Thanatophoric Dysplasia, Type I

Alternative Names
Lethal Short-Limbed Platyspondylic Dwarfism, San Diego Type
Platyspondylic Lethal Skeletal Dysplasia, San Diego Type
TD
TD1
Thanatophoric Dwarfism
Thanatophoric Dysplasia
Achondroplasia, Severe, with Developmental Delay and Acanthosis Nigricans
SADDAN

Record Category
Disease phenotype

WHO-ICD
Congenital malformations, deformations and chromosomal abnormalities > Congenital malformations and deformations of the musculoskeletal system

Incidence per 100,000 Live Births
6-10

OMIM Number
187600

Mode of Inheritance
Autosomal dominant

Gene Map Locus
4p16.3

Description
Thanatophoric dysplasia is the most frequent form of lethal osteochondrodysplasias with an estimated frequency of nearly of 1 in 20,000 births. Thanatophoric dysplasia is classified into two types: TD type 1 patients have curved femurs with or without a cloverleaf skull, and in the second type patients always have straight femurs and a cloverleaf skull. Affected individuals usually die within minutes or days after birth.

Thanatophoric dysplasia is an autosomal dominant disorder. Prenatal diagnosis is commonly accomplished in the second-trimester scan, but occasionally thanatophoric dysplasia may not be clearly distinguished from the other osteochondrodysplasias, with consequent important prognostic implications. However, in order to confirm the diagnosis, complementary radiological, pathological and molecular studies are mandatory.

Molecular Genetics
Essentially, all thanatophoric dysplasia patients had mutations in the transmembrane domains of the fibroblast growth factor receptor 3 gene, located on the short arm of chromosome 4 (4p16.3). A sporadic mutation causing a Lys650Glu change in the tyrosine kinase domain of FGFR3 was found in 16 of 16 individuals with one type of thanatophoric dysplasia.

Epidemiology in the Arab World
Oman
Sawardekar (2005) conducted a study to establish the prevalence of major congenital malformations in children born during a 10-year period in Nizwa Hospital. Of the 21,988 total births in the hospital, seven children were born with Thanatophoric Dysplasia. Sawardekar (2005) hinted for a possible genetic contribution in these children.

Morocco
Chemke et al. (1971) and Graff et al. (1972) described thanatophoric dwarfism in two male offspring of first-cousin Moroccan Jewish parents. In the second-born affected sib the diagnosis was made antenatally by X-ray. However, after review of the radiographs of one, Rimoin (1975) concluded that this was not thanatophoric dwarfism. Thus, Rimoin (1975) concluded that 'there are no well-documented examples of familial thanatophoric dwarfism; a genetically lethal autosomal dominant mutation or an environmental agent could explain' its occurrence. Knowles et al. (1986) and Borochowitz et al. (1986) suggested that the disorder reported by Chemke et al. (1971) and Graff et al. (1972) was the same as the 'new'

autosomal recessive dysplasia they described under the designation of Schneckenbecken dysplasia.

United Arab Emirates

Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth in Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 to January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Single gene disorders accounted for 24% of the cases, 21% were due to autosomal dominant disorders. In their study, Al Talabani et al. (1998) observed one case of thanatophoric dysplasia in a family from the United Arab Emirates. Recurrence was not reported in other members of the family. Al Talabani et al. (1998) concluded that this study is very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as this study included over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

In a 5-year prospective study for newborns at Al Ain Medical District, Al-Gazali et al. (2003) defined the pattern and birth prevalence of the different types of osteochondrodysplasias in the United Arab Emirates. Among the 38,048 births during the study period, 36 (9.46/10,000 births) had some type of skeletal dysplasia of which three had thanatophoric dysplasia. The mean paternal and maternal age for thanatophoric dysplasia were 39.8 and 31.2 years, respectively. Al-Gazali et al. (2003) calculated the birth rate of this type of osteochondrodysplasia in the United Arab Emirates to be 0.78/10,000 births (0.09-0.60/10,000 worldwide) and the mutation rate to be 0.39/10,000. Al-Gazali et al. (2003) also noted that the birth prevalence of new dominant skeletal dysplasias is higher in the UAE population than those reported for other populations (0.2/10,000, with a range of 0.06-0.3).

Simsek et al. (2003) described Emirati patient(s) with type I Thanatophoric Dysplasia with a mutation in the FGFR3 gene.

Bekdache et al. (2010) described a female infant born to non-consanguineous parents with Thanatophoric Dysplasia, Type I. At 23-weeks of pregnancy, the mother was referred for fetal skeletal evaluation. The examination showed markedly shortened long bones and bowed femur, strawberry shaped head, bilateral clubfeet, short ribs, narrow thorax, and platyspondyly. The baby was delivered at 33-weeks, weighing 1,730 grams. She was transferred to the NICU after inserting an endotracheal tube and after having intermittent positive pressure. She was on nasogastric tube feeding and antibiotics were prescribed at the age of 2-months, after one month the baby was on assisted ventilation. The infant died at the age of 93 days, her condition being incompatible with life. Postnatal DNA sequencing of FGFR3 gene identified a heterozygous mutation.

References

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Related CTGA Records

Fibroblast Growth Factor Receptor 3

Schneckenbecken Dysplasia
Short Rib-Polydactyly Syndrome, Type III

External Links

http://www.genetests.org/profiles/td
http://www.orpha.net/data/patho/GB/uk-Thanatophoric-dysplasia.pdf

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