Prenatal Sonographic Evaluation of Short-limbed Dwarfism: An Algorithmic Approach

Beverly A. Spir, MD
Michael Oliphant, MD
Ronald H. Gottlieb, MD
Lawrence P. Gordon, MD

Prenatal sonographic evaluation of short-limbed dwarfism is initiated when a significantly shortened femur is found or by referral of a patient with a family history of skeletal dysplasia. If a short femur is demonstrated, all the long bones are measured and evaluated for bowing, fractures, and mineralization. The bone dysplasia is categorized according to whether it is mesomelic, rhizomelic, or micromelic and whether bowing or fractures are present. The fetal spine, head, thorax, hands, and feet are carefully evaluated to differentiate the type of bone dysplasia and to determine whether it is lethal. Serial examinations may be necessary. This approach will provide sufficient information to counsel the family, manage the pregnancy, and direct the postnatal evaluation.

INTRODUCTION
Skeletal dysplasias occur in approximately 0.024% of births (1). A prenatal sonographic evaluation for a short-limbed dwarf may be initiated because of the incidental finding of a shortened or bowed extremity or as a result of a referral because of a family history of skeletal dysplasia. It is essential to remember that the definitive diagnosis of bone dysplasia is made postnatally based on clinical and radiographic criteria. The purposes of prenatal detection are to counsel the family, manage the pregnancy, and direct the appropriate postnatal radiologic evaluation. We present an organized approach to the detection and evaluation of bone dysplasias in utero.

Index terms: Bones, osteochondrodysplasias, 40.151, 40.152 • Fetus, abnormalities, 856.871, 856.873 • Fetus, US studies, 856.1298 • Pregnancy, US studies, 856.1298


1 From the Departments of Radiology (B.A.S., R.H.G.) and Pathology (L.P.G.), SUNY Health Science Center, 750 E Adams St, Syracuse, NY 13210 and the Departments of Medical Imaging (M.O) and Pathology (L.P.G.), Crouse Irving Memorial Hospital, Syracuse, NY. From the 1988 RSNA annual meeting. Received January 31, 1989; revision requested April 20 and received June 30; accepted November 15. Address reprint requests to B.A.S.

2 Current address: Department of Radiology, Wilson Memorial Hospital, Johnson City, NY.

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It is especially important to identify those bone dysplasias that are lethal (listed in order of decreasing frequency (1–3)): thanatophoric dysplasia; osteogenesis imperfecta, type II; achondrogenesis, types I and II; Jeune syndrome (may be nonlethal); hypophosphatasia (congenital lethal form); chondroectodermal dysplasia (usually nonlethal); chondrodysplasia punctata, rhizomelic type; camptomelic dysplasia; short-rib polydactyly syndromes I, II, and III; and homozygous achondroplasia.

The gestational ages at which the different skeletal dysplasias are seen vary; therefore, the diagnosis of an abnormality should not be excluded if it is not visualized during a single in utero examination. Often, serial examinations are necessary (eg, for achondroplasia [4]). The classification we present is intended as a starting point and is based on the present understanding of skeletal dysplasias. Although not all the abnormalities and variants fit neatly into groups, the categories are sufficiently broad to accommodate most cases. All types are not illustrated, and some are not shown sonographically because of their rarity.

**APPROACH**

The diagnosis of short-limbed dwarfism should be suspected when the femur length is below the 95% confidence limits. To determine whether one is dealing with a generalized bone dysplasia, all long bones of the fetus must be measured and evaluated for bowing, fractures, and mineralization (Fig 1).

The sonographic evaluation of mineralization is difficult. Useful signs of decreased mineralization include an unusually prominent falx (5), absent or decreased visualization of the spine (6), decreased bone echogenicity, and nonuniform or weak acoustic shadowing (7).

The dysplasia can then be characterized according to which limb segments are most prominently involved and whether bowing is the predominant feature (Figs 2, 3). Evaluation of the other parameters listed in algorithm 1 aid in the differential diagnosis within each classification (Figs 4–6).

