

## Early Antenatal Sonographic Recognition of Thanatophoric Dysplasia with Cloverleaf Skull Deformity

Patricia E. Burrows,<sup>1,2</sup> Michael W. Stannard,<sup>1,3</sup> Jerry Pearrow,<sup>1</sup> Sandy Sutterfield,<sup>1</sup> and Max L. Baker<sup>4</sup>

Sonographic measurement of fetal femur length, especially when correlated with biparietal diameter (BPD), is a reliable method in the identification of certain forms of short-limbed skeletal dysplasias [1-4]. Using this technique, we identified a fetus with thanatophoric dysplasia at 19.7 weeks gestation. Thanatophoric dysplasia is a uniformly lethal condition and when associated with polyhydramnios or fetal macrocephaly causes increased obstetric morbidity. Sonography, supported by radiography and possibly fetoscopy, can diagnose this condition early in gestation, so that termination of pregnancy may be considered.

### Case Report

A 27-year-old gravida 2, para 1 woman underwent an obstetrical sonographic examination at Arkansas Children's Hospital 19.7 weeks after her last menstrual period. The examination revealed mild polyhydramnios and a single live male fetus with short, thick extremities. We obtained the following measurements: the abdominal circumference was 14.8 cm, consistent at the 50th percentile with a gestational age of 19.6 weeks; BPD measured 46 mm, consistent with 20.4 weeks gestation. Femur, humerus, tibia, and radius measured 22, 24, 21, and 17 mm, respectively, all except the humerus being below the 95th percentile reported by Jeanty et al. [5, 6]. The correlation between BPD and femur length fell well below the 99% confidence limits reported by Filly et al. [1], as well as those determined in our laboratory. At this initial examination we could also see that the fetus had a relatively small thorax, and that the long bones of the extremities were thick and abnormally shaped. The number of digits was normal.

Abdominal radiographs of the mother to confirm the diagnosis of severe, short-limbed bony dysplasia demonstrated the short extremities, short ribs, small iliac bones, curved proximal femurs, and small vertebral ossification centers characteristic of thanatophoric dysplasia.

The mother elected to carry her pregnancy to term and allowed us to examine the fetus sonographically every 3 weeks. The growth curves of the fetal long bones showed abnormally slow growth and plateaued after 22 weeks gestation (fig. 1). The abnormal shape of the long bones also became more pronounced with advancing ges-

tational age. In particular, the tibias became more curved with a sigmoid configuration. Fetal activity diminished progressively. The asymmetry between the size of the thorax and the abdomen became more obvious with growth. At 25.6 weeks gestation the circumference of the chest at the level of the heart was 16.8 cm, compared with the abdominal circumference of 21.3 cm. The abdominal circumference was appropriate for the gestational age (at the 50th percentile) on each examination. Very slight lateral bowing of the middle cranial fossa was present on the initial examination at 19.7 weeks gestation. This progressed and was associated with a disproportionate increase in the BPD without dilatation of the cerebral ventricles (fig. 1). At 34.5 weeks gestation, the BPD measured 10.4 cm (greater than the 95th percentile).

The male infant was delivered at 38 weeks gestation by cesarean section. He had typical clinical features of thanatophoric dysplasia and died at 18 hr of age. Postnatal radiographs showed typical findings of thanatophoric dysplasia. A mild kleeblattschaedel, or cloverleaf skull deformity, was evident on both clinical examination and radiographs. The diagnosis of thanatophoric dysplasia was confirmed by histologic examination of tissues from vertebrae and femur at the Division of Medical Genetics, Harbor-UCLA Medical Center.

### Discussion

Different forms of skeletal dysplasias appear to have different extremity growth patterns [2, 3]. In general, affected fetuses show a progressive decrease in the growth rate of the long bones throughout gestation, so that in some forms the femur length is normal early in the second trimester and then falls below the normal range later in gestation [1]. Dysplasias diagnosed before 22 weeks gestation include achondrogenesis [3], chondroectodermal dysplasia [2, 4], diastrophic dysplasia [1, 2], and unclassified forms of severe dwarfism [2]. Filly and Golbus [3] reported that thanatophoric dysplasia can be diagnosed before 22 weeks gestation, but to our knowledge this has not yet been demonstrated in the literature. Other dysplasias diagnosed later in the second trimester include heterozygous achondroplasia [1], camptomelic dysplasia [2], and Robert syndrome [2].

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<sup>1</sup> Department of Radiology, Arkansas Children's Hospital, Little Rock, AR 72202.

<sup>2</sup> Present address: Department of Radiology, Hospital for Sick Children, 555 University Ave., Toronto, Ontario, Canada M5G 1X8. Address reprint requests to P. E. Burrows.

<sup>3</sup> Present address: Department of Radiology, Midland General Hospital, Midland, TX 79701.

<sup>4</sup> Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR 72205.

