

Anaesthetic considerations in little people

Part 1: Campomelic Dysplasia

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Case Report

A 3½ year old 12kg boy with campomelic dysplasia presented for lengthening of both Achilles tendons. He was a happy child but did not verbalise. He had a short stature; anterior bowing of both tibia - with a cutaneous dimple over the apex - and deficient proximal fibulae; short femurs, bowed antero-laterally with lateral sclerosis of the cortex in the upper third on X-ray. The acetabulae were abnormally steep. His chest was small, bell shaped, with significant kyphoscoliosis and small shoulder blades. He had a chronic cough and stridor ascribed to tracheomalacia that had been present since birth. He had been admitted on numerous occasions for pneumonia, viral bronchiolitis and failure to thrive. Gastro-oesophageal reflux had been excluded.

His head was not enlarged (circumference 50th centile) but his face was broad and flat with a high forehead, a relatively small jaw, flat nasal bridge, long philtrum and low set ears. His ears were low set but had a normal configuration. (Fig 1) The previous repair of the soft palate was visible. No chromosomal studies were performed since his external genitalia were normal male (i.e. no sex reversion). He had delayed milestones, some attributed to a hearing deficit. He was born by normal vaginal delivery at term weighing 2.84kg. His parents and two siblings were normal. He had had previous uneventful anaesthetics for cleft palate repair, bilateral myringotomies and dental extractions (caries). The dental extractions were complicated by bleeding - an underlying coagulopathy was excluded. When sedated for a recent CT scan he had developed respiratory difficulties.

Campomelic dysplasia

Campomelic dysplasia is a rare form of severe osteochondrodysplasia and congenital dwarfism which has a potentially lethal outcome as a result of respiratory insufficiency in the newborn period. The incidence is estimated at 0.05-0.9 per 10000 births¹ and affects all ethnic groups. The chromosomal sex ratio is approximately 1:1 but a preponderance of female phenotype occurs as a consequence of sex reversal.

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Figure 1: Three year old boy with campomelic dysplasia with typical facial features; anterior bowing of the tibia with overlying skin dimple; and kyphoscoliosis.



Campomelic dysplasia was first described in the 1950's^{2,3} but recognised as an entity in 1970.⁴ The term campomelia, from the Greek word campos meaning curved and melia meaning limb, was adopted⁵ although camptomelic from a Greek word camptos meaning bent was first suggested by Bianchine.⁶ Both are used interchangeably in the literature. The condition is also known as CMD1 and CMPD1. The syndrome has many other skeletal and extra-skeletal manifestations⁷ but the bent limbs are the most obvious and may be present at birth.

Genetic profile. Campomelic dysplasia is an autosomal dominant condition caused by mutations involving the SOX-9 gene, an SRY-related gene located on chromosome region 17q24.3-q25.1.^{1,8} (SRY is the sex determining region on the Y chromosome in mammals). The SOX9 gene encodes a transcription factor which is involved in bone formation (regula-

tor in Type II collagen expression in chondrogenesis), control of testicular development and determination of phenotypic sex characteristics.¹

An unusual aspect of campomelic dysplasia is that 75% of affected individuals with a male karyotype may have female or ambiguous genitalia.⁷ The abnormal SOX 9 gene, located on chromosome 17, fails to stimulate the testes to develop and produce hormones (testosterone, mullerian inhibiting substance). In the absence of these hormones female external genitalia develop even in genetic males (XY) - a phenomenon known as sex reversal.

