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A guide to the recognition of skeletal disorders in the fetus

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Abstract The discovery of fetal skeletal abnormality on prenatal US mandates an extended study of the fetus. This extended examination includes specific views and measurements of the fetal skeleton. Lethality can be predicted if severe pulmonary hypoplasia is present. Specific diagnosis of a fetal osteochondrodysplasia is difficult; a collaborative approach among obstetric, neonatal and genetic services is necessary to provide the parents with all available information regarding the pregnancy. Pediatric radiologists who have experience in radiologic assessment of osteochondrodysplasias of infants and children can provide expertise in this area.

Keywords Fetus · Skeletal anomalies · Skeletal dysplasia · US · Radiography

Introduction

Pediatric radiologists have the training and experience to bridge the border between prenatal and postnatal imaging. They can be a link among obstetricians, pediatricians and pediatric surgeons, and provide guidance for further imaging when a fetal anomaly is detected [1]. Because of their knowledge of the radiographic evaluation of osteochondrodysplasias in infants and children, pediatric radiologists can act as a resource in those rare situations where the fetus is found to have abnormal bones on US. This guide to the evaluation of the fetal skeleton reinforces reviews published in *Pediatric Radiology* by Lachman in 1994 [2] and Avni et al., in 1996 [3]. It is updated from a presentation given at the Postgraduate Course of ESPR in Dublin, 2005.

What is osteochondrodysplasia?

From a radiologic perspective, osteochondrodysplasia (or the more familiar but looser term, skeletal dysplasia), refers to one or more of the following: abnormal length of bones; abnormal shape of bones; abnormal number of bones; and abnormal density of bones. From a geneticist's viewpoint, each osteochondrodysplasia is the result of an abnormal cellular product or process, which in turn results from a defective chromosome. In the most recent classification, disorders of the skeleton have been divided into seven groups based on their known molecular-pathogenetic etiologies (Table 1) [4].

The disease that we know as osteogenesis imperfecta is a good example of a defect in an extracellular structural protein, specifically collagen. Although we think of collagen as a single entity, it is a family of 19 or more different molecules [5]. Furthermore, each collagen molecule is a triple-stranded helical structure—a rope formed by tightly twisted alpha chains, of which 25 have been identified. Each alpha chain is encoded by a separate gene. Collagen is secreted into the extracellular matrix, typically by a fibroblast, where it makes up 25% of our total mass of protein [6]. A defect in the genes encoding the alpha 1 and alpha 2 chains of type 1 collagen (the most common and distributed in skin and bone) causes the clinical phenotypes of osteogenesis imperfecta [7].

When there is a defect in the gene that sends out instructions for manufacture of fibroblast growth factor receptor 3 (FGFR3), the result might be one of several dysplasias, including thanatophoric dysplasia, achondroplasia, and some of the craniosynostoses [4]. There is not a direct, tidy correlation between genetic defect and clinical phenotype in all cases, indicating that other moderating factors are involved. As more research has been done on skeletal dysplasias, more overlap has resulted. For example, there is a radiographic division between type I and type II thanatophoric dysplasia, where clover leaf skull is the major differentiating feature. However, in a report from Zurich, the same mutation in the FGFR3 gene was iden-

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Table 1 Genetic disorders of the skeleton

Defects in extracellular structural proteins
Defects in metabolic pathways
Defects in folding and degradation of macromolecules
Defects in hormones and signal transduction mechanisms
Defects in nuclear proteins and transcription factors
Defects in oncogenes and tumor suppressor genes
Defects in RNA and DNA processing and metabolism

See Reference 4 for more details, including clinical phenotypes

tified in two patients, one with type I and the other with type II thanatophoric dysplasia [8].

There are approximately 200 disorders of skeletal growth and development [4]. Their names have been derived from their appearance, e.g. osteogenesis imperfecta (Latin) and diastrophic dysplasia (Greek), from the presumed etiologic flaw, e.g. achondroplasia, or from the authorship of early publications, e.g. Rubenstein Taybi syndrome. Not all dysplasias are associated with short bones, and use of the term “dwarfism” is disappearing from medical literature. “Thanatophoric dysplasia”, which has replaced “thanatophoric dwarfism”, is a case in point. The mixed nomenclature and classification has been confusing and in some cases misleading. With the ongoing discoveries in cell biology, a review of osteochondrodysplasias was initiated in 2001. This resulted in publication of “The International Nomenclature of Constitutional Disorders of Bone” [9, 10].

Prenatal diagnosis

There are four salient points regarding prenatal diagnosis of skeletal disorders:

- 1) The prenatal recognition of skeletal abnormality is almost always achieved with US alone. If used at all, radiography and MRI have ancillary roles. The role of MRI might expand in the future. The gestational age of the fetus, the size of the mother in terms of adequacy of scans, the fetal lie, equipment used, and experience and expertise on the part of the examiner are all variables in obstetric US. An ultrasonographer working full-time for 50 weeks every year and doing only obstetric scanning of pregnant patients at 18–20 weeks’ gestation in a community practice might encounter one fetus affected by a skeletal dysplasia in two years. In fact, an ultrasonographer would probably miss diagnosing the most common of skeletal dysplasias, achondroplasia, because the short bones of achondroplasia typically become obvious in mid- or late second trimester—after routine scanning is performed. Overall prevalence of skeletal dysplasias was calculated to be 2.4/10,000 deliveries in one large study [11], but the incidence varies with the population.
- 2) Skeletal dysplasias can be classified as lethal or non-lethal (Table 2). Lethality is caused by pulmonary

Table 2 Criteria used to diagnose lethal skeletal dysplasia

Early, severe, micromelia
Femur length: abdominal circumference <0.16
Thoracic circumference <5th percentile
Thoracic circumference: abdominal circumference <0.79
Cardiac circumference: thoracic circumference >0.60

hypoplasia from an abnormally formed, therefore restrictive, thorax [12–16]. Severe micromelia refers to long bones that are four or more standard deviations below the mean for gestational age. This finding is characteristic of thanatophoric dysplasia, achondrogenesis, and osteogenesis imperfecta type II, all of which are lethal. The discovery of a lethal skeletal dysplasia might result in the family electing to terminate the pregnancy. In other cases where the dysplasia might not be lethal by virtue of pulmonary hypoplasia but would lead to suffering and poor quality of life for the child, the family might also elect to terminate the pregnancy. Therefore, depending on the society in which one practices, the number of living children affected by skeletal dysplasia might vary [11].