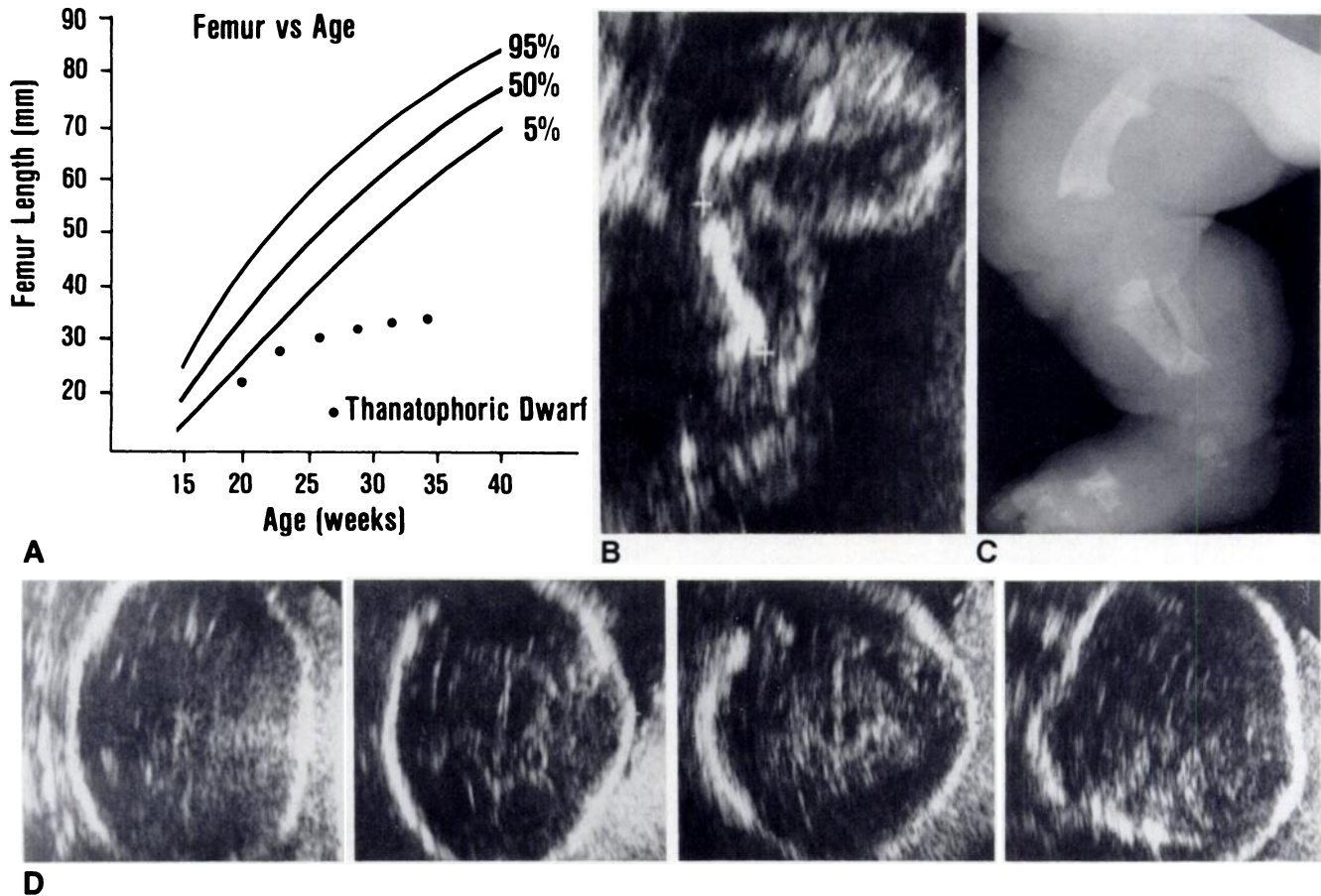


Fig. 1.—A, Femur length measurements from 19.7 to 34.5 weeks gestation in fetus with thanatophoric dysplasia show grossly abnormal growth pattern. (Values for normal fetuses are from [5, 6].) B, Sagittal sonogram of leg at 22.6 weeks showing abnormally short, thick bones and soft tissues. C, Lateral

radiograph shows thick, soft tissues and short, thick, curved bones. D, Axial sonograms of head at 19.7, 25.6, and 34.5 weeks gestation and coronal image at 34.5 weeks (left to right) show progressive lateral bulging of middle cranial fossa (cloverleaf deformity).

Thanatophoric dysplasia should be included in the differential diagnosis of short-limbed dwarfism identifiable by abnormal femur length before 22 weeks gestation. This lethal form of short-limbed dwarfism is usually sporadic [7]. Radiologic findings are characteristic and include normal trunk length with small, flat vertebral ossification centers and lack of normal progression of lumbar interpediculate distance; extremely short ribs; small, short iliac bones; marked shortening of the tubular bones of the extremities; and a distinctive bowing of the proximal femora [8]. Some of the characteristic features of this disease that can be demonstrated sonographically include the relatively narrow thorax; the thickened soft tissues of the extremities; the short, thick, curved tubular bones, especially in the lower extremities; and, in our fetus, cloverleaf skull deformity. Although the femur length was slightly below the 95th percentile for gestational age at 19.7 weeks, the abnormal length was much more obvious when plotted against BPD. We could not document sonographically lack of progression of the interpediculate distance in the

lumbar spine nor the flattening of the vertebral ossification centers. Polyhydramnios is frequently associated with thanatophoric dysplasia [9].

Infants with thanatophoric dysplasia are usually described as having distended abdomens. The measurements we obtained demonstrate that the prominence of the abdomen is only relative compared with the small thorax, as the measurement of abdominal circumference was appropriate for the gestational age by menstrual history throughout pregnancy.

The association of kleeblattschaedel, or cloverleaf skull deformity, with thanatophoric dysplasia and other chondrodysplasias is well known [10]. This deformity consists of a trilobed skull with prominence of the vertex and both temporal regions. Many of the affected infants have hydrocephalus, which was absent in our fetus. A more severe cloverleaf skull deformity could complicate the interpretation of BPD-femur correlation. In these cases, the abdominal circumference could be used to predict the gestational age.

Fetal long-bone measurements, therefore, together with

characteristic morphologic abnormalities, allow identification of thanatophoric dysplasia in utero when termination may be considered.

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