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# Antenatal diagnosis of short-limb dwarfism: sonographic approach

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This paper is dedicated to Jacques Sauvegrain.

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**Abstract** Based on the findings in 12 patients with skeletal dysplasia diagnosed antenatally, the authors propose a tailored approach to the evaluation of foetuses with shortened long bones, depending on the time of discovery, the degree of shortening and the associated findings. During the second trimester, a very short femur [2 standard deviations (SD) – 5 mm and less] most probably corresponds to a bone dysplasia, although the differential diagnosis is mainly early intra-uterine growth retardation, and the foetal skeleton should be surveyed completely in order to find supplementary features suggestive of dwarfism. Anomalies of long bones in their shape, thickness or contour, or spinal ossification disorders or undermineralisation (best evaluated at the level of calvarial bones) are most helpful in determining the type of dysplasia. A short femur (between 2 SD and 2 SD – 4 mm) may indicate growth retardation, a chromosomal anomaly or dwarfism. Follow-up examinations are mandatory in order to differentiate between them. During the third trimester a very short femur may indicate a bone dysplasia and the work-up should be the same as in the second trimester. A short femur may correspond to dwarfism of late development, a growth-retarded foetus or constitutional shortness. Various ratios, especially that of the femur/foot, are helpful in differentiating between them. In case of previous family history, a short or very short femur usually indicates recurrence of the dwarfism. In all cases of antenatal diagnosis, confirmation of the sonographic findings should be obtained either by foetal or neonatal radiographs. The approach proposed by the authors should provide sufficient information to counsel the family not only for the ongoing pregnancy but also for subsequent ones.

## Introduction

Obstetric ultrasound (US) allows the antenatal detection of foetuses affected by a skeletal dysplasia. In recent years, numerous reports in the literature describe the in utero features of various bone dysplasias [1–7]. Most cases are detected on the basis of abnormal measurements of long bones (mainly a short femur [1, 2]). Although many descriptions have been published, a precise diagnosis is not always easy to achieve in utero and the sonographer plays a central role in determining whether the short femur is effectively part of a bone dysplasia or corresponds to any other disorder.

The aims of this study, based on 12 cases of bone dysplasia with an antenatal diagnosis, are to describe the sonographic features highly suggestive of dysplasias and to propose a logical work-up in order to differentiate short-limbed dwarfisms from the other potential diagnoses for a short femur.

## Materials and methods

A retrospective study was undertaken of 12 pregnancies complicated by foetal short-limbed dwarfism evaluated by US during a 6-year period from 1988 to 1994, and for which confirmation had been obtained by skeletal radiographs. The criteria studied retrospectively on the sonogram included foetal age at diagnosis, biparietal diameter, abdominal circumference, measurements, shape and outlines of long bones, degree of spine and skull ossification and any additional anomaly. The measurements of the long bones were classified according to the method of Kurz et al. [1]. A very short femur (or other long bone) was defined as shorter than 5 mm below 2 SD and a short femur as between 2 SD and 2 SD – 4 mm. The results of chromosomal analysis and final outcome were also recorded. Foetal or neonatal radiographs were evaluated in order to confirm the type of dysplasia and to appreciate the accuracy of antenatal diagnosis.

## Results

Data of each patient are summarized in Table 1. In all 12 patients, the detection of bone dysplasia was not anticipated (family history was completed only after the US examination in case 4). Among the 12 patients, the mean gestational age at discovery was 27.4 weeks (range 21–30 weeks), 6 cases being detected during the second and 6 during the third trimester. The mildest shortening of the long bones was observed in two cases of achondroplasia (SD – 2 mm); major shortening was observed in a case of diastrophic dwarfism and of hypophosphatasia (2 SD – 22 mm).

Associated anomalies of the long bones were observed in eight cases, thickened irregular bones in four, bowed femur in two, stippled epiphysis in one and wavy bone in another. A small chest was an associated skeletal finding in four patients. One patient presented trisomy 21 on chromosomal analysis.

Based on the sonographic data, a correct diagnosis was already proposed in utero in eight cases (mainly achondroplasia: three patients, and osteogenesis imperfecta (OI): two patients). Termination of pregnancy was elected in eight cases and one perinatal death occurred for an unknown reason. Three patients are alive (two with achondroplasia and one with Conradi-Hünermann syndrome).

