Acknowledgement

The authors wish to thank the Dean, Dr. P.M. Pai for giving us permission to publish this article.

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Thanatophoric Dysplasia

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Thanatophoric dwarfism (TD) literally meaning death seeking dwarf is the most common form of lethal bone dysplasia and is characterized by severe micromelia and other malformations.

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Received for publication: December 12, 1993; Accepted: May 2, 1994

TD has an estimated prevalence of 0.28 to 0.60 per 1000 births(l). In Indian literature, a few isolated cases are described(2). In this report we describe five cases of thanatophoric dwarfism picked up during a period of 2 years. Four cases were out of 13,244 births (live births + still born) in 3 hospitals attached to medical college, Davangere (3 per 10,000 births) and the other case was delivered outside but was brought to our hospital in gasping state and later died. In one case an antenatal diagnosis was made. The rarity of the disorder and the information regarding the prevalence during our period of study, prompted us to report these cases.

Case Reports

Case I: A 24-year-old, healthy, non-consanguineously married woman with history of one previous abortion was brought to the hospital at 22 weeks of gestation for antenatal evaluation. The pregnancy was reported uneventful. Ultrasound examination showed a single live fetus, and amniotic fluid was adequate. Biparietal diameter of the fetus was corresponding to 22 weeks of

gestation. Femur, humerus and other long bones were very short with femoral length corresponding to 14-15 weeks. The thoracic cavity was small and irregular. With these findings, thanatophoric dwarfism was considered. A second ultrasound scan performed 2 weeks later confirmed the previous findings and a diagnosis of thanatophoric dwarf was made. A medical termination of pregnancy was performed at 25 weeks of gestation.

On examination, the fetus was weighing 700 grams and was small in length. There was macrocephaly, frontal bossing, depressed nasal bridge, chest was funnel shaped and face appeared small. Both the upper and lower limbs were grossly shortened and brachydactyly was present.

Radiological examination showed a narrow thoracic cage, shortening of all the long bones with bending of both the femora and metaphyseal flaring. There was brachydactyly and the pelvis was small. The vertebrae were 'H' shaped with a narrow vertebrae.

The other four cases were still born. In all the cases the mothers were admitted to hospital only just before the delivery. The details of all the five cases studied are given in *Table I.*

Discussion

Thanatophoric dwarfism presents with extreme shortness of limbs, bowing of long bones of the extremities, short thorax, protruded abdomen and excessive subcutaneous fat and skin creases. The skull is disproportionately large compared to facial dimensions with frontal bossing, enlarged fontanelle, depressed nasal bridge and prominent eyes. Hydramnios is frequent. Characteristic radiologic findings include excessive shortening of the long bones, telephone receiver shape of femur, disproportionate thorax with short ribs and pelvis malformed, with flat spiculated acetabulum(2).

At present two forms of thanatophoric dysplasia are recognized(3). TD type I is characterized by curved femora and very flat vertebral bodies and Type II by straighter femora, wider bones, flatter vertebral bodies and clover leaf skull(3,4). Some authors suggest TD with clover leaf skull as a distinct clinical entity(l). However, others argue that it represents a more severe spectrum of skull deformity that occur in TD(4). Recently, Corsello *et al.* described clover leaf skull in association with long bone abnormalities which were typical of TD type I in monozygotic twins(l), thus making it difficult to use the presence of the clover leaf skull as a differential manifestation between the two types of TD. In four of our cases the clover leaf deformity was present in association with long bone abnormalities characteristic of type I.

TD is now considered as an autosomal dominant condition with a high new mutation rate(l) but there have been a few reports of familial occurrence suggesting autosomal recessive inheritance.

The two conditions which present a difficulty in diagnosis are achondroplasia and achondrogenesis. In classical achondroplasia limbs are longer, neonatal deaths uncommon, long bones not curved and metaphyseal abnormalities less marked. In rare patients with homozygous achondroplasia, the differentiation becomes still difficult, while a family history of dwarfism makes differentiation possible. In achondrogenesis radiological features of extreme degree of deficient ossification in vertebral bodies is highly suggestive(5).

TABLE I—*Summary of Clinico Radiological Findings*

Clinical features	Case I	Case II	Case III	Case IV	Case V
	Abortion	Still born	Still born	Still born	Still born
Gestational age	25 weeks	37 weeks	36 weeks	40 weeks	32 weeks
Paternal age	30 years	36 years	28 years	35 years	30 years
Maternal age	24 years	28 years	22 years	30 years	28 years
Short stature	+	+	+	+	+
Short limbs	+	+	+	+	+
Brachydactyly	+	+	+	+	+
Macrocephaly	+	+	+	+	+
Small face	+	+	+	+	+
Depressed nasal bridge	+	+	-	+	-
Frontal bossing	+	+	-	+	-
Widening of cranial sutures	-	-	+	-	-
Funnel shaped chest	+	+	+	+	+
Anal atresia	-	-	+	-	-
Radiological findings					
Shortening of long bones	+	+	+	+	+
Clover leaf skull	-	+	+	+	+
Brachydactyly	+	+	+	+	+
Bend femur	+	+	+	+	-
Metaphyseal dysplasia	+	+	+	+	+
Widening of cranial sutures	-	-	-	-	+
Narrow thoracic cage	+	+	+	+	+
Small scapulae	-	-	-	-	+
Small pelvis	+	+	+	+	+
Platyspondyly	-	+	+	+	+
Narrow sacro sciatic notch	-	-	-	-	+
Narrow veretebral interpedicular growth		+	+	+	+ +

