Prenatal Sonographic Diagnosis of Focal Musculoskeletal Anomalies

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Focal musculoskeletal anomalies vary, and can manifest as part of a syndrome or be accompanied by numerous other conditions such as genetic disorders, karyotype abnormalities, central nervous system anomalies and other skeletal anomalies. Isolated focal musculoskeletal anomaly does, however, also occur; its early prenatal diagnosis is important in deciding prenatal care, and also helps in counseling parents about the postnatal effects of numerous possible associated anomalies. We have encountered 50 cases involving focal musculoskeletal anomalies, including focal limb dysplasia [radial ray abnormality (n=3), mesomelic dysplasia (n=1)]; anomalies of the hand [polydactyly (n=8), syndactyly (n=3), ectrodactyly (n=1), clinodactyly (n=6), clenched hand (n=5)]; anomalies of the foot [clubfoot (n=10), rockerbottom foot (n=5), sandal gap deformity (n=1), curly toe (n=2)]; amniotic band syndrome (n=3); and anomalies of the focal spine [block vertebra (n=1), hemivertebra (n=1)]. Among these 50 cases, five [polydactyly (n=1), syndactyly (n=2) and curly toe (n=2)] were confirmed by postnatal physical evaluation, two (focal spine anomalies) were diagnosed after postnatal radiologic examination, and the remaining 43 were proven at autopsy.

For each condition, we describe the prenatal sonographic findings, and include a brief review.

Index terms:
Fetus, abnormalities
Fetus, US
Fetus, skeletal system

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Focal musculoskeletal anomalies can occur in isolation or in association with a large variety of syndromes, malformations and disorders. Thus, the early and accurate prenatal diagnosis of anomalies is important not only for detecting the anomaly itself, but is also helpful with regard to these other, associated, anomalies. We describe and summarize various musculoskeletal anomalies, which may be categorized as focal limb dysplasia (n=4), anomalies of the hand (n=23), foot (n=18), and focal spine (n=2) and amniotic band syndrome (n=3). Forty-three cases were diagnosed at autopsy, five were confirmed by postnatal physical examination and the remaining two were diagnosed after postnatal radiologic examination.

Focal Limb Dysplasia

Radial ray defect or abnormality

A prenatal diagnosis of radial ray hypoplasia should be based on ultrasound findings of severe shortening or absence of the radius, absence of the thumb, and abnormal posture of the hand (sharp radial deviation) (Fig. 1). Sonographic evaluation of fetal limb bones is sometimes difficult due to forearm posture (pronation or supination) and abnormal amniotic fluid volume. If there are many severe associated defects involving, for example, the heart, central nervous system, kidneys or abdominal wall, visualiza-

tion of the ulnar and radius should not even be attempted.

When radial ray abnormality is detected, important additional differential diagnosis can be made (1). The anomalies associated are Holt-Oram syndrome (cardiac defects and congenital defects of the thumb), TAR syndrome (thrombocytopenia-absent radius, autosomal recessive), VATER or VACTERL association (vertebral, anal and cardiac anomalies; tracheoesophageal fistula; and radial/limb defects), Fanconi's anemia, and chromosomal anomalies (trisomy 18, trisomy 13) (1).

Mesomelic dysplasia

Mesomelic dysplasia is characterized by shortening of the middle segment of the limbs, with or without hand and foot involvement, and other possible associated anomalies, and can be diagnosed by ultrasound from the early part of the second trimester onwards (Fig. 2). Several subtypes are known to exist, including the Langer, Campailla-Martinelli, Maroteaux, Nievergelt, Robinow, Reinhardt-Pfeiffer and Werner types (2). Langer mesomelic dwarfism is an extensively reported type of mesomelic dysplasia, in which a hypoplastic ulna, fibula and mandible can be detected, together with an inconstant finding of cubital deviation of the hand. Shortening of the lower limbs is commonly more prominent than that of the forearms. If kyphoscoliosis is accompanied by mild shortening of the forearms and lower legs, Campailla-Martinelli-type acromesomelic dwarfism is suggested. Where shortening of the forearm or lower leg is

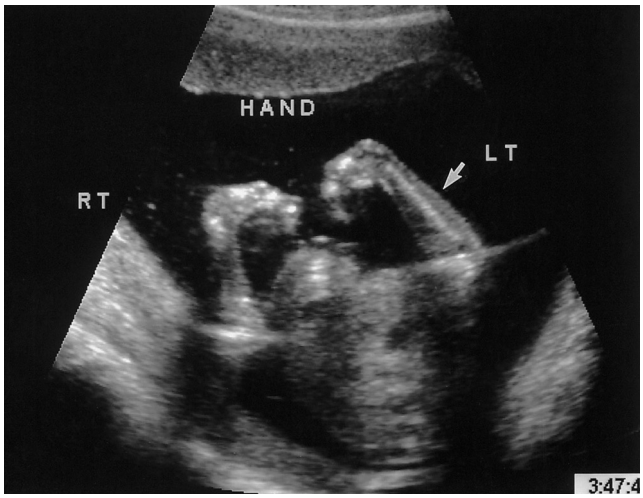


Fig. 1. Radial ray abnormality.
Second-trimester ultrasound reveals that the forearm consists of only the ulna (arrow), with sharp radial deviation of the hand. The thumb is not well visualized, consistent with radial ray abnormality.

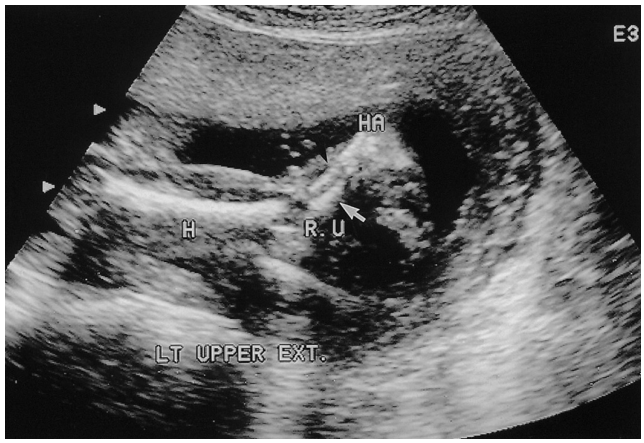
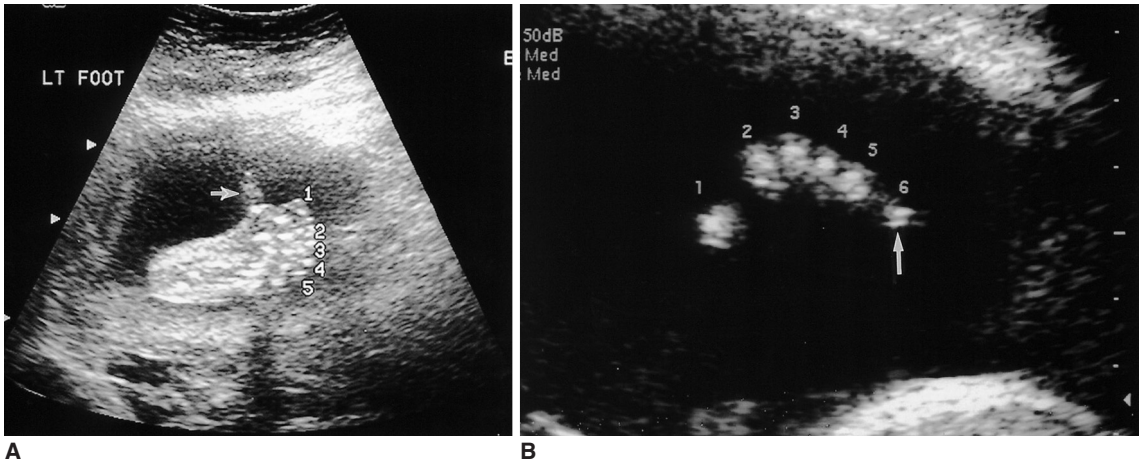


Fig. 2. Focal skeletal dysplasia: mesomelia.
Fetal sonography performed at week 20 demonstrates the typical finding of mesomelic dysplasia. The forearm (radius and ulnar, arrows) is markedly shortened compared with the humerus.



A B

Fig. 3. Polydactyly.
A. Prenatal ultrasound reveals that the foot, viewed radially, has an extra digit (preaxial polydactyly) (arrow).
B. An extra digit at the ulnar side of hand, viewed axially, suggests postaxial polydactyly (arrow).

mild, further skeletal anomalies and fetal structures must be detected if various other congenital diseases are to be differentiated. The prognosis of these different types of mesomelic dwarfism varies according to the results of the orthopedic procedures aimed at correcting limb deformities.

Anomalies of the Hand

Polydactyly

Polydactyly, the condition in which more than five digits are present, may be classified as one of two main types: pre- or postaxial. Preaxial polydactyly involves the radial aspect of the hand, while the postaxial type involves the ulnar aspect (Fig. 3). The central type can also occur, and involves duplication of the index, middle, or ring fingers. Polydactyly may be accompanied by multiple structural anomalies such as cardiac malformations, the absence of the corpus callosum, cephalocele, and short rib-polydactyly (SRPD) syndrome (3). Castilla et al., in an epidemiologic analysis of newborns with polydactyly, noted that in 14.6% of cases other congenital anomalies were present (4). In most cases of fetal polydactyly, a detailed ultrasonographic survey and fetal karyotyping will provide sufficient information for appropriate prenatal parental counseling. Supernumerary digits may arise from the hand or from another digit, and may consist solely of soft tissue elements or may contain bone; the former may be particularly difficult to distinguish sonographically. Isolated polydactyly, especially without skeletal structure, is associated with a favorable outcome (5).

Syndactyly

Syndactyly, involving the fusion of digits, may manifest as the fusion of bones or of soft tissues (Fig. 4). This anomaly is suggested when digits consistently appear to be stuck together during ultrasound examination, but is difficult to detect, especially where soft tissue fusion has occurred. Syndactyly is associated with many syndromes, including SRPD syndrome, triploidy and Down synrome, and its diagnosis thus leads to the detection of associated anomalies and chromosomal abnormalities similar to those found in polydactyly (3).

Clenched hand

Clenched hand deformity is the typical abnormal posture of a trisomy 18 fetus, in which the fourth and fifth fingers deviate radially and the second finger deviates in an ulnar direction over the third finger (Fig. 5). Compared with a normal fetus in which changes in the configuration of the

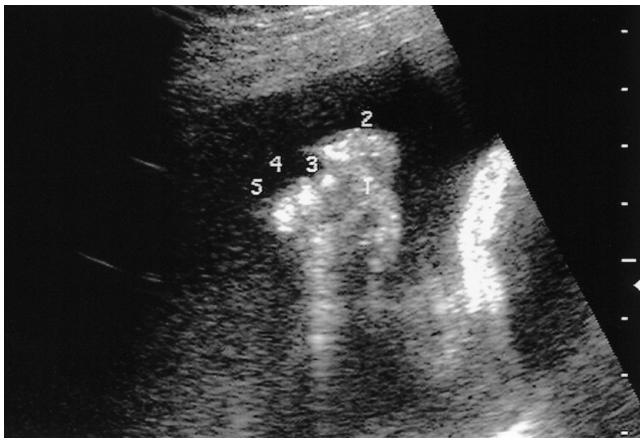
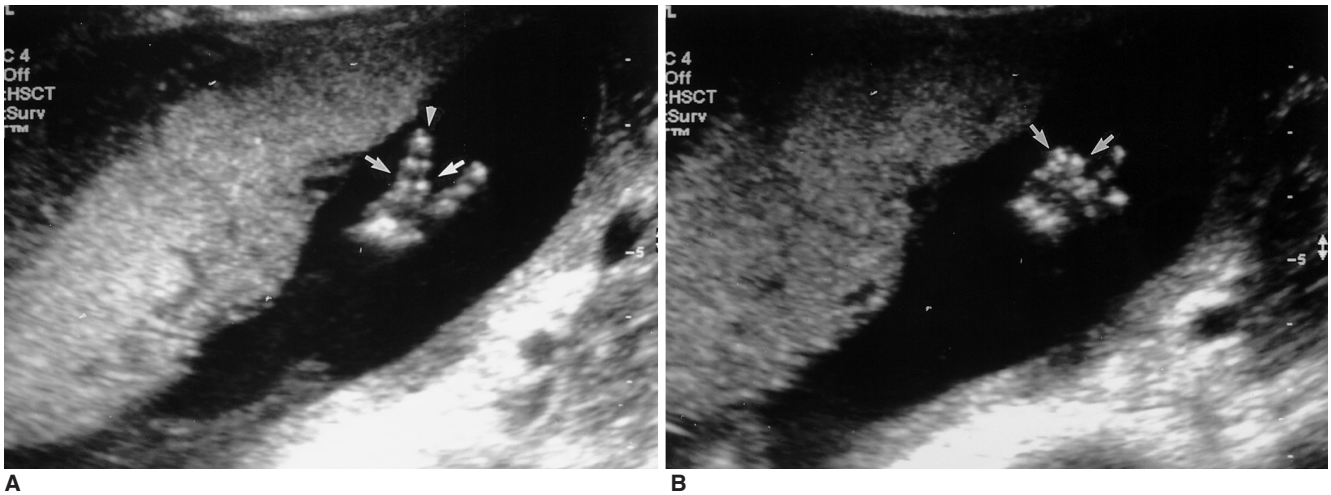


Fig. 5. Clenched hand deformity.
At fetal ultrasound, overlapping of the fourth and fifth fingers radially, and the second finger in an ulnar direction, are observed consistently in a fetus with trisomy 18.



A **B**

Fig. 4. Syndactyly.
A, B. At prenatal sonography, two digits (arrows) at the ulnar side of a fetal hand are seen to be stuck together. The distal phalanges of these digits are observed as one bony segment (arrowhead).

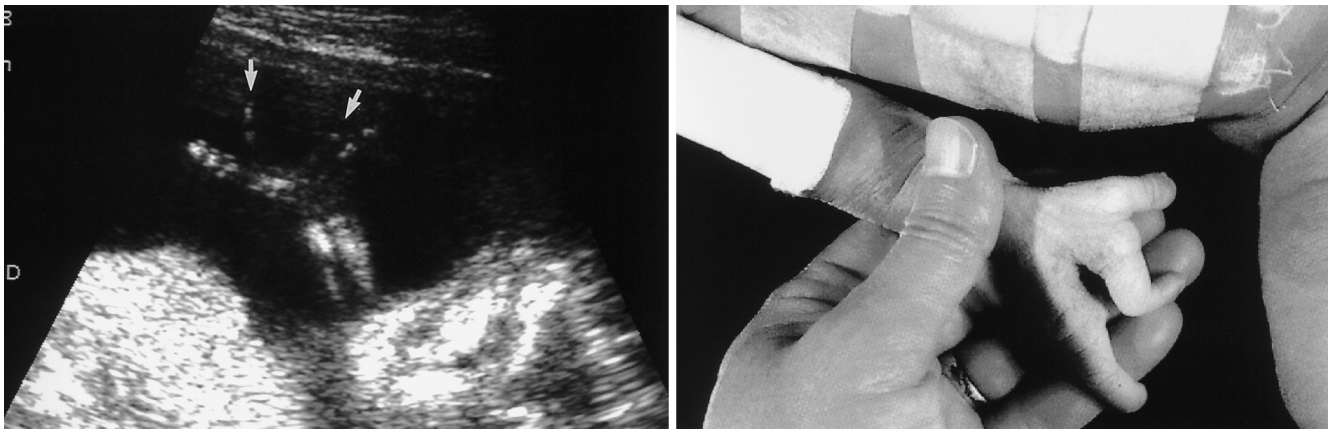
hand and fingers are observed, this characteristic posture, without opening of the hand, is constantly apparent during ultrasonographic examination. Tongsong et al. (6) found that at sonographic examination of 25 fetuses with trisomy 18, abnormalities of the extremities, especially a clenched hand, were present in ten (40%) (6). Quintero et al. have claimed that the abnormal posture results in part from muscle variations along the radial margin of the forearm and hand, the absence of thenar muscles, anomalous tendons and attachments among the forearm groups, and fusion among the arm flexor group (7).