## Discussion

Skeletal dysplasias occur in 0.024–0.07 % of births. Several of these disorders are associated with a poor prognosis for post-natal life [1–5]. Prenatal detection of these disorders may influence the obstetric and perinatal management of affected foetuses. Obstetric US offers a unique opportunity for an antenatal diagnosis that is usually suspected either by the detection of shortened long bones or as a result of a referral because of family history; the time of diagnosis can be as early as the end of the first trimester, but is usually during the second and third trimesters [2, 8]. In Belgium, in the course of most uncomplicated pregnancies three US examinations are routinely performed (one per trimester), and the femur is systematically measured during the second and the third trimester examinations, so a shortened femur is easily detected. Yet, a short femur does not necessarily indicate a bone dysplasia. Therefore, we propose a tailored approach to the detection of a short femur based on the time of discovery, the degree of shortness, previous family history and the skeletal anomalies observed by US.

Kurz et al. have shown that the number of millimeters below the 2 SD line is an accurate, easy criterion for evaluating femoral shortening. On this basis, two groups of patients can be defined: the group with femur length 1–4 mm below the SD line (short femur) and the group of patients with femur length more than 5 mm below the 2 SD line (very short femur [1]).

In our study, all patients with bone dysplasia detected during the second trimester presented a *very short femur* and, as shown by many authors, a very short femur is highly suggestive of dwarfism [1–7]. The only alternative diagnosis is an early growth-retarded foetus, a condition that can mimic bone dysplasia [9]. In this type of growth retardation the outcome is poor, and we have encountered several cases of karyotype anomalies. In families with a previous history of bone dysplasia, the detection of a very short femur means recurrence of the disease and if the disorder is lethal, parents may elect at this stage to terminate the pregnancy [5]. In case of an unanticipated detection, a systematic foetal survey should be undertaken in order to find supplementary information that could establish the diagnosis and prognosis of the dwarfism as precisely as possible and help to differentiate it from a growth-retarded foetus [9]. First, all long bones should be measured in both extremities and compared with nomograms in order to confirm the degree of shortening and determine its predominant form (mainly rhizomelic or micromelic; mesomelic dwarfism would not be detected by the measurement of the femur only) [4, 7]. The long bones should be analysed thereafter for any shape or contour abnormalities; long bone bowing, angulation, fractures or thickening secondary to callus formation can be observed; bone fractures appear as an interruption in the bone contours, thickened or irregular contours may correspond to callus formation (Fig. 1 a, b); both features strongly suggest OI of type II [10–12]. Bowed or angulated femurs may correspond to several dysplasias [13]; in one of the two cases where bowed femurs were detected (Fig. 2 a), the presence of bowed tibias suggested camptomelic dwarfism. In case 4, the exceptional visualisation of a stippled epiphysis (Fig. 3 a, b) along with femoral asymmetry led us to re-analyse the family his-

**Table 1** Data of 12 antenatal diagnoses of bone dysplasia (*AC* abdominal circumference, *Bip* biparietal diameter, *CD* chest diameter, *D* dysplasia, *F* femur, *H* humerus, *LMP* last menstrual period, *OI* osteogenesis imperfecta, *T* tibia, *TOP* termination of pregnancy, *U* ulna)

| | Gestational age in weeks (LMP) | Long bone measurements (mm below 2 SD)/ long bone anomalies | Other skeletal measurements (mm below 2 SD); other skeletal findings | Other sonographic findings | Outcome | Final diagnosis (complete diagnosis in utero (yes/no)) |
|---|---|---|---|---|---|---|
| Case 1 | 21 | F – 8; H – 13 (Fig. 1 a, b)? Callus formation; thickened long bones | Bip 2 SD – 3; AC 2 SD – 8; CD – 2 (Fig. 1 c); undermineralisation of skull (Fig. 1 d) | – | TOP | OI type II (yes) (Fig. 1 e) |
| Case 2 | 22 | F – 16; T – 14; bowed femur and tibia | – | Hydramnios | TOP | Camptomelic D (yes) |
| Case 3 | 22 | F – 16; T – 13; bowed femur (Fig. 2 a) | – | Fetal hydrops; bilateral hydronephrosis | TOP | Camptomelic D with Down syndrome (no) (Fig. 2 b) |
| Case 4 | 22 | Left F – 4; right F – 6; stippled epiphysis (Fig. 3 a) | – | – | Normal birth | Conradi-Hünermann syndrome (familial history positive) (yes) (Fig. 3 b) |
| Case 5 | 22 | F – 9; H – 6 | Absent ossification of cervical and lumbo-sacral spine (Fig. 4 a) | Hydrocephalus | TOP | Achondrogenesis type I (yes) (Fig. 4 b) |
| Case 6 | 23 | F – 18; H – 7; T – 10; fracture; thickened long bones | CD – 4; undermineralisation of skull | – | TOP | OI type II (yes) