnosed as CD on the basis of these findings. One of them was born to a diabetic mother, none of them showed sex reversal and only one survived the first year of life. Genetic counseling was given to the families of the patients.

Keywords: Campomelic dysplasia, diabetic mother, sex reversal, counseling

INTRODUCTION

Campomelic dysplasia is a rare cause of short limbed dwarfism. The incidence is reported to be 1 per 200000 births [1]. The term "campomelia" means curved limb. The hallmark features of CD are angular bowing and shortening of long bones with pretibial skin dimpling, hypoplastic scapulae, missing pairs of ribs, narrow thorax and hip dislocation. In 10% cases of CD, campomelia is absent and it is called acampomelic CD [2]. A secondary feature of CD is a male to female sex reversal which occurs in two-thirds of patients with an XY karyotype [3]. CD is a frequently lethal skeletal dysplasia with 77% of deaths occurring neonatally and 90% of deaths before first two years of age [4]. To the best of our knowledge, this is the first reported case of CD in a baby of a diabetic mother though it has previously been reported in acampomelic CD [5].

CASE SERIES

Case 1

A male newborn weighing 2.7 kg was born to a primigravida mother at 40 weeks of gestation by LSCS. There was no history of consanguinity. The mother was suffering from gestational diabetes mellitus which was controlled with insulin. Her HbA1c at ninth month of gestation was 6.8. Anthropometry of the neonate revealed a head circumference of 34 cm, length of 41 cm and a upper segment: lower segment ratio of 2.7:1. There was proximal shortening of both lower limbs. Physical examination revealed hypertelorism, micrognathia, cleft palate and congenital dislocation of hips (Fig 1). The examination of other systems were within normal limits. The Chest X- Ray showed hypoplastic scapulae. X -Ray Pelvis showed shortening and bowing of both femurs (Fig 2 & 3). USG whole abdomen and brain were normal. Based on the clinical and radiographic findings, the patient was diagnosed to be suffering from Campomelic dysplasia. The karyotype was 46,XY hence no sex reversal was present. Genetic study was not done due to financial constraints. The neonate was managed conservatively and discharged on Day 6 of life. He has survived the first year of life and is currently fourteen months old.