Ectrodactyly: the 'lobster claw' anomaly

Ectrodactyly is a relatively rare condition involving the absence of digits. It can manifest as the absence of a single finger or, in its severe form, as the absence of all but the fifth digit. Usually, this heterogeneous group of hand and foot malformations is characterized as the split hand/foot deformity due to the absence of the third digit, with clefting into the proximal portion of the hand or foot and syndactyly of the remaining digits on each side of the cleft. The hand typically resembles a lobster claw (Fig. 6). This anomaly occurs either sporadically or in association with a number of genetic and non-genetic syndromes, including the well known autosomal-dominant ectrodactyly syndrome and ectrodactyly-ectodermal dyplasia-cleft palate (EEC) syndrome (8).

Clinodactyly

The term clinodactyly (or camptodactyly) is used to describe the permanent curvature or flexion of one or more fingers, together with shortening, usually over an adjacent



A **B**

Fig. 6. Ectrodactyly (split hands or feet).
A. The hand of this fetus has only four fingers, with abnormal widening between the second and third finger (arrows).
B. Neonatal photograph demonstrates lobster claw deformity of the hand.

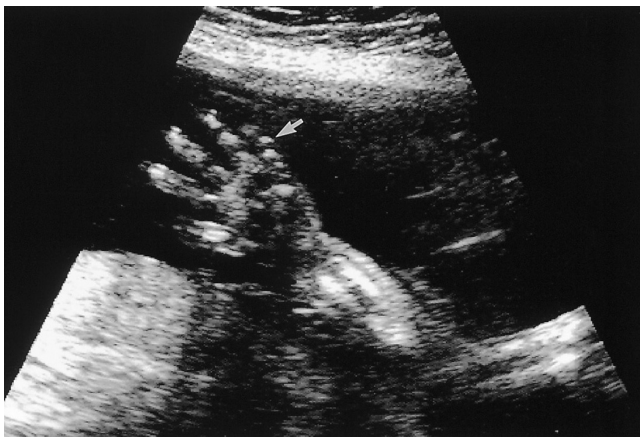


Fig. 7. Clinodactyly.
Second trimester ultrasound reveals shortening and radial deviation of the middle phalanx of the fifth finger (arrow), a condition frequently associated with karyotype abnormality such as trisomy 21,18 and 13.

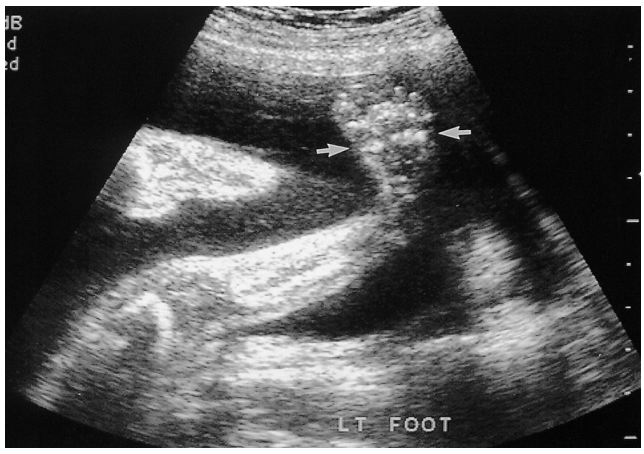


Fig. 8. Clubfoot.
At 22 second weeks' gestation, the forefoot (arrows) is oriented in the same plane as the lower leg.

finger (most commonly the fifth) (Fig. 7) (9). The presence of overlapping digits can lead to a clenched hand configuration. Karyotype abnormality, most notably trisomy 18 and trisomy 13–15, as well as autosomal-dominant congenital malformation syndromes, are frequently associated, and contracture syndromes such as one of the arthrogryposis syndromes, Pena-Shokeir syndrome, or multiple pterygium syndromes may also be present (3).

Anomalies of the foot

Clubfoot

Where prenatal ultrasonography indicates that the lower leg bones and sole of the foot are not perpendicular, clubfoot is diagnosed. The foot may be oriented in the same plane as the lower leg, or parallel to and alongside it (Fig. 8). Laterally, the lower leg and the hind part of the foot may form a round-shaped continuum. Clubfoot may occur in isolation or in association with numerous other conditions, including general musculoskeletal disorders, arthrogryposis and genetic syndromes, and CNS and karyotype abnormalities. In 10–14% of cases it is associated with other structural malformations, and in 6–22% of cases, there is also significant risk of karyotype abnormality (3).

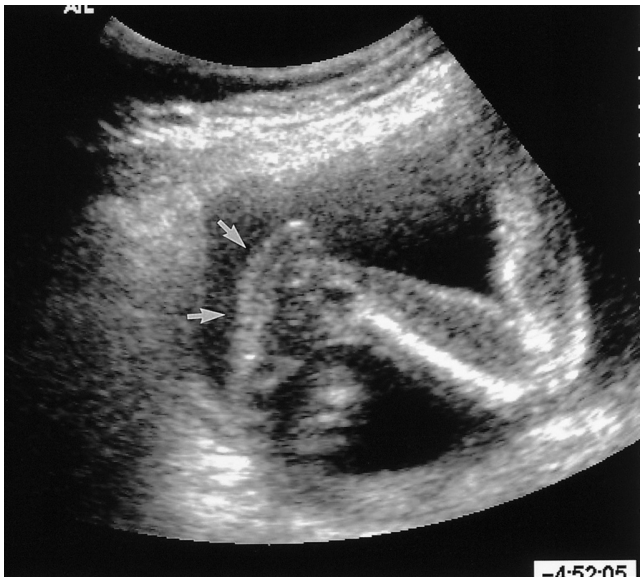


Fig. 9. Rockerbottom foot.
Prenatal ultrasound demonstrates eversion of the plantar arch (arrows).