A complete evaluation of the fetal head, spine, thorax, hands, and feet should be performed (Fig 1). Examination of the thorax should include measurement of the cardiothoracic ratio and thoracic circumference to differentiate a cardiac from a pulmonary abnormality.

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**Figure 1.** Algorithm 1 for prenatal evaluation of short-limbed dwarfism.

**Figure 3.** Algorithm 2 for classification of short-limbed dwarfism on the basis of long-bone measurements. S = syndrome.
Figure 2. Drawings depict the skeletal characteristics of the three classifications of short-limbed dwarfism as they are seen in the leg. (a) Normal leg. (b) In mesomelic dwarfism, there is disproportionate shortening of the tibia and fibula. (c) In rhizomelic dwarfism, there is disproportionate shortening of the femur. (d, e) In micromelic dwarfism, there is disproportionate shortening of the entire leg. This classification is further subdivided into mild (d), mild and bowed, and severe (e).
Mesomelic: differential diagnosis, prognosis

- Normal C.T. ratio, thoracic circumference
- Normal spine
- Normal head
- No polydactyly

Syndromes as in Algorithm II:
NONLETHAL

*If any of these parameters are abnormal, obtain serial measurements and consider moving to another category.

Figure 4. Algorithm 3 for diagnosis of mesomelic dwarfism. C.T. = cardiothoracic.

Micromelic: differential diagnosis, prognosis

- Mild
  - Decreased thoracic circumference
  - Increased C.T. ratio
  - May have polydactyly
  - Jeune syndrome (ATD)*
  - Ellis-Van Creveld**
  - MAY BE LETHAL

- Diastrophic dwarf
  - NONLETHAL
  - (except for rare lethal form
    associated with tracheal hypoplasia)

b. Micromelic: differential diagnosis, prognosis

- Severe
  - Increased C.T. ratio
  - Decreased thoracic circumference
  - Normal mineralization, fractures
  - Thanatophoric Dwarf
  - Homozygous Achondroplasia
  - (Achondrogenesis)
  - LETHAL
  - Osteogenesis imperfecta
  - (Type II)
  - (Hypophosphatasia)
  - LETHAL
  - Polydactyly
  - Short Rib Polydactyly syndrome
  - LETHAL

- Camptomelic dwarf
  - NONLETHAL
  - LETHAL

- Osteogenesis imperfecta
  - (Type III)
  - NONLETHAL

- Abnormal cervical spine
  - Increased C.T. ratio
  - Decreased thoracic circumference

- Abnormal tibia/fibula
  - Disproportionate Scapula

Figure 5. Algorithm 4 for diagnosis of rhizomelic dwarfism. C.T. = cardiothoracic.

- Stippled epiphyses**
- Chondrodysplasia punctata.
- Rhizomelic form
  - LETHAL
- Heterozygous achondroplasia
  - NONLETHAL
  - "Has not been reported on
    in utero ultrasound"

b. Figure 6. Algorithm 5 for diagnosis of mild (a), mild and bowed (b), and severe (c) micromelic dwarfism. ATD = atrial septal defect. C.T. = cardiothoracic.

■ MESOMELIC DWARFISM

Mesomelic dwarfism (Fig 4) is characterized by a shortening of the radius and ulna or tibia and fibula (Fig 2b). This sign is one of the major characteristics of the Langer, Nievergelt, Reinhardt, Robinow, and Werner syndromes. These syndromes are all hereditary autosomal dominant conditions except for Langer syndrome, which is an autosomal recessive condition.

The mesomelic syndromes are not lethal, and the definitive diagnosis is made postnatally on the basis of clinical and radiographic criteria. Patients with Robinow syndrome may be mentally retarded; patients with the
other syndromes should have normal intelligence.

■ RHIZOMELIC DWARFISM
Rhizomelic dwarfism (Fig 5) is characterized by shortening of the humerus or femur (Fig 2c). Two conditions belong to this classification: heterozygous achondroplasia and chondrodysplasia punctata, rhizomelic type.

Heterozygous Achondroplasia.—This condition is the most common nonlethal bone dysplasia, with a prevalence of one in 26,000 births (2). The condition may be inherited (autosomal dominant pattern), or it may arise due to new mutation of genes.

On in utero sonograms of a fetus with heterozygous achondroplasia, the proximal long bones are shortened, have normal mineralization, and have no fractures. The cardiothoracic ratio is normal. Initially, the lengths of the femurs are normal, but by 27 weeks gestational age, the lengths are shorter than the usual range (<95% confidence limit) (Fig 7). Therefore, one cannot exclude the diagnosis of heterozygous achondroplasia until after the third trimester.

On neonatal radiographs, the lumbar pedicles are shortened, and the normal progressive widening of the lumbar interpediculur distance does not occur. Rhizomelic shortening of the long bones is seen. The iliac bones are flat and nonflared, with small sacrosciatic...
notches. The base of skull and foramen magnum are small, and the hands have a trident shape.

**Chondrodysplasia Punctata.**—The rhizomelic type of this lethal condition is inherited in an autosomal recessive pattern.

On neonatal radiographs, the vertebral bodies are irregular, with coronal clefts. Rhizomelic shortening, with metaphyseal splaying and stippled epiphyses, is seen in the long bones (Fig 8). Extracartilaginous stippling is seen as well.

Although, to our knowledge, antenatal diagnosis has not been reported, the findings of hypertelorism and stippled epiphyses accompanying rhizomelic bone dysplasia would be suggestive of chondrodysplasia punctata.

**MICROMELIC DWARFISM**

Micromelic dwarfism may vary in severity, the shape of the bone, and the degree of mineralization. They may be categorized as mild, mild and bowed, and severe.

- **Mild Micromelic Dwarfism**

  The algorithm for this classification is featured in Figure 6a. The differential diagnoses include Jeune syndrome, Ellis–van Creveld syndrome (or chondroectodermal dysplasia), and diastrophic dwarfism.

**Jeune Syndrome.**—This often lethal syndrome is also known as asphyxiating thoracic dysplasia. It is a hereditary autosomal recessive condition and cannot be distinguished from Ellis–van Creveld syndrome in utero. Associated renal disease may occur.

On in utero sonograms, the long bones are proportionately shortened. The thorax is small, with a decreased circumference and increased cardiothoracic ratio. Polydactyly is occasionally seen.

On neonatal radiographs, the spine is normal. The extremities are shortened, with occasional polydactyly. The pelvis has a tridentate appearance, with small, flattened ilia, and the thorax is small in both anteroposterior and transverse dimensions (Fig 9).

**Ellis–van Creveld Syndrome.**—This hereditary autosomal recessive condition is usually not lethal. About 50% of the patients with this syndrome have a cardiac anomaly (usually atrial septal defect).
Figure 9. Jeune syndrome. Neonatal radiograph shows small thorax, short limbs, and trident pelvis (arrow). Note polydactyly of left hand.

On in utero sonograms, the long bones are proportionately shortened. The thorax is small, with a decreased thoracic circumference and increased cardiothoracic ratio. Congenital heart defects (usually atrial septal defect) and polydactyly are frequently seen.

Radiographs of the neonate demonstrate a normal spine and proportionately shortened long bones with frequent polydactyly. A trident pelvis with small, flattened ilia is seen. The thorax appears small in both anteroposterior and transverse dimensions, and a cardiac anomaly is commonly present.

Ellis–van Creveld syndrome is difficult to distinguish from Jeune syndrome, since polydactyly, narrow thorax, and trident pelvis occur in both entities. Occasionally, a patient with Ellis–van Creveld syndrome will have mesomelic shortening of the long bones. However, the abnormal thorax enables the radiologist to distinguish this entity from other mesomelic syndromes.

Diastrophic Dwarfism.—Infants with this hereditary autosomal recessive condition may have a characteristic facial expression and cauliflower ears. Normal intellectual development occurs, and the condition is usually not lethal.

In utero sonography demonstrates proportionately shortened long bones, with associated hand and foot deformities (hitchhiker’s thumb, clubfeet) (Figs 10, 11). Joint contractures and abnormal spinal curvature may be seen.

Neonatal radiography reveals moderately flattened vertebral bodies. Progressive kyphoscoliosis of the cervical, thoracic, or lumbar spine occurs. The lumbar interpedicular spaces are narrow. Radiography also shows proportionate shortening of the long bones, with flattened epiphyses and widened metaphyses. The first metacarpal is hypoplastic and oval (hitchhiker’s thumb); talipes equinovarus may be present (10,11).

• Mild, Bowed Micromelic Dwarfism
The algorithm for this classification is given in Figure 6b. The differential diagnoses include camptomelic dysplasia and osteogenesis imperfecta, type III.

Camptomelic Dysplasia.—The inheritance pattern for this condition is either sporadic or autosomal recessive. The condition is usually not lethal. When deaths occur, most are due to respiratory insufficiency in the neonatal period.
Figure 10. Diastrophic dwarfism. Sonograms obtained at 37 weeks gestational age show short femurs (a) and abnormal thumb (arrowhead in b). (c) Corresponding neonatal radiograph of hand shows hitchhiker thumb and small, oval first metacarpal (arrow). Note bone dysplasia and elbow dislocation. (d) Lumbosacral lordosis (arrows) seen on sonogram is confirmed on neonatal lateral radiograph (e).
Figure 11. Diastrophic dwarfism. (a) Graph of femoral and tibial measurements (in millimeters) obtained from serial sonograms beginning at 15 weeks gestational age. Comparison of these measurements with the usual ranges indicates the presence of micromelic shortening. (b, c) Scans obtained at 27 weeks show short femur (cursors in b) and clubfoot (arrowheads in c). Arrow = tibia. Visualization of the metatarsal bones and tibia and fibula at right angles in the same coronal plane is diagnostic of clubfoot (8,9). (d) Neonatal anteroposterior radiograph shows oval first metacarpal (arrow), mildly flattened vertebral bodies, and hypoplastic cervical vertebrae. Kyphoscoliosis is not yet evident.

On in utero sonograms, femurs and tibias are bowed and fibulas are short (Fig 12). Thoracic circumference is decreased, and scapulae are hypoplastic. Cleft palate may be detected.

Neonatal radiography reveals hypoplastic vertebrae (especially in the lower cervical area) and scapulae. Tracheal narrowing may be present. Femurs are bowed. Tibias are bowed anteriorly, with an associated soft-tissue dimple. Fibulas are short.
Figure 12. Camptomelic dysplasia. (a, b) Sonograms obtained at 34 weeks gestational age show bowed femur (arrows in a) and short fibula (arrowhead in b). (c–e) Neonatal radiographs show angulation of distal tibias, hypoplastic scapulas (arrowheads in c), and marked cervical lordosis. Note tracheal narrowing (arrow in d). (f) Pretibial dimple (arrow) is a classic clinical finding (cf arrow in e). (Figure 12a and 12b courtesy of Gerald Segal, MD, Utica, NY.) (Reprinted, with permission, from reference 12.)
Osteogenesis Imperfecta, Type III.—This nonlethal, progressively deforming disorder has a heterogeneous inheritance pattern (ie, it can be autosomal dominant, autosomal recessive, or sporadic).

On in utero sonograms, the long bones are short and bowed (Fig 13), with fractures. However, the humeri may be almost normal in shape (13). Acoustic shadowing is present. Thoracic size is within normal limits.

On neonatal radiographs, the vertebrae and pelvis are normal. Long bones are short, bowed, and fractured. However, fractures usually heal well, in the shape of the bone. Humeri are usually less involved (13,14). Rib fractures may be present.

Infants with type III osteogenesis imperfecta have normal sclerae. Joint hyperlaxity is present in 50% of children with this disorder (13). Progressive deformities of the limbs occur during childhood. The spine be-

Figure 13. Osteogenesis imperfecta, type III, progressive deforming type. (a, b) Sector scans obtained at 27 weeks gestational age show short, thick, bowed left femur (arrow in a) and left tibia (arrowhead in b). Open arrow in b = foot. (c) Scan taken at 32 weeks shows short, bowed right femur (arrows) and bowed tibia (arrowheads). Open arrow = foot. (d) Neonatal radiograph reveals the same findings in the lower extremities. The mother was similarly affected. (Reprinted, with permission, from reference 12.)
comes progressively abnormal during late childhood or adolescence.

There are four major types of osteogenesis imperfecta (13). Types I and IV are autosomal dominant types: Type I is characterized by blue sclerae, and type IV by normal sclerae. Both are considered to be "tarda" forms, being found after birth. (In type I cases with fractures at birth, the fractures are considered to have occurred during delivery [13].) Normal findings at in utero sonography do not mean that the diagnoses of types I and IV, or milder forms of type III, osteogenesis imperfecta should be excluded.

**Severe Micromelic Dwarfism**
The algorithm for this classification is presented in Figure 6c. The differential diagnoses include thanatophoric dysplasia; heterozygous achondroplasia; osteogenesis imperfecta, type II; achondrogenesis; hypophosphatasia, congenital lethal form; and short-rib polydactyly syndromes.

*Thanatophoric Dysplasia.—*This lethal condition is the most common bone dysplasia, with a prevalence of one in 6,400 (2) to one in 16,700 (1) births. The inheritance pattern is sporadic.

Distinguishing features on in utero sonograms include polyhydramnios (71% of cases), narrow thorax, macrocrania (including hydrocephalus), and cloverleaf skull deformity (Figs 14–16). Femurs may be bowed. Major neonatal radiographic findings include marked platyspondyly; short, broad, bowed long bones; small pelvis; narrow thorax; macrocrania; and cloverleaf skull deformity.

*Homozygous Achondroplasia.—*This rare entity resembles thanatophoric dysplasia. It is hereditary, with an autosomal dominant pattern, and lethal.

*Osteogenesis Imperfecta, Type II (Perinatal Lethal Form).—*This condition has either an autosomal recessive or sporadic inheritance pattern (15).

In utero sonograms demonstrate fractured long bones and ribs, with minimal acoustic shadowing from bones. Neonatal radiographs reveal platyspondyly, spinal osteopenia, and a poorly mineralized skull (Figs 17–19). The long bones have short thick shafts, generalized osteopenia, and multiple fractures.

Babies with type II osteogenesis imperfecta have blue sclerae. Demise is usually due to pulmonary hypoplasia.

*Achondrogenesis.—*This autosomal recessive condition may be subclassified into two types. Both types are lethal. The radiologic findings of type 1 include poorly or nonossified spine and calvaria; flared, fractured ribs; poorly ossified pelvis; absent sacrum; and absent pubis. In type 2, there is variable ossification of the spine and skull, no rib fractures, ossified iliac bones, and deficient sacrum and pubis (Figs 20, 21).

*Hypophosphatasia (Congenital Lethal Form).—*Fetuses with this hereditary autosomal recessive condition have short, poorly mineralized extremities; short, poorly ossified ribs; and poorly mineralized calvaria and spine on sonograms (Figs 22, 23).

On neonatal radiographs, the vertebrae are poorly ossified, especially the neural arches. No ossification of whole long bones is present; irregular metaphyseal defects are seen. Pelvic bones are small. Major portions of the calvaria, base of the skull, and facial bones are not ossified.