It is possible to recognize short limbs in fetuses beginning as early as 13 weeks of gestation, when femur length can be routinely measured(5). The sensitivity of ultrasound in this regard is high as shown by Weldneref *al.(6).*

Achondrogenesis, camptomelic dwarfism, chondrodysplasia punctata, homozygous achondroplasia, severe hypophosphatasia and severe osteogenesis imperfecta need to be differentiated from TD during prenatal sonography(5). The reported

Fig. 1. Thanatophoric dysplasia (Case II) with tetramicromelia, small face and frontal bossing.

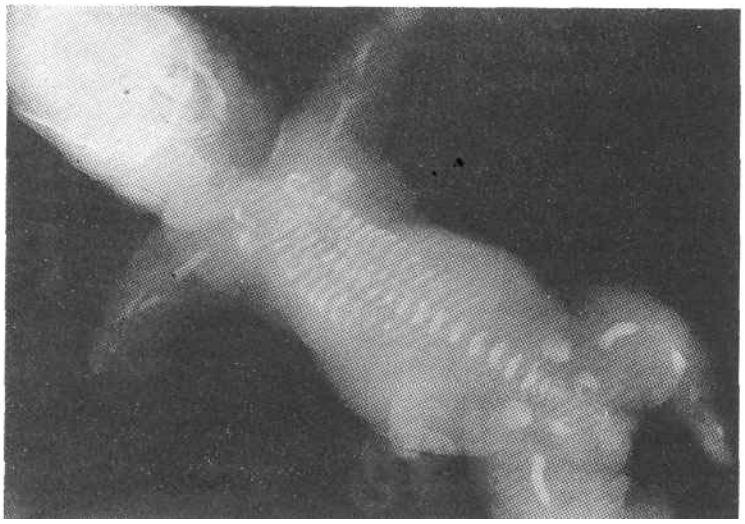

Fig. 2. Thanatophoric dysplasia (Case II) showing typical deformities of long bones.

sonographic features of TD include hydramnios, marked shortening of the major long bones, bowing of extremities, narrow thorax, protruberant abdomen, ventriculomegaly and clover leaf skull, Platyspondylosis has been difficult to diag-

Fig. 3. Thanatophoric dysplasia (Case IV) showing deep skin folds, depressed nasal bridge and bell shaped thorax.

nose sonographically(5). Although, clover leaf skull is also seen as an isolated entity, its presence with short limbs is highly suggestive of TD type 11(1,5). Recently, cephalometric analysis by ultrasound is used for prenatal diagnosis of TD(7). All long bones should be examined to determine distal versus proximal limb shortening. Osteogenesis imperfecta is suggested by fractured limbs or ribs, while achondrogenesis is characterized by fewer than three ossification centers per spinal segment(5). When lethal forms of dwarfism are suspected, fetal radiographs are recommended to provide corroborative data regarding the specific type of dwarfism.

In the present report, all except one had no antenatal check-ups and were admitted to the hospital just before delivery.

Early neonatal death in TD may be due to reduced thoracic dimensions causing pulmonary hypoplasia. Malformations, deformations and potentially significant neuroaxial injury, principally at the level of the atlas vertebrae may also contribute to the death(8,9).

Recently, many reports of patients with TD surviving the neonatal period have been documented in literature and one patient had survived 5.2 years(8). Respiratory failure is the common cause of death. Brain stem compression resulting from hydrocephalus which may develop beyond the neonatal period also contributes to ventilatory insufficiency(8,9). Surgical interventions by decompressions of brain stem in small foramen magnum has allowed prolonged survival in some of these cases(8,9).

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Ehlers-Danlos Syndrome: Variable Expression in Sibs

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Ehlers-Danlos Syndrome (EDS) is a genetically determined disorder of connective tissue. It was first described by Van Meekeran in 1682(1). The condition derives its name from reports by Edvard Ehlers, a Danish dermatologist and Henri Danlos, a French physician. Though, more than 1000 cases have been reported in world literature, current interest centres around the recognition of increasing heterogeneity in EDS(2). We report here two sibs with EDS who had different severity of manifestations.

Case Report

A ten-year-old girl born of a non-consanguinous marriage was brought to us

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Received for publication: August 3, 1993; Accepted: June 2, 1994