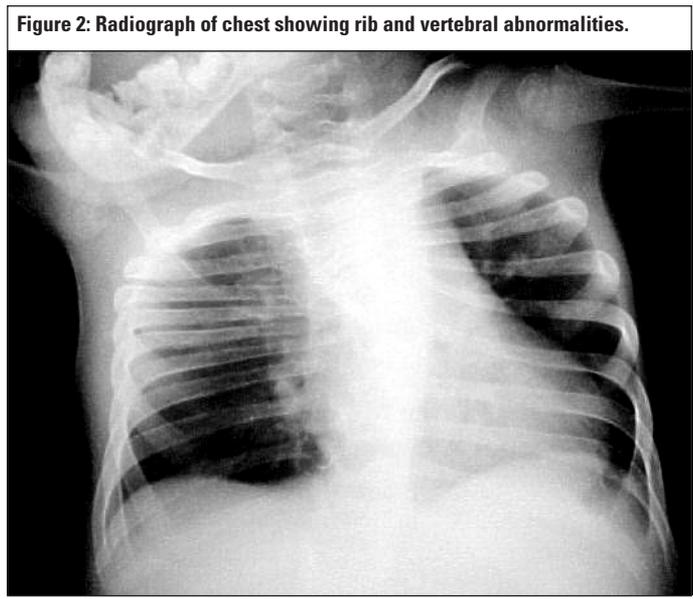
Since the SOX- 9 gene produces a multidomain protein it is likely that mutations in different domains may cause a variation in the phenotype. Because of the importance of SOX-9 in bone formation, it is likely that nullisomy for the SOX-9 gene is lethal⁸ - most deaths occurring in the neonatal period. Individuals who have chromosomal rearrangements have a milder phenotype and better prognosis.

Clinical Features

The facial features of campomelic dysplasia are typical (Fig 1) and are characterised by macrocephaly (87%) with a high forehead, a large anterior fontanelle, small flat face, hypertelorism and an antimongoloid slant to the eyes. The nasal bridge is flat with a long philtrum while the ears are low set and posteriorly rotated.^{1,5,7} Some may have hearing difficulties.⁷

Although there are several typical orthopaedic features associated with campomelic dysplasia the predominant anaesthetic concern is respiratory . The small bell -shaped thoracic cage with deficient ribs (Fig 2), reduced laryngeal diameter and tracheo-bronchial cartilage hypoplasia are characteristic features. The structurally abnormal tracheobronchial cartilage are reduced in number in the large airways and absent in the smaller bronchi. Kyphoscoliosis develops early and progresses to such an extent that it affects cardiopulmonary function at a very early age (1-4.5years)^{5,9}, further compromising an already precarious respiratory function.

These children are an aspiration risk for a number of reasons. Kyphoscoliosis is commonly associated with reflux because of the altered oesophageal and lower oesophageal sphinc-



ter function. Upper airway abnormalities, which include micrognathia and cleft palate (usually soft palate), together with hypotonia, may also contribute. Many of these abnormalities also predispose to upper airway obstruction and obstructive sleep apnoea.

Intubation may be difficult. The upper airway abnormalities (micrognathia, cleft palate) in association with limited neck movement and macrocephaly contribute to this difficulty. Cervical spine instability (odontoid hypoplasia, hemivertebrae, kyphosis)⁵ should be excluded preoperatively.

Communication may be difficult in some individuals in view of hearing loss secondary to structural abnormalities of the incus and stapes and cochlea hypoplasia.¹ The absence of olfactory bulbs and tracts have been noted at post mortem.⁷ Other anomalies that need to be assessed prior to surgery include renal and cardiac defects. There is a high incidence of hydro-nephrosis (up to 38%) while ventricular septal defects are seen in 20% of patients.^{1,7,10}

Phenotypic females with 46-XY karyotype have an increased risk of developing gonadoblastomas and surgical removal of the gonads is indicated.¹¹

Orthopaedic manifestations

No single skeletal abnormality is pathognomonic of campomelic dysplasia but combinations of skeletal, radiological and nonskeletal abnormalities define the disorder (Table 1). Three of the 5 radiological features; seven or more of the 11 clinical signs; or the combination of sex reversal and bowed lower limbs is considered diagnostic.^{1,7}

Table 1: Diagnostic criteria and likelihood of occurrence modified from Khoshlal¹ and Mansour⁷

Clinical : Seven or more of	%	Radiological	%
Macrocephaly *	87	Hypoplastic scapulae	92
Micrognathia	93	Bowed femora *	
Cleft palate *	66	Bowed tibia *	
Flat nasal bridge *	90	Vertically narrow iliac wings *	93
Low set ears	88	Poorly developed pubic bones	100
Talipes equinovarus *	94	Abnormal ischial bones	96
Congenital dislocation of hips	82	Non mineralised thoracic pedicles *	77
Bowed femora *	69	Abnormal cervical vertebrae *	77
Bowed tibiae *	91	Non mineralised sternum	
Pretibial skin dimples *	88	Small thoracic cage, * 11 ribs	72
Respiratory distress *	96	Short 1st metacarpal	100
or			
Sex reversal and bowed lower limbs			
* Present in our patient			