*Short-Rib Polydactyly Syndromes.—*Fetuses with this lethal, hereditary autosomal recessive condition have a narrow thorax, short ribs, and polydactyly on sonograms. Major neonatal radiographic findings include short, horizontally oriented ribs and polydactyly.
Figure 14. Thanatophoric dysplasia. (a) Sonogram obtained at 26 weeks gestational age shows short femur (arrow). (b) Another scan shows narrow thorax (black arrows), macrocrania, and hydrocephalus (white arrow). Photograph (c) and radiograph (d) of neonate show large head, narrow thorax, and severe micromelia. (Reprinted, with permission, from reference 12.)
Figure 15. Thanatophoric dysplasia. (a) Fetal sonogram obtained at term shows short, non-bowed femur. (b–e) Other scans reveal abnormal, lobular configuration of the calvaria (arrows in b–d), consistent with cloverleaf skull deformity. This is distinguished from encephalocele by the presence of calvaria around the entire brain. A large monoventricle (V) with a partial interhemispheric fissure (curved arrow in e) is seen, consistent with semilobar holoprosencephaly.
Figure 16. Findings on neonatal radiographs of the fetus in Figure 15 confirm diagnosis of thanatophoric dysplasia with cloverleaf skull (kleeblattschädel) deformity.

Figure 17. Osteogenesis imperfecta, type II. (a) Sonogram obtained at 18 weeks gestational age shows short, angulated femur (cursors). Acoustic shadow is absent. (b) Cross-sectional scan of the thorax shows fractured rib (arrows). S = vertebral body. (c) Another scan shows unusually bright falx (curved arrow) because of demineralization of skull (S).
Figure 18. Anteroposterior (a) and lateral (b) radiographs of same 18-week-old fetus as in Figure 17 show short, fractured, demineralized long bones and ribs, consistent with osteogenesis imperfecta, type II. Note demineralization of skull.
Figure 19. Osteogenesis imperfecta, type II. (a) Sonogram obtained at 35 weeks gestational age shows short, angulated humerus (cursors) with poor acoustic shadow. (b) Cross-sectional view of thorax shows abnormally increased cardiothoracic ratio (see cursors). The thoracic circumference was decreased. (c) Scan of the fetal head taken at 30 weeks shows bright falx (arrow), a finding indicating poor mineralization of skull. (d) Findings on neonatal radiograph confirm the diagnosis.
Figure 20. Achondrogenesis, type II. (a, b) Sonograms obtained at 33 weeks gestational age show very short femur with poor acoustic shadow ( cursors in a) and poorly visualized spine (arrowheads in b), a finding indicating poor mineralization. Arrow in b = nuchal cystic hygroma, H = fetal head. Note lack of acoustic shadows from spine. Compare b with c, a sonogram of a normal fetal spine at 25 weeks gestational age.

Figure 21. Neonatal photograph (a) and radiograph (b) of fetus in Figure 20 show severe micromelia. Spine is poorly mineralized, and sacrum and pubis are absent. Arrow = femur.
Figure 22. Hypophosphatasia, congenital lethal form. (a) Sonogram taken at 22 weeks gestational age shows short, bowed femurs (arrows). (b) Scan taken at 29 weeks shows short, thin, bowed tibia and fibula. Arrows = foot. (c) On sonogram obtained at 22 weeks, the falx (arrow) is more prominent than the calvaria, a finding indicating a poorly mineralized skull. (Courtesy of Richard Gerle, MD, Syracuse, NY; reprinted, with permission, from reference 12.)

Figure 23. Neonatal radiographs of fetus in Figure 22 show minimally ossified calvaria; thin, short, poorly ossified long bones; and ribs with widened, irregular ends. (Reprinted, with permission, from reference 12.)
SUMMARY
Evaluation of bone dysplasia is initiated by the finding of a significantly shortened femur or a referral of a pregnancy at risk. If a short femur (length less than the 95% confidence limit) is demonstrated, all long bones should be measured and evaluated for bowing, fractures, and mineralization. In the case of suspected heterozygous achondroplasia, serial measurements should be obtained up to at least 27 weeks gestational age.

If a bone dysplasia is present, it should be classified as mesomelic, rhizomelic, micromelic (mild or severe), and bowed and/or fractured. The fetal spine, head, thorax, hands, and feet should be evaluated to aid in the differential diagnosis.

It is important to determine whether the fetus has a lethal or possibly lethal form of short-limbed dwarfism. Although the final diagnosis cannot be made until after birth, the above evaluation will provide sufficient information to counsel the family during the pregnancy and to direct the postnatal evaluation for definitive diagnosis.

REFERENCES