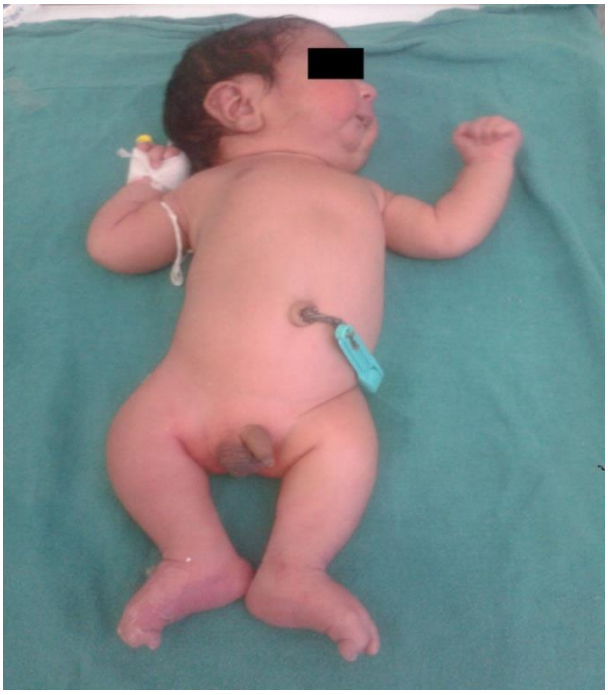

Fig-1: proximal shortening of lower limb and pierre-robin sequences

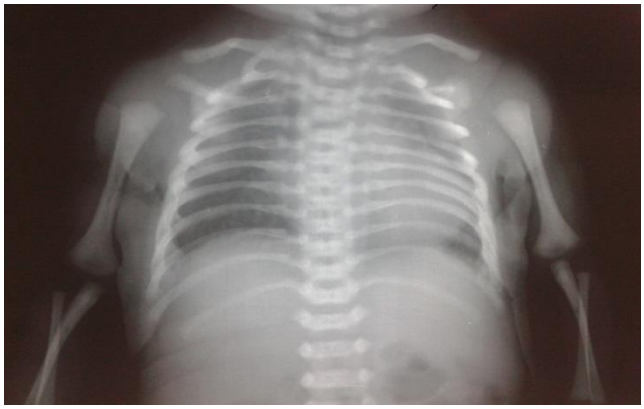

Fig-2:CXR shows hypoplastic scapulae

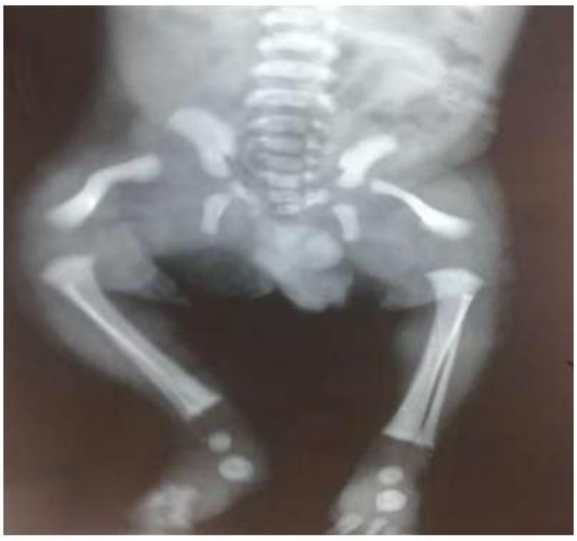

Fig-3: X-Ray Lower limbs shows bilateral shortening and bending of femurs

Case 2

A female newborn weighing 2.45 kg, born at 38 weeks of gestation by LSCS to a second gravida mother was admitted in our NICU for respiratory distress. The mother had a non consanguineous marriage and her first child was healthy. Anthropometry revealed a head circumference of 33.5 cm, length of 44 cm and upper segment: lower segment ratio of 2.3:1. Physical examination revealed micrognathia and cleft palate (Fig 4).The sepsis screen was negative. Chest X - Ray showed hypoplastic scapulae, X- Ray pelvis revealed bilateral shortening and bowing of femurs (Fig 5 & 6). USG KUB showed mild hydronephrotic changes in the left kidney. Here also, Campomelic dysplasia was diagnosed and karyotyping was done which showed no sex reversal. Genetic study was not done. The neonate was managed conservatively and discharged on Day 9 of life. The infant died due to pneumonia at 3 months of age.

