Dyssegmental Dysplasia, Silverman-Handmaker Type

Alternative Names
DDSH
Silverman-Handmaker Type of Dyssegmental Dysplasia

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
224410

Mode of Inheritance
Autosomal recessive

Gene Map Locus
1p36.1

Description
Dyssegmental dysplasia, Silverman-Handmaker type (DDSH) is a rare lethal form of chondrodysplasia characterized by anarchic ossification of vertebra, camptomelia (bending of the long bones) and micromelia (short limbs). Individuals with DDSH also have cephalocele, a flat face, abnormally small jaws, cleft palate, short neck, elongated scapula, abnormal size, cardiac defects, hydromeophrosis, and reduced joint mobility. In addition, DDSH is associated with either stillbirth or death within a few days after birth. Hispanic origin individuals are heavily affected with the disease. Studies show equal number of affected sibs in males and females with the ratio being 1:1.

Molecular Genetics
Dyssegmental dysplasia, Silverman-Handmaker type is an autosomal recessive disorder. It is suggested that null mutations of the perlecan gene heparan sulfate proteoglycan 2 (HSPG2), essential for cartilage development, are associated with DDSH.

Epidemiology in the Arab World

Lebanon
Prabhu et al (1998) reported the case of a male infant born with clinical and radiographic evidence of a lethal form of dyssegmental dysplasia most compatible with the Silverman-Handmaker type. The parents were first cousins of Druze-Lebanese origin supporting an autosomal recessive mode of inheritance. The infant was born at 39 weeks of gestation to a 16-year-old woman. At 26 weeks gestation, a fetal sonogram was done detecting oligohydramnios, micromelia with marked disorganization of the vertebral bodies, and the absence of acetylcholine esterase. The infant showed poor respiratory effort and bradycardia shortly after birth. Consequently, he was incubated and supported with a conventional ventilator. Most DDSH features were observed in the case like; severe micrognathia with glossoptosis, low-set ears, short neck, cleft palate, and decreased mobility at the joints. CT scan and MRI of the brain displayed arachnoid cyst and venous angioma which were not reported previously with DDSH. Oral feeding was difficult due to gastroesophageal reflux; therefore, he was fed by introducing a gastrojejunostomy tube. Ophthalmological examination demonstrated subluxation of the lenses and prominent choroidal vasculature in the fundus. The infant failed hearing evaluation. He had hyperthermia, with temperature spikes as high as 40 degrees Celsius, two to three times per week which was referred to a central origin. Severe alterations in the architecture of the vertebra were observed by radiological examination. His physical growth was severely delayed. At age of 8 months, he was discharged home to his parents with 24-hour nursing care. He had increasingly frequent episodes of bradycardia and cyanosis and died at home two weeks later. Prabhu et al (1998) found that this case is not compatible with DDSH due to the prolonged survival, and the abnormalities of the eyes and the CNS. The
prolonged survival period was attributed to the neonatal intensive care, the presence of a gene that improved pulmonary function, or to the representation of an intermediate phenotype between DDSH and dyssegmental dysplasia Rolland-Desbuquois type. The study proved the presence of the gene of DDSH in the Middle East gene pool. This was probably the first report on dyssegmental dwarfism Silverman-Handmaker type in Lebanese Druze.

References

Contributors
Abeer Fareed: 13.5.2006