- 3) Differential diagnoses of skeletal dysplasias that are encountered in prenatal imaging only roughly match those seen in pediatric practice. For example, neurofibromatosis, multiple exostoses, and Marfan syndrome are diagnosed after the neonatal period. Prenatal diagnosis is skewed toward syndromes that present on US with obvious shortening or malformation of bone, in particular the femur, which is imaged on every scan as part of biometric assessment.
- 4) Consultation of radiologist/ultrasonologist with geneticist, neonatologist and pathologist is crucial in arriving at a diagnosis or, in some cases, a list of possible diagnoses for an affected patient. When the patient is a fetus, discussion can occur at a fetal medicine panel after consultants review the clinical details of the pregnancy and the images of an abnormal fetus. Only 48–65% of specific diagnoses are correct; however, the identification of a lethal dysplasia is highly accurate [13, 14]. If a pregnancy is terminated or if a fetus or neonate dies, formal review of the case must occur with presentation of postmortem clinical evaluation, postmortem imaging, and pathologic examination when available. The family gets the best medical care and appropriate genetic counseling when such processes are in place. Through such a review, the consulting services involved in diagnosis and treatment add to their base of knowledge. High-resolution postmortem radiographs, such as those available with Faxitron (General Science X-ray, Wheeling, Ill.), or mammographic film are ideal. Anteroposterior and lateral views of the fetus are the minimum required. Published normal standards are available for comparison [17]. When pathologic examination is declined by the family, postmortem US is useful for evaluation of intraabdominal and intracranial contents; in relevant situations it might add information regarding morphology of cartilage columns in the

epiphyses. Postmortem MRI is best suited to the evaluation of craniospinal neuroanatomy [18], but as experience in the technique increases it might play a greater role, particularly in the evaluation of cartilage [19].

How is an antenatal diagnosis made?

If there are family members who have a known osteochondrodysplasia and if the parents are willing to pursue investigation, a fetus can be scanned with US early and often in the pregnancy. It is worth re-emphasizing that many dysplasias do not become apparent in the fetus until the third trimester, after birth, or well into childhood [10]. Therefore, genetic testing via chorionic villous sampling or amniocentesis can be done if requested and if available for the particular dysplasia. There must be coordination between the genetics and scanning departments in this regard.

Most diagnoses of skeletal anomaly are made in the absence of any family history. Of prenatally diagnosed dysplasias, 90% or more are the result of new spontaneous mutations or the appearance of recessive disease carried by phenotypically normal parents [12].

A fetus affected by a skeletal dysplasia might be identified by virtue of having an abnormally thick nuchal translucency on screening scans performed during a window from 11 to 14 weeks' gestational age [20]. With widespread use of such screening, early diagnosis of the severe dysplasias might increase. In such cases, it is likely that nuchal thickening reflects an abnormal extracellular matrix [21, 22].

Guidelines for assessment of a fetus with possible skeletal dysplasia

Standard measurements acquired at screening obstetric US include biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femoral length (FL). Comparison of these values with standardized measurements based on known gestational age (from last menstrual period or first trimester scan), allows assessment of normal versus abnormal biometry. The discovery of short or malformed femurs or other bones mandates completion of the routine US examination of the fetus and the addition of measurements that are not standard. This extended examination of the fetal skeleton follows completion of the routine scan, which includes evaluation of brain, heart and abdominal contents according to specific guidelines. Assessment of fetal gender is not routine but should be included when a skeletal abnormality is detected. This can be very useful information in certain situations, e.g. gender reversal of males, present in camptomelic dysplasia [22]. Both the American Institute of Ultrasound in Medicine [23] and the Australian Society of Ultrasound in Medicine have guidelines listed on their websites [24].

When an extended examination is necessary, the parent(s) should be told that the examination will be longer than

Table 3 Fetal skeletal survey

Sagittal and coronal views of long bones; measurements
Transverse view and measurement of clavicles
Sagittal view and measurement of scapulae
Length and shape of ribs
Thoracic/abdominal circumference (TC/AC)
Axial and sagittal view of the feet; length of foot
Number of digits
Sagittal, transverse, coronal views of spine
Facial profile, coronal view of orbits
Shape, sutures, softness of skull

usual and alerted to the fact that measurements of many bones will be performed. It is the duty of the examiner to explain the need for further information in as calm and gentle a manner as possible. Careful, compulsive examination, identification, and measurement of bones must follow. An interim discussion with the parents after scanning is complete can be followed by a more detailed conversation with the family after there has been consultation with perinatal specialists. Additional views required for an extended skeletal examination are listed in Table 3 and discussed below.

Length of all long bones: femur, humerus, ulna, radius, tibia and fibula

The diaphysis is measured in its long axis with care to avoid obliquity, which would cause apparent decrease in length. The epiphysis, whether cartilaginous or ossified, is excluded. Both femurs should be measured. A single short femur is more likely to be focal femoral dysplasia or an isolated anomaly rather than part of a generalized skeletal dysplasia. Femur length should equal foot length in the normal fetus [25] (Fig. 1). Tibia and fibula have to be differentiated based on their position relative to the knee. The ulna extends more proximally than does the radius; distal ulna and radius should end at the same level. Radial ray anomalies might be syndromic but might be part of the VACTERL association [26]. Standards for lengths of long bones are available in textbooks, from manufacturers of US equipment by inclusion as software, and on the Internet. The values from different authors differ slightly; it is reasonable to pick one standard and use it in all cases while remembering that individuals of some ethnic groups are typically short. Reports should document the standards used. The site of shortening helps narrow the differential diagnosis; categories include micromelia (entire limb), rhizomelia (humerus, femur), mesomelia (radius/ulna, tibia/fibula), acromelia (hands, feet).