Table 1. Anomalies and Syndromes associated with Focal Musculoskeletal Anomalies

Focal Limb Dysplasia	Radial Ray Defect	VACTERL association, chromosomal aberrations (trisomy 18, mosaic trisomy 18, trisomy 13), Fanconi's anemia, TAR syndrome, Holt-Oram syndrome, etc.
	Mesomelic Dysplasia	Hypoplastic mandible, kyphoscoliosis, enlarged head, small hands and feet, clubfoot, genital hypoplasia, facial abnormalities, polydactyly, aplasia of the thumb, cleft lip, congenital cardiopathy, etc.
Anomalies of the Hand	Polydactyly	Hydrolethalus (hydrocephalus and heart defect), Meckel-Gruber syndrome, Ellis-van Creveld syndrome, hypochondroplasia, Jeune thoracic dystrophy, SRPD syndrome, VATER association, trisomy 13, etc.
	Syndactyly	SRPD syndrome, EEC syndrome, Holt-Oram syndrome, Robert's syndrome, VATER association, trisomy 10, triploidy, Down syndrome, etc.
	Clenched Hand	Trisomy (18, 13, 9), amniotic band syndrome, arthrogryposis, Pena Shokeir syndrome, multiple pterygium syndrome, etc.
	Ectrodactyly	Amniotic band syndrome, EEC syndrome, trisomy (18 ,13), etc.
	Clinodactyly	Camptomelic dysplasia, EEC syndrome, Holt-Oram syndrome, chromosomal abnormalities (trisomy 21,13,18, etc.), etc.
Anomalies of the Foot	Clubfoot	Arthrogryposis, caudal regression syndrome, amniotic band syndrome, Camptomelic dysplasia, trisomy (18, 9), etc.
	"Rockerbottom" foot	Neural tube defects, caudal dysplasia sequence, chromosomal abnormalities, etc.
	Sandal gap deformity	Trisomy 21
	Curly toe	Not known
Amniotic Band Syndrome		Limb defects (asymmetric constriction of limbs or digits, amputations, clubbed feet, clenched hands), anterior abdominal wall defects (gastroschisis, omphalocele), cranial abnormalities (encephalocele, asymmetric anencephaly), facial clefting, micrognathia, limb-body wall defects, etc.
Foca Spine Anomalies	Hemivertebra and block vertebra	VATER association, Noonan syndrome, caudal regression syndrome, cloacal exstrophy, Klippel-Feil syndrome, Marfan syndrome, etc.

Note.—TAR syndrome=Thrombocytopenia-absent radius syndrome, SRPD syndrome=Short rib-polydactyly syndrome
EEC syndrome=Ectrodactyly-ectodermal dysplasia-clefting syndrome
Table 1 is taken from reference 15

Rockerbottom foot

A "rockerbottom" foot is due to a deformed talus and calcaneus, the talus having assumed a vertical position on account of plantar flexion. Externally, eversion of the plantar arch, i.e. a convex plantar surface is observed, together with posterior bulging of the calcaneus (Fig. 9)(9). Sonographically, this convexity plus protrusion behind the posterior calf line of the heel can be observed. A rockerbottom foot is most often associated with karyotype abnormality, particularly trisomy 13. It may also occur as an isolated anomaly; together with a caudal dysplasia sequence, neural tube defects, or neuromuscular disorders; or as part of the Potter sequence (3).

Sandal gap deformity

Sandal gap deformity involves medial displacement of the great toe, giving rise to a greater than normal space between the first and second toes (Fig. 10). Separation of the great toe has been reported in 45% of children with Down syndrome, but is not a typical finding in other syndromes (10). The deformity may, however, be a normal variant, occurring in many normal fetuses or neonates. If the findings of prenatal sonographic examination suggest sandal gap deformity, a careful search for other risk factors for Down syndrome is recommended. An awareness and un-