Symmetric anterolateral bowing of the femurs and anterior bowing of the tibiae (with a skin dimple over the apex) are common findings. These and other lower limb anomalies are probably vascular in origin (anterior tibial artery). The fibula is either hypoplastic, straight but more commonly bowed, proximal to the tibial bow. (Fig 3) Foot abnormalities are frequent and include clubfeet (talipes equinovarus), calcaneo-valgus deformity with characteristic fanning of the toes with a wide space between the first and second toes.⁵ Hypoplasia of the pelvic bones (vertical ilia, pubis) frequently give rise to secondary subluxation or dislocation of the hips. The caudal space may be difficult to identify in the presence of pelvic and hip abnormalities. This was true in the case described and a sacro-intervertebral block was performed

Figure 3: Radiograph of limb showing typical lateral bowing of femur and anterior bowing of tibia.

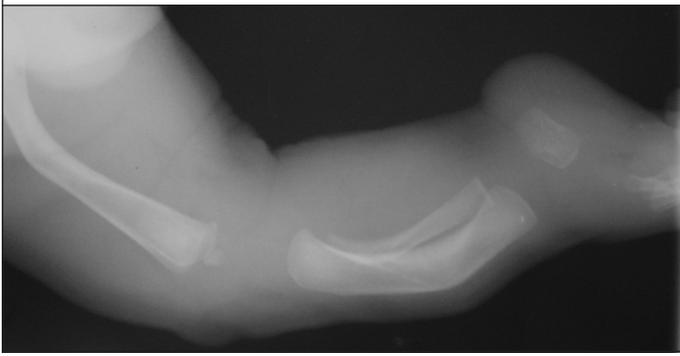


Figure 4: Radiograph of shoulder demonstrating the hypoplastic shoulder blade



to provide regional analgesia for the lower limbs.

The upper limbs are less likely to be bowed. The hypoplasia of the scapula body (small, without blade)(Fig 4) is a consistent feature.^{12,13} The hands may show brachydactyly, clinodactyly, camptodactyly and or hypoplasia of the fingers. A short first metacarpal is a characteristic radiographic sign.

The spine is affected at all levels. The cervical spine may be unstable and kyphotic. The thoracic pedicles may be absent or their ossification may be delayed. More than 50% of individuals have only 11 ribs associated with six lumbar vertebrae implying normal segmentation of the spine. Congenital scoliosis or progressive kyphoscoliosis of the thoracolumbar spine may present at an early age. This may not only compromise cardio-respiratory function but may cause neurological problems (paraplegia in 33% of cases). Surgical correction by instrumentation is difficult if not impossible since the bones are fragile, the connection between the posterior elements and vertebral bodies is poor, and there is close proximity of the spinal cord to the laminae, in the presence of abnormal thoracic pedicles. Autogenous bone grafting from the hypoplastic iliac bones is also difficult.

Conclusion

Most children with campomelic dysplasia die of respiratory failure at an early age (66-75% in neonatal period⁷). Advances in respiratory care¹⁴ has lead to improved survival but few progress to adulthood. These children pose significant anaesthetic challenges. The severity of respiratory deficit is not only determined

by the phenotype but also the age of the child, the severity of the airway narrowing and the kyphoscoliosis. Laryngoscopy and intubation may be difficult and reflux poses an aspiration risk. The choice of anaesthetic will be influenced by the severity of the respiratory problems, the presence of obstructive sleep apnoea and the degree of hypotonia. Central and peripheral nerve blocks may be difficult in view of the orthopaedic abnormalities.

Geneticists continue to unravel the complexities of the phenotypic expression and the links between chondrogenesis and sex determination.^{15,16} Recent studies suggest that significantly milder forms of the disease may be detected in parents of affected children.¹⁷ and the condition may be under diagnosed.¹⁸

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