Mineralization of long bones is very difficult to assess with US. The bones, even if consisting of poorly mineralized tissue, still act as reflective surfaces to the US beam. Detection of both cortical surfaces on a single scan indicates under-mineralization as does lack of distinct posterior shadowing (Fig. 2).

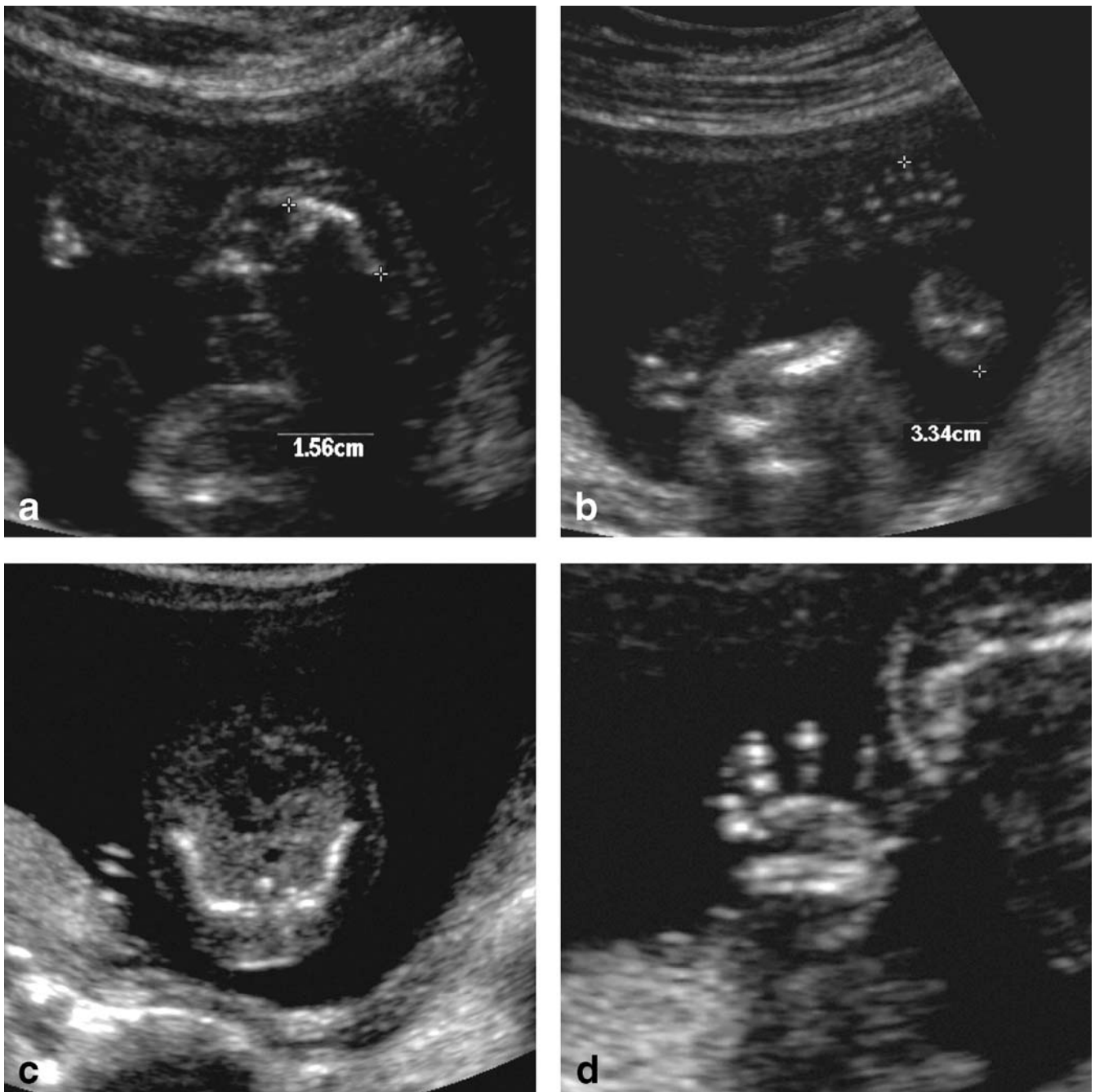


Fig. 1 Thanatophoric dysplasia. **a** The bowed femur is extremely short for gestational age of 18 weeks and measures less than the foot (**b**). **c** The ribs are short, forming only one-half the circumference of the chest. **d** The open hand shows stubby fingers. Thoracic circumference (**e**) is 0.79 of the abdominal circumference (**f**). The

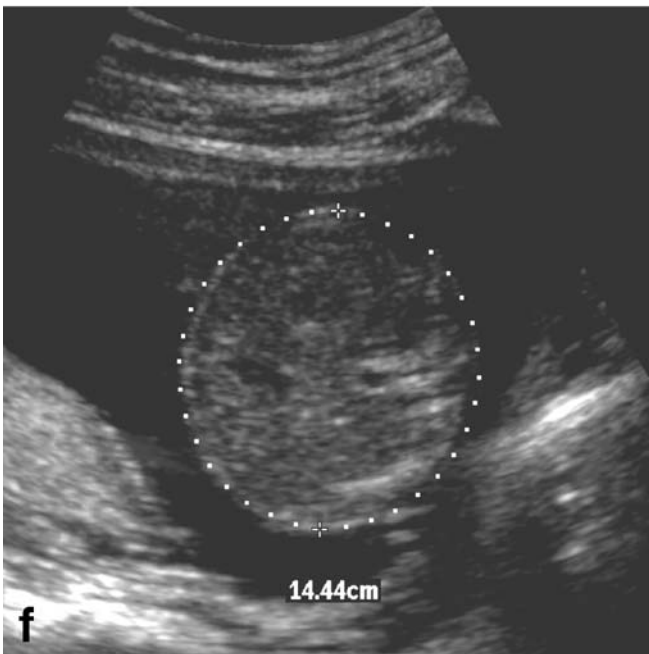
skull, not shown, was normally shaped and ossified. This combination of findings, in association with extreme shortening of other bones, is typical of thanatophoric dysplasia. Postmortem anteroposterior radiograph (**g**) demonstrates platyspondyly, short ribs, short long bones with proximal bowing, and abnormally shaped pelvis

Sagittal and coronal views of long bones

Ultrasonographers tend to forget that bones need evaluation in at least two orthogonal planes in order to characterize their shape. “Bent” bones might be fractured, e.g.

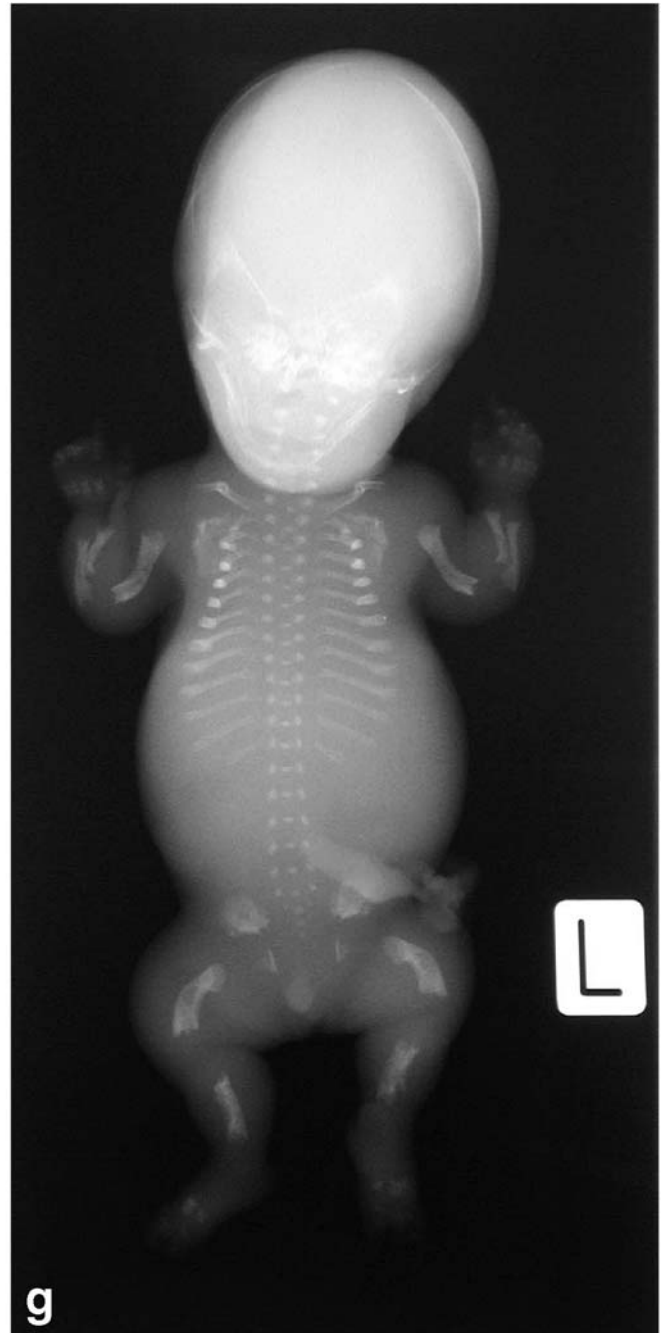
osteogenesis imperfecta, or dysplastic, e.g. campomelic (camptomelic) dysplasia. It is often difficult to accurately assess bones from the distal limbs in two orthogonal planes.

Fig. 1 (continued)