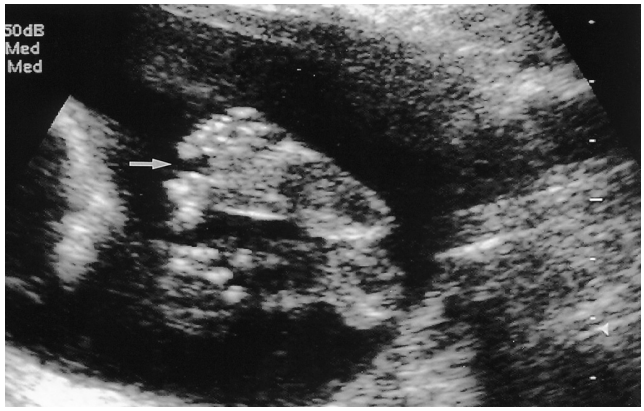
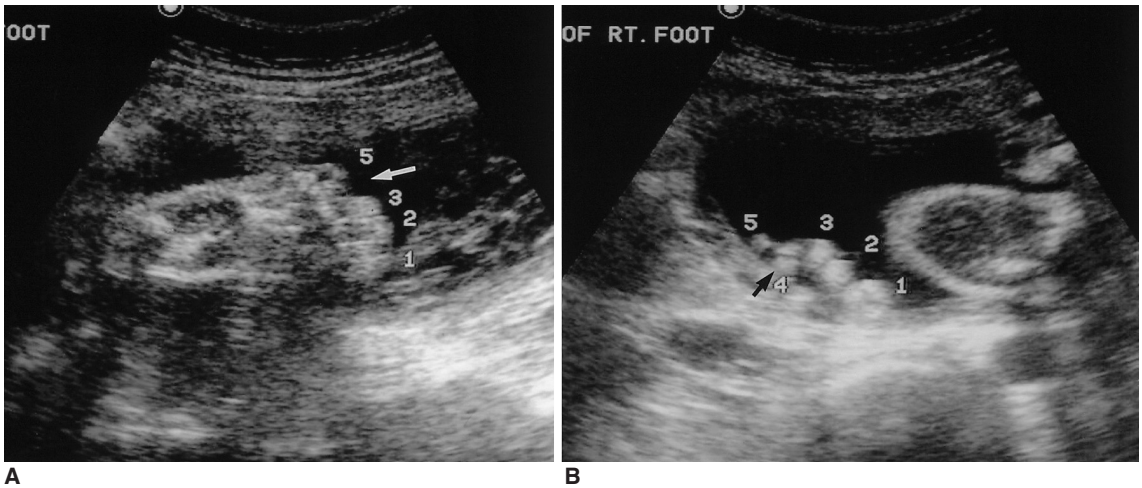


Fig. 10. Sandal gap deformity.
Plantar view of the foot in a fetus with Down syndrome reveals an abnormal degree of separation between the great toe and the second toe (arrow).



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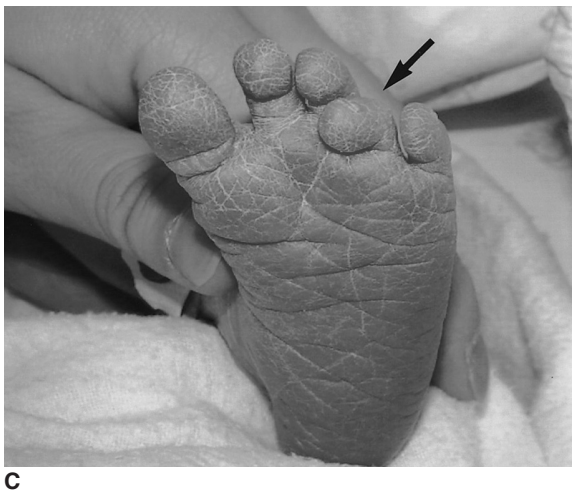


C

Fig. 11. Curly toe.
A, B. Prenatal sonography indicates that the fourth toe (arrow) deviates medially and plantarly (**A**, axial scan; **B**, coronal scan).
C. Neonatal photograph confirms the presence of a congenital underlapping fourth toe (arrow).

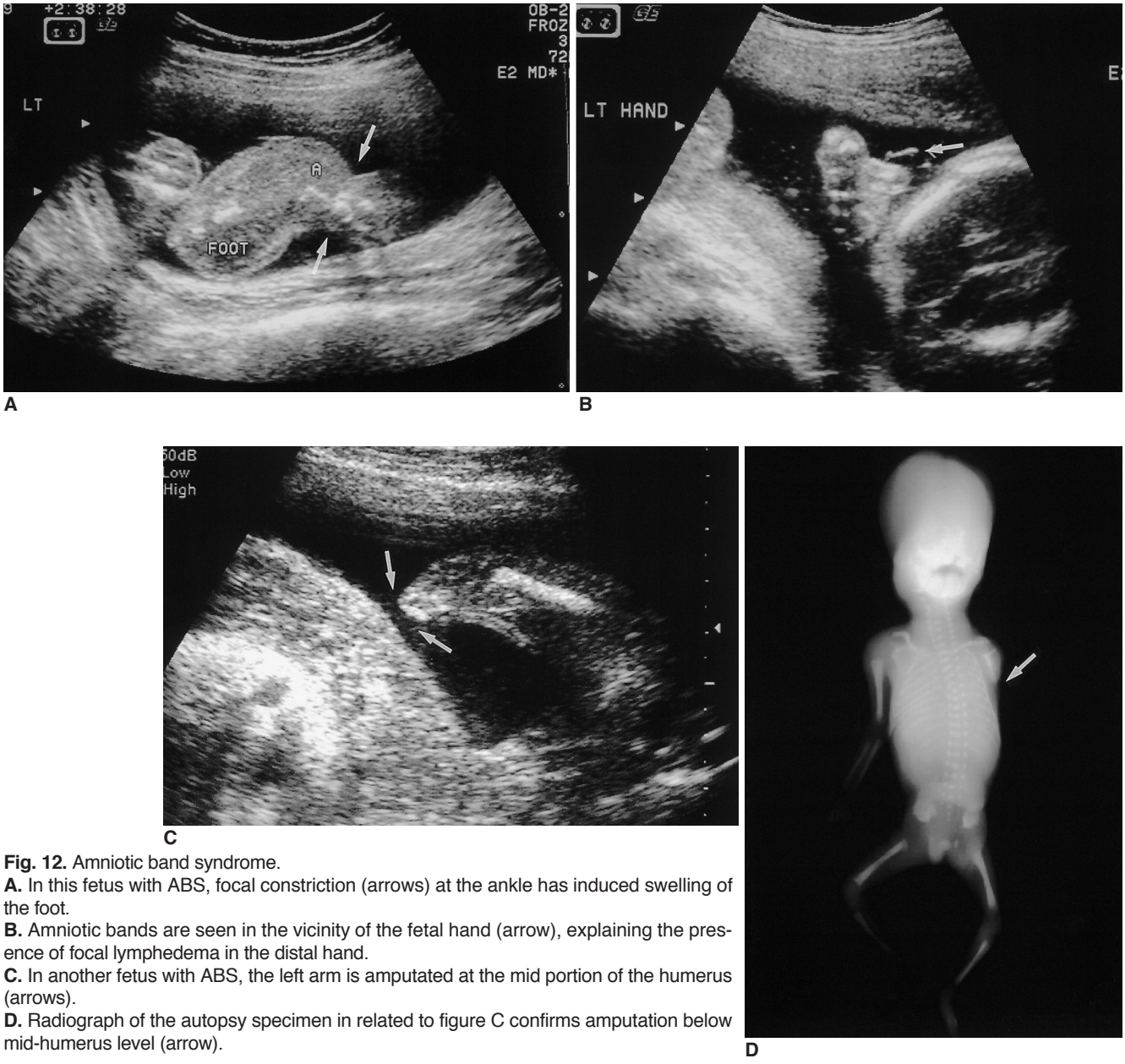
derstanding of any such abnormalities, even subtle ones, should -especially with regard to karyotyping- increase a practitioner's confidence during parental counseling. If no other abnormality is present, including clinical risk factors, separation of the great toe can be accepted as a normal variant (10).

