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Special Feature / Diagnosis

Diagnosis and Discussion: Campomelic Dysplasia

Figure 1. Characteristic features include large head, flat face, low-set ears, micrognathia, and bowed legs with pretibial dimple of the right leg.

Figure 2. Anteroposterior plain radiograph shows short femora with anterior bowing, 11 paired thin ribs, small hypoplastic scapulae, small narrow lilac wings, and widely separated ischia.

Figure 3. Dissection of the femur shows angulation anteriorly.

Campomelic dysplasia (CD) is a rare, often lethal, congenital osteochondrodysplasia, short-limbed dwarfism characterized by anterior bowing of the long bones of the lower limbs. The incidence varies from 0.05 to 2.0 per 10,000 births.[1, 2] There is an association with a variety of extraskeletal anomalies involving the cardiac, respiratory, urinary tract, and central nervous systems.[1, 3] The term *campomelia* is derived from Greek, meaning bent or curved limb.[1, 4-6] Most recently, it has been linked to rearrangements in the sex-determining region Y–related *SOX9* gene on chromosome 17 (q24.3-q25.1).[7, 8] These mutations disrupt skeletogenesis and chondrocytic differentiation and produce defective testicular development often resulting in sex reversal with female phenotype in chromosomal XY males.[1-3, 5-7]

Most believe CD is autosomal recessive; however, rare reports strongly favor an autosomal dominant inheritance.[1, 7-9] The sex ratio is approximately 1:1. Approximately 75% of genotypic XY males will exhibit female or ambiguous genitalia, varying from bifid scrotum with hypospadias to an enlarged clitoris.[1, 7] Genotypic XX females remain phenotypically female.[1, 3] The cause for sex reversal is believed to be related to the absence of the sex-determining region Y antigen (testis-determining factor) expressed in pre-Sertoli cells during gonadal ridge development.[5, 6, 8, 9]

Characteristic features are skeletal hypoplasias and anomalies affecting the face, head, scapulae, spine, pelvis, and upper and lower limbs. The limbs are short with anterior bowing of the legs and/or thighs, often with pretibial skin dimples.[1, 3, 5, 6] The head is macrocephalic, with flattened facies and nasal bridges, high forehead, low-set ears often with associated deafness, hypertelorism, long philtrum, small mouth, and micrognathia. Two thirds of patients will have cleft palate.[1, 3] The trunk is short and the chest may be bell shaped. Radiography reveals severely hypoplastic bladeless scapulae, vertically narrow iliac wings, agenesis of the sacral wings, poorly developed ischiopubic rami, 11 paired thin ribs, nonmineralized thoracic pedicles, and delayed ossification.[1, 3, 5-7]

The cause of death is primarily respiratory owing to airway and pulmonary defects, lack of laryngotracheobronchial cartilages, and hypotonia resulting in apneic spells, atelectasis, aspiration, and pneumonia. Death occurs in most patients in the neonatal period.

Polyhydramnios is present in 30% of cases.[1, 5, 6] Infants who survive suffer from feeding difficulties, stridor, retractions, frequent otitis media, bronchitis, and poor growth.[3] Patients who survive several years may be mentally retarded and show variable breakpoints within the vicinity of chromosome 17 (q21-q25).[3, 9, 10] The oldest reported CD survivor was 17 years old with an IQ of 45.[3]

Other extraskeletal anomalies involve the central nervous system (macrocephaly, hydrocephalus, polygyria, absent olfactory bulbs and/or tracts), cardiovascular system (patent ductus arteriosus, ventricular septal defects, coarctation of the aorta), and genitourinary system (hydronephrosis, hydroureter, renal hypoplasia, renal cortical and medullary cysts).[1, 3, 5, 6] The epiphyseal resting cartilage is histologically unremarkable.[5, 6] No biochemical defects of bone collagen, ground substance, or mineralization are evident despite limb bowing.[5, 6] Diagnosis can be established by ultrasonography as early as 18 weeks' gestation.[1, 3] Gonadectomy is advocated in surviving phenotypic females with Y chromosome fragments owing to the increased risk of gonadoblastoma.[11] Recognition of CD is imperative for assistance in genetic counseling and its diagnosis in affected future pregnancies.[1, 3, 12]

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Accepted for publication April 30, 1999.

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SECTION EDITOR: ENID GILBERT-BARNESS, MD