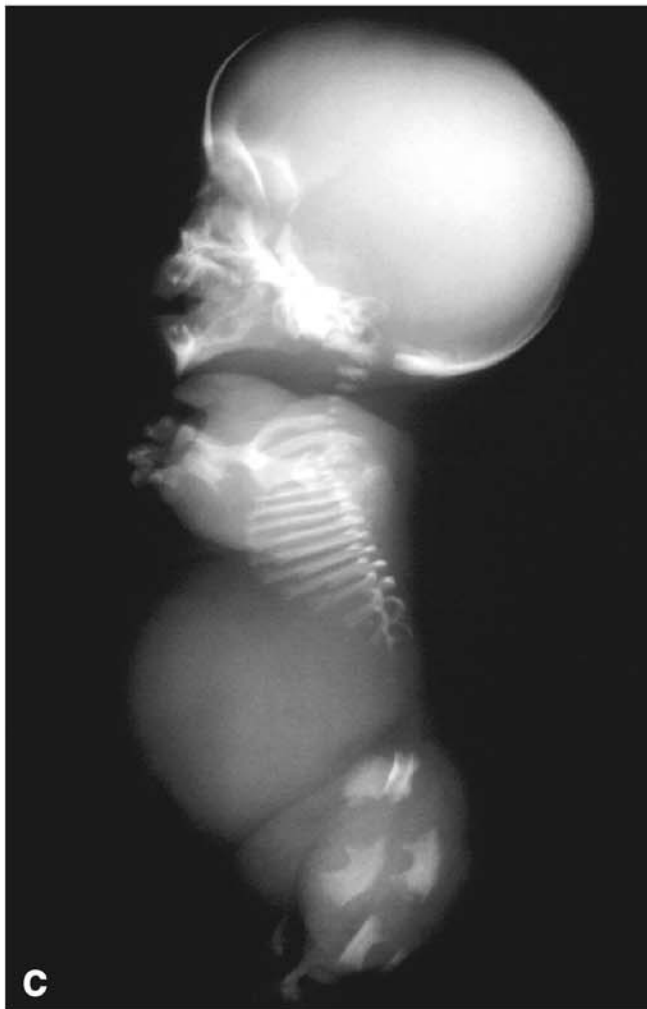
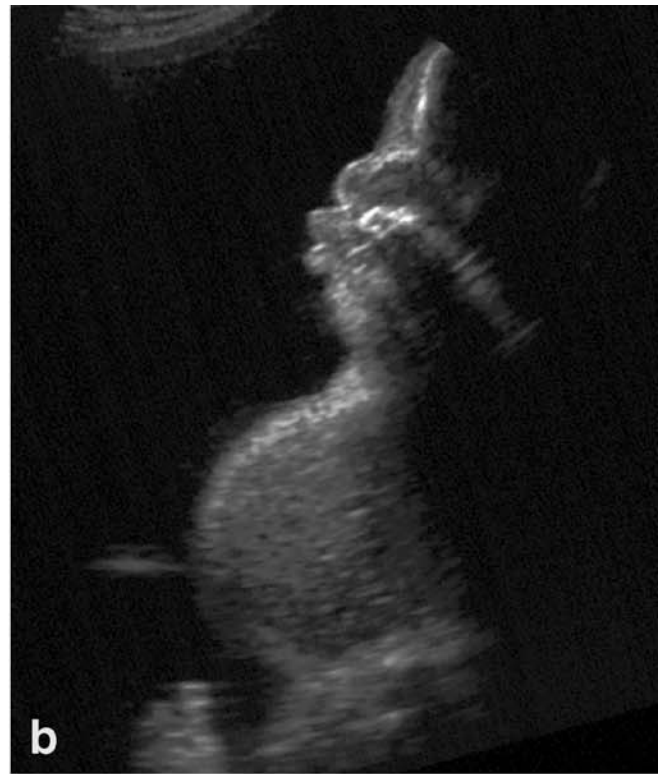
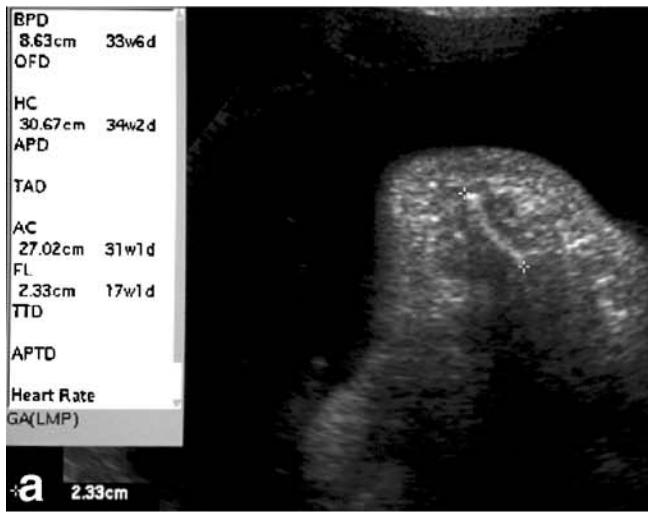
Transverse view of the clavicles with measurement of length

The clavicle is the first bone to ossify in the fetus [17] and the last to fuse its epiphysis in the adolescent or young adult [27]. Clavicular growth is normally 1 mm/week gestational age [28]. Cleidocranial dysplasia is the obvious syndrome associated with short or dysplastic clavicles.



Sagittal views and measurement of the scapulae

The scapula is hypoplastic in campomelic dysplasia [29]. It might be smaller than normal in syndromes where all bones are small for gestational age, such as hypochondrogenesis. It is high-riding with segmentation anomalies of the cervical spine (Klippel Feil/Sprengel deformity) [30].



◀ **Fig. 2** Achondrogenesis II. **a** The biometric data show the marked discrepancy between femur length and other measurements. Ossification of distal vertebral bodies is absent. **b** Midsagittal view of fetal face, chest and abdomen through polyhydramnios is oriented to match the lateral radiograph (**c**) of this fetus, who did not survive. **c, d** Note the extreme micromelia, lack of distal vertebral ossification centers and the normally ossified skull

Length and shape of ribs

The ribs should extend around two-thirds of the circumference of the thoracic cavity. Published normal standards are available [31]. Short ribs are associated with thanatophoric dysplasia (Fig. 1), Jeune thoracic dysplasia and the short rib-polydactyly syndromes, among others [32]. Ribs should be smooth in contour. Irregular, beaded ribs are associated with osteogenesis imperfecta (Fig. 3). As with long bones, the angulation and beading of ribs might be appreciated in one plane but not another.

Thoracic circumference/abdominal circumference

The measurement of thoracic circumference should be at the level of the four-chamber view of the heart and around the ribs [13, 33, 34]. The ratio of thoracic-to-abdominal circumference should be 80–100% [14] (Fig. 1). Lower values indicate the presence of pulmonary hypoplasia. There is often considerable inter- and intraobserver variation for this measurement, and several should be obtained. Midsagittal view of the fetal chest and abdomen provides a subjective impression of the degree of thoracic hypoplasia when present.

Axial and sagittal views of the feet with measurement of foot lengths

Talipes and rocker bottom foot can be diagnosed prenatally. However, scans in late pregnancy are less reliable because fetal positioning might result in pseudotalipes. In normal fetuses, the length of the foot will equal the length of the femur [25].

Number of digits of hands and feet, if possible

Persistently clenched hands are abnormal and indicate probable neurologic and/or chromosomal abnormality. Partially opened hands are adequate for counting digits, but an open hand is best. A small accessory digit might be completely missed. Also, absent first metacarpal or other subtle radial ray anomaly might be undetectable. Counting toes is much more difficult than counting fingers. Three-dimensional (3-D) US has a role here [32]. Discovery of polydactyly directs the differential diagnosis toward

trisomy 13, short rib polydactyly syndromes, chondroectodermal dysplasia and Meckel Gruber syndrome.