Curly toe (congenital underlapping toe)

This is a common deformity, often involving the fourth and fifth toes. One or more toes are bent plantaward, deviated medially, and usually rotated laterally at the distal interphalangeal joint level (11). The prenatal sonographic finings are mild shortening of the fourth or fifth toe, as viewed axially, together with medial and plantar deviation of this same toe when the foot is viewed in the coronal plane (Fig. 11). The condition usually occurs bilaterally and symmetrically, and there is a high familial incidence. Associated or chromosomal anomalies have not yet been reported. The cause is unknown, but hypoplasia of the intrinsic muscles of the affected toe has been suggested. If the deformity is mild and asymptomatic, no treatment is necessary; however, if symptomatic, and conservative treatment fails, then surgery is indicated (11).

Amniotic band syndrome

Amniotic band syndrome (ABS) is a complex collection of multiple disfiguring and disabling manifestations. It involves a wide spectrum of defects, ranging from minor



A B C D

Fig. 12. Amniotic band syndrome.
A. In this fetus with ABS, focal constriction (arrows) at the ankle has induced swelling of the foot.
B. Amniotic bands are seen in the vicinity of the fetal hand (arrow), explaining the presence of focal lymphedema in the distal hand.
C. In another fetus with ABS, the left arm is amputated at the mid portion of the humerus (arrows).
D. Radiograph of the autopsy specimen in related to figure C confirms amputation below mid-humerus level (arrow).

constriction rings and lymphedema of the digits to major craniofacial and visceral defects. This congenital malformation includes severe and often lethal deformities such as acrania, microcephaly, encephalocele, cleft palate and gastroschisis. The most common triad of clinical manifestations is congenital distal ring constrictions, intrauterine amputations and acrosyndactyly (12). For live births, the reported incidence is 7.7:10,000, though may be as high as 178:10,000 for spontaneous abortions. Early rupture of the amnion is followed by intrauterine entrapment of fetal structures by mesodermal fibrous strands originating from the chorionic side of the amnion. A characteristic feature is the presence of amniotic bands in direct contact with fetal parts whose motion is significantly restricted (Fig. 12) (13). When only restricted fetal movement and characteristic asymmetric fetal anomalies are observed, regardless of the presence or absence of fibrous membranes, the possibility of ABS should be considered.

Anomalies of the Focal Spine (Hemivertebra and block vertebra)

Hemivertebrae or butterfly vertebrae are caused by failure of vertebral segment formation, and can lead to scoliosis and kyphosis. A hemivertebra acts as a wedge within the vertebral column, resulting in curvature away from the side on which it is present. However, when it occurs at the