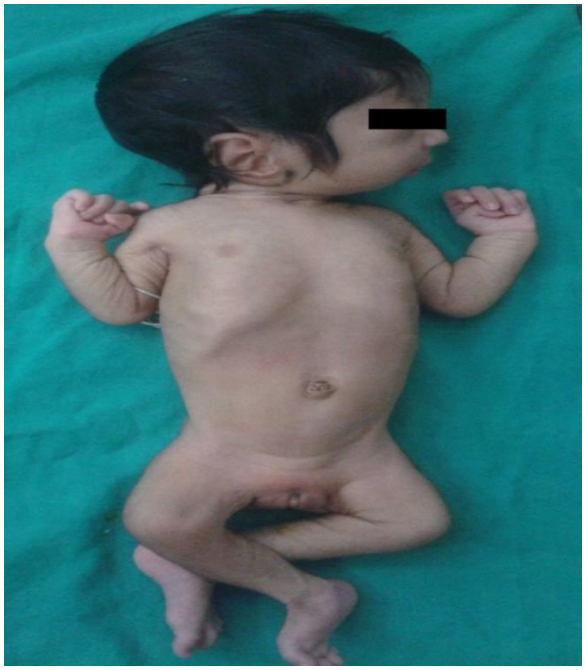

Fig-4: showing proximal shortening of lower limb and pierre –robin sequences

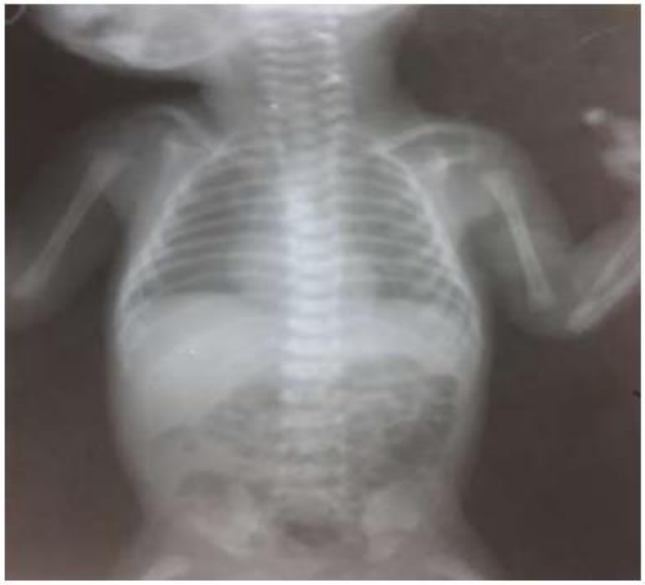

Fig-5:CXR shows hypoplastic scapulae

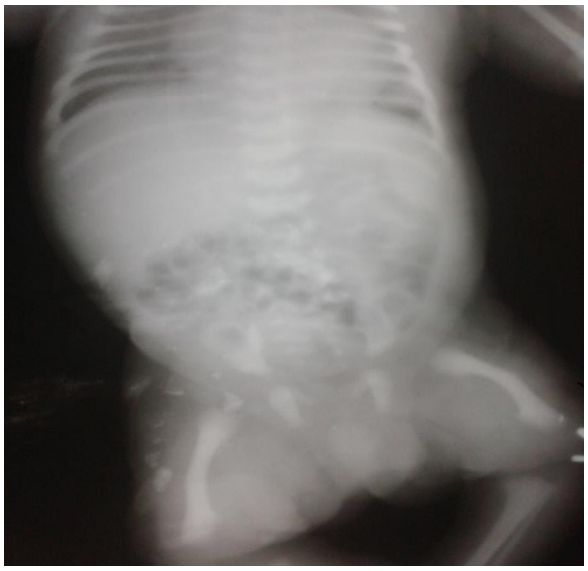

Fig-6: X Ray Pelvis shows bilateral shortening and bending of femurs

DISCUSSION

Campomelic dysplasia is a rare, often lethal skeletal dysplasia usually associated with sex reversal. Most cases are due to mutations in the *SOX9* gene – a member of the *SOX* (SRY-related HMG box) gene family – located on 17q23–qter, which plays a role in chondrogenesis and sex determination [6]. The diagnosis of CD is based on clinical and radiographic findings, the latter providing the most reliable diagnostic clues [7]. The clinical findings are hypertelorism, flat nasal bridge, Pierre Robin sequence, hypotonia, narrow thorax, kyphoscoliosis, bowed lower limbs, hip dislocation and CTEV. The suggestive radiological findings are bowed femora and tibiae, hypoplastic scapulae, slender thoracic cage with eleven pairs of ribs, non mineralized thoracic pedicles, narrow iliac wings etc. The important differential diagnoses are osteogenesis imperfecta, achondroplasia, thanatophoric dysplasia, hypophosphatasia and Stickler syndrome.

The high rate of neonatal deaths in CD is due to respiratory insufficiency due to laryngotracheobronchomalacia. Infants who survive suffer from recurrent respiratory tract infections, mental retardation, sensorineural deafness, progressive kyphoscoliosis and short stature. Antenatal ultrasonography can detect the condition as early as 18 weeks of gestation [8]. Genetic counseling is needed as there is recurrence risk in a sibling if one of the parents is a mosaic and in an offspring if the patient survives to the reproductive age.

Management is in the form of supportive medical care, orthopedic treatment of skeletal malformations and gonadectomy in case of XY phenotypic females with male gonads to prevent the risk of gonadoblastoma.

Though acampomelic dysplasia was being reported in the literature, our case of typical CD in an infant of diabetic mother (IDM) is the first one in this row. Congenital anomalies occur more frequently in IDMs than in infants of non-diabetic mothers [9]. The most common fetal structural defects associated with maternal diabetes are cardiac malformations, neural tube defects, renal agenesis and skeletal malformations. Metabolic control of diabetes in early pregnancy is correlated with malformations seen in IDMs. Studies have shown a relation between elevated HbA1c in the first trimester and major anomalies in IDMs [10].

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