Sagittal, transverse, and coronal views of the spine

As with evaluation of long bones, US views of the vertebral elements are reflective only. Each vertebra should have three ossification centers obvious on US. A sagittal view of the spine provides a relative measure of bony vertebral center compared to its enveloping cartilage and adjacent disc space. Platyspondyly can be diagnosed when there is obvious widening between vertebral ossification centers. Defective ossification of vertebral bodies is typical of achondrogenesis/hypochondrogenesis [35, 36] (Fig. 2). The contour of the spine and the presence of soft-tissue abnormality/defect should be noted. Persistent tail is a feature of metatropic dysplasia [37].

Profile and coronal views of the face with 3-D view if available

Micrognathia can be assessed on direct sagittal views of the face, as can frontal bossing. Hypo/hypertelorism is established based on orbital measurements and comparison with standards. The rule of three is known by artists and helpful to sonographers: in normal facial proportions, there is space for a third eye between the other two. The geneticist and pediatric pathologist can often use information from the contours of the face to aid with diagnosis (Figs. 4 and 5), and 3-D US is particularly helpful in this regard [38]. Fetal position is key to acquiring the data needed for good 3-D reconstructions. Prone position and arms and hands over the face do not allow diagnostic images. Four-dimensional (4-D) US—3-D with the added dimension of realtime imaging—is likely to be even more revealing [39]. Aneuploidy is frequently associated with stereotypical facies.

Skull: shape, sutures, softness

By virtue of the typical position of a fetus, the skull is usually evaluated in transverse plane. A skilled sonographer can usually recognize an unusual shape. A cloverleaf skull, or kleeblatschadel, is associated with thanatophoric dysplasia type II. The frontal bossing associated with achondroplasia is best identified on sagittal view of the face and anterior skull. Clear identification of intracranial structures (particularly in the near field where reverberation usually obscures detail) is a sign of decreased ossification, typically associated with osteogenesis imperfecta or hypophosphatasia (Fig. 3). Also, gentle pressure with the examining transducer can flatten the abnormally ossified skull. Three-dimensional US has been used in assessing shape and sutural anatomy [40].

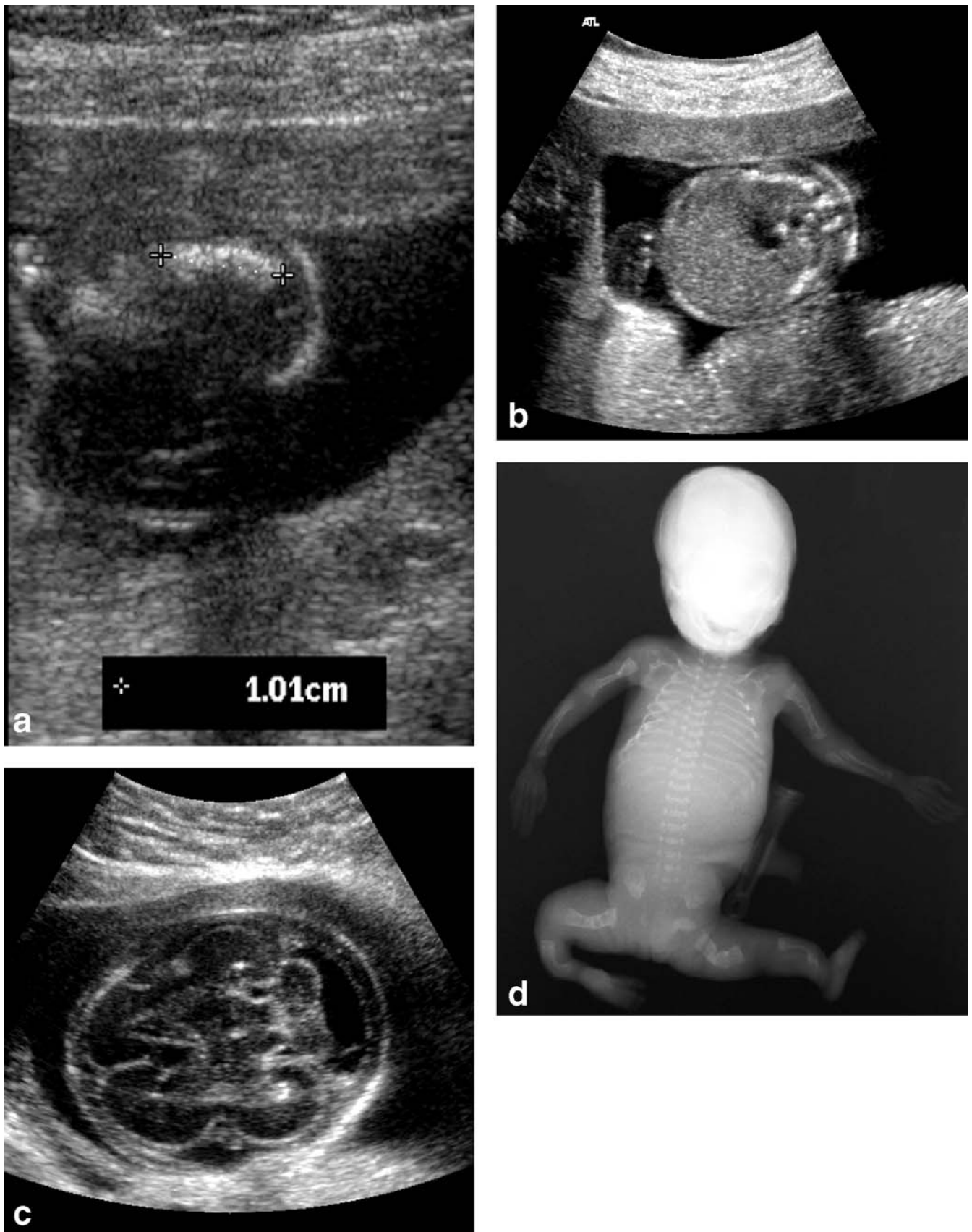


Fig. 3 Osteogenesis imperfecta type II. **a** Femoral length of 1.01 cm is half the expected femoral length of 2.2 cm for 17 weeks gestational age. **b** The lower ribs shown on this transverse view are short and irregular. **c** The detailed anatomic delineation of the brain

results from poor ossification of the membranous calvaria, which allows penetration of the US beam. **d** Postmortem anteroposterior radiograph shows abnormally mineralized, short long bones and gracile ribs. Multiple fractures are present