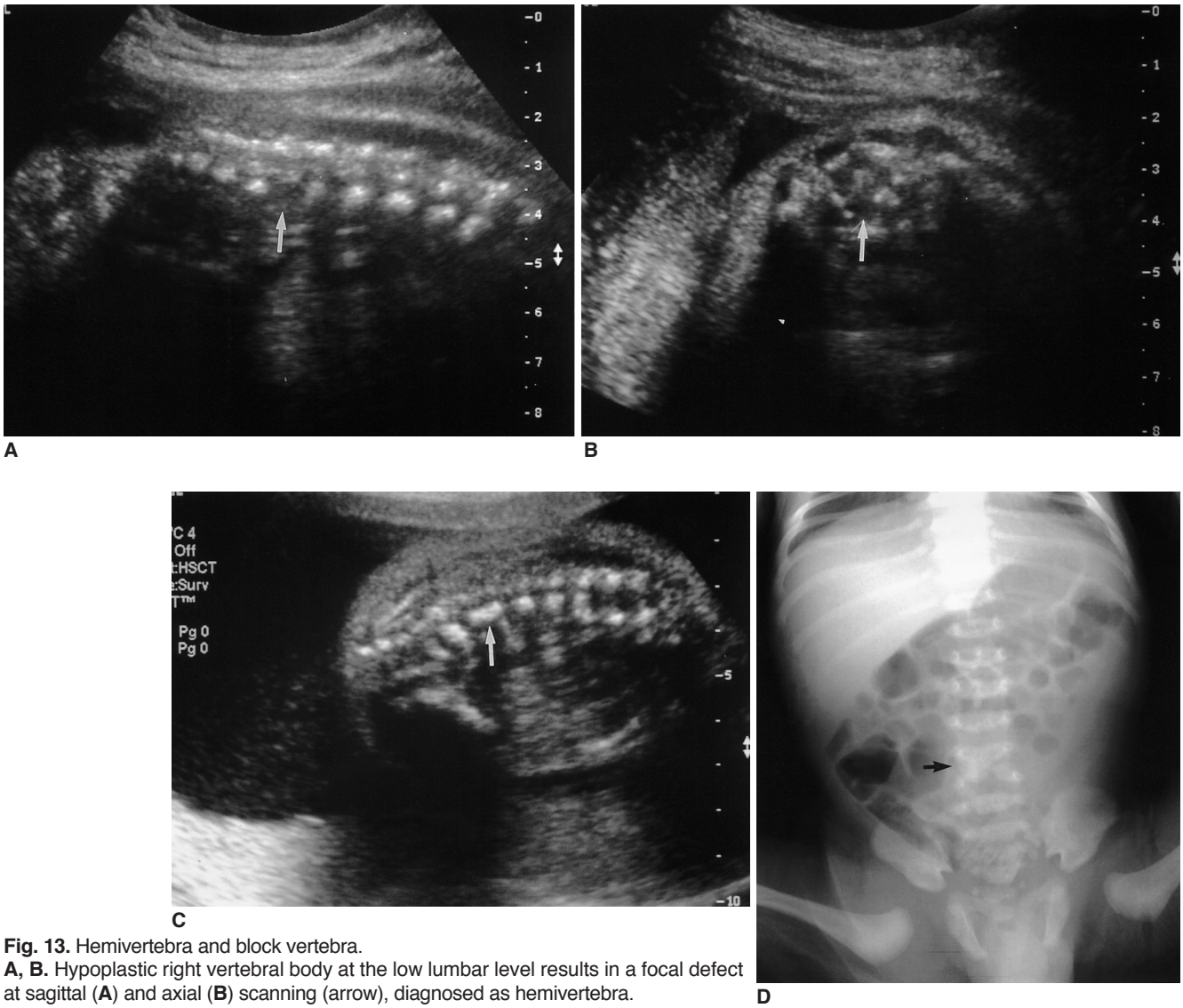


Fig. 13. Hemivertebra and block vertebra.
A, B. Hypoplastic right vertebral body at the low lumbar level results in a focal defect at sagittal (**A**) and axial (**B**) scanning (arrow), diagnosed as hemivertebra.
C. Oblique coronal prenatal ultrasound scan obtained at the low lumbar level suggests the fusion of two vertebral bodies, leading to an abnormally elongated vertebral column compared with other normal body contours.
D. Postnatal plain film of the fetus in **Fig.12C** demonstrates block vertebra at the right side between the fourth and fifth lumbar vertebral bodies (arrow).

low lumbar to sacral level, deformity is not commonly associated. The prenatal sonographic findings include the asymmetrical appearance of a vertebral body at sagittal or coronal scanning, while axially, a focal defect is seen at either side of the vertebral column (Figs. 13A, B).

Segmentation failure causes block vertebrae, resulting in various degrees of scoliosis, lordosis, kyphosis, and shortening of the spine (Figs. 13C, D). The most common site of vertebral anomalies has been found to be the lower thoracic region; regardless of the type of anomaly, the thoracolumbar region has shown the worst prognosis (14). Vertebral body anomalies of the thoracic spine often accompany rib defects; also reported to accompany vertebral defects are renal, lower extremity, heart, and gastrointestinal anomalies.

VATER or VACTERL syndrome involves the non-random association of anomalies with vertebral abnormalities, and when a fetal vertebral anomaly is suggested sonographically, a careful search for other fetal anomalies should thus be undertaken. If none are detected, the outcome for the newborn is excellent, though scoliosis commonly progresses with advancing age.

Summary

As indicated in this brief review, the severity of fetal musculoskeletal anomalies varies widely. Although prenatal ultrasound may suggest severe deformity, several anomalies may show an excellent outcome, or the neonate may be normal. Curly toe anomaly and sandal gap deformity, for example, can occur in normal fetuses and their prognosis is good. When occurring in isolation, soft tissue syndactyly and polydactyly both have a relatively good postnatal outcome. On the other hand, most limb dysplasias, hand and foot anomalies, amniotic band syndrome and vertebral anomalies are associated with multiple skeletal anomalies and may be a part of wider chromosomal abnormality. Among the conditions mentioned, a more thorough prenatal examination is recommended for clinodactyly and sandal gap deformity, since these are frequently associated with Down syndrome.

Thus, no apparently trivial finding suggesting musculoskeletal anomaly of prenatal sonography should be overlooked, and a detailed search for associated abnormalities should always ensue.

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