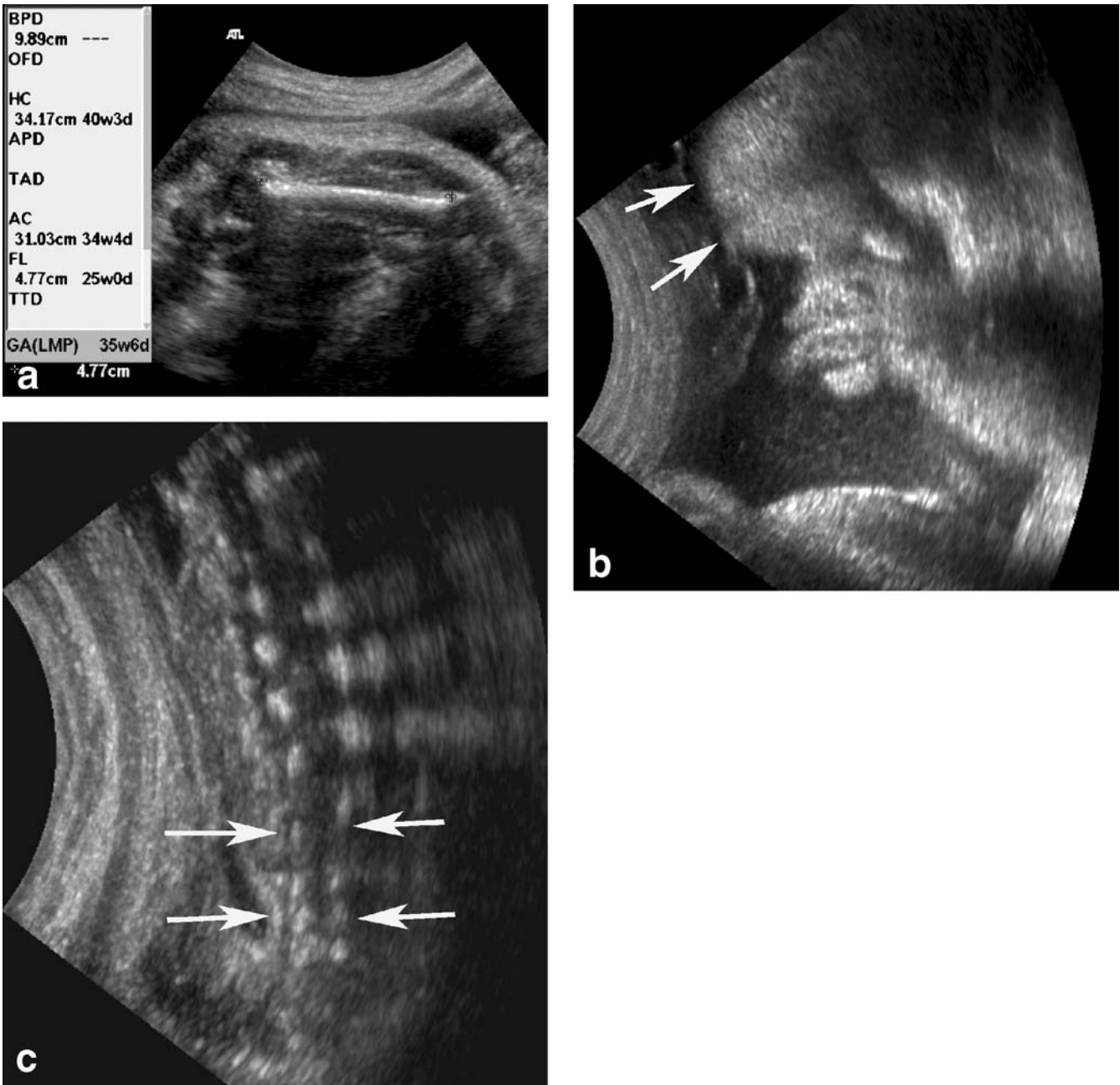


Fig. 4 Achondroplasia. **a** This late third trimester scan shows marked shortening of the femur and relatively large head circumference compared to abdominal circumference. **b** The fetal face could not be scanned in mid-sagittal plane, but this coronal view hints at frontal bossing (arrows). The scan has been oriented in

anatomic position. The left eye and cheek is partially covered by the left hand of the fetus. **c** Coronal view of the lower spine, oriented in anatomic position, demonstrates subtle narrowing of the lumbar interpediculate distances (arrows)

Caveats

Children tend to resemble their parents. A short mother and father are likely to have a short baby who is perfectly normal.

Intrauterine growth restriction (IUGR) can be severe enough that the fetal skeleton lags far behind the normal in growth and development. Short limbs and delayed ossification centers can result and mimic skeletal dysplasia in utero. Symmetric growth restriction can result from chro-

mosomal anomaly or early intrauterine infection. Asymmetric IUGR (relative sparing of head with abdominal and soft-tissue restriction of growth from poor intrauterine nutrition) usually becomes apparent in the second trimester, after 24 weeks. Sequential measurements on growth charts are useful in the diagnosis, particularly if there are early scans as a baseline. There is typically other evidence such as maternal hypertension, uterine anomaly or large fibroid(s), abnormal placental perfusion as demonstrated by abnormal Doppler examination of uterine arteries,

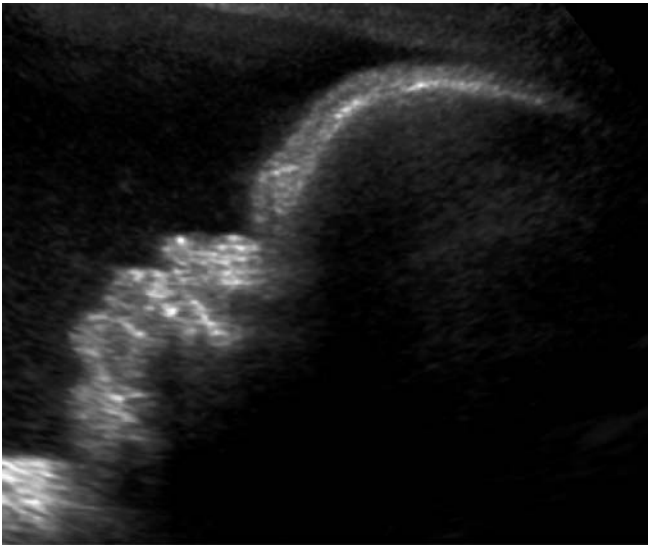


Fig. 5 Achondroplasia. This sagittal view of the anterior skull and face demonstrates the frontal bossing that is associated with achondroplasia. This fetus had femoral measurements well within the normal range at 18 weeks gestational age. On a scan performed late in the third trimester for obstetric reasons, he was identified as having short long bones

Table 4 Typical features of skeletal dysplasia

Thanatophoric dysplasia	Polyhydramnios Thickened soft tissues Micromelia Extremities at 90° to trunk Bowed femur (telephone receiver) Platyspondyly Frontal bossing, depressed nasal bridge Cloverleaf skull (type II)
Achondrogenesis	Polyhydramnios Thickened soft tissues Micromelia Absent ossification of vertebral bodies Normal calvarial ossification (type II) Small thorax, some with rib fractures (type IA)
Osteogenesis imperfecta IIA	Asymmetric micromelia Irregular/thickened bones Angulated bones Beaded ribs, small thorax Poorly ossified skull
Osteogenesis imperfecta IIB	Lower extremities more affected Less beading of ribs Poorly ossified skull
Osteogenesis imperfecta IIC	Thin bones, multiple fractures Thin beaded ribs Poorly ossified skull
Achondroplasia	Rhizomelia, mild mesomelia Stubby fingers Frontal bossing Narrowed interpediculate distance

oligohydramnios or elevated umbilical artery Doppler to indicate that the fetus is failing to thrive because of lack of nutrition. But this is not always the case, and a false-positive diagnosis of skeletal dysplasia might be assigned to the fetus [41].

Any mother who has a fetus with abnormal bones needs a review of her medical history and careful questioning of intake of medications or other substances. Teratogens associated with skeletal dysplasia are warfarin [42], glucose (uncontrolled maternal diabetes mellitus, type 1 or 2) [43], alcohol [44], phenylalanine (maternal phenylketonuria) [45], and thalidomide, which is now being used for treatment of leprosy and other illnesses [46].

Aneuploidy is frequently associated with skeletal dysplasia (Table 4). In particular, Down syndrome might present with mildly short femurs and humeri and no other discernable anomaly. Maternal age is an important factor. Punctate epiphyseal calcifications are a hallmark of the chondrodysplasia punctata syndromes but are rarely obvious until the third trimester.

Of the 200 or more osteochondrodysplasias, the four most commonly diagnosed prenatally are thanatophoric dysplasia (Fig. 1), achondrogenesis (Fig. 2), osteogenesis imperfecta type II (Fig. 3), and achondroplasia (Figs. 4 and 5) (Table 5). Of these, only achondroplasia is a nonlethal skeletal dysplasia. As noted previously, the achondroplastic fetus typically is identified on a scan that is performed in the third trimester of pregnancy. Therefore, the diagnosis results from incidental discovery in most cases. However, because achondroplasia is the result of a more frequent genetic mutation compared to other dysplasias, it is among the most commonly diagnosed.

Conclusions

The discovery of osteochondrodysplasia in a fetus during routine screening US is an unusual occurrence. A careful, complete evaluation of the skeleton of the fetus with US should follow identification of one or more short bones. Most osteochondrodysplasias that are diagnosed prenatally

Table 5 Skeletal manifestations that might accompany the common trisomies

Trisomy 13	Short long bones from intrauterine growth restriction Polydactyly/club hand/overlapping fingers Club foot/rocker bottom foot Microcephaly/hypotelorism
Trisomy 18	Short long bones from intrauterine growth restriction Clenched, overlapping fingers Limb defects, particularly radial ray Strawberry-shape skull Micrognathia
Trisomy 21	Mildly short femur Mildly short humerus “Sandal gap” toes Clinodactyly of little finger Flattened facial profile

fall into the four groups of thanatophoric dysplasia, osteogenesis imperfecta type II, achondroplasia, and achondrogenesis. Specific diagnosis may not be possible prenatally, but a lethal skeletal dysplasia can be identified with confidence.

Preliminary discussion of findings with parents should follow directly after scanning; it is wise to avoid specific diagnostic labels unless absolutely certain. Use all textbooks, journal articles and Internet resources available. Cellular biology is advancing rapidly, with the direct consequence of uncovering the causes of osteochondrodysplasias and, sometimes, changing their names.

Consultation with clinicians from other services, specifically obstetrics, neonatology, and genetics, should be scheduled. A Fetal Medicine Panel fulfills this role on a routine basis. Consideration of other imaging such as 3-D or 4-D views [47], radiography, and MRI depends on the US findings.

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<http://www.ibis-birthdefects.org>. Includes information regarding osteochondrodysostrophies and links to other sites.

<http://www.ncbi.nlm.nih.gov/Omim>. Online Mendelian Inheritance in Man: produced by Johns Hopkins and hosted by the National Library of Medicine in the USA

<http://ghr.nlm.nih.gov/>. A service of the National Library of Medicine with information on gene-related disorders

<http://www.emedicine.com/ped/topic625.htm>. A pediatric and clinical overview of skeletal dysplasias with links to other articles

<http://www.thefetus.net/index.php>. An ultrasonographic teaching file of fetal anatomy, normal and abnormal

<http://www.vh.org/pediatric/provider/pediatrics/ClinicalGenetics/Contents.html>. Provides instruction on basic genetics

<http://www.encyclopedias.families.com>. An excellent “lay” resource with information in plain English

Further readings

Textbooks and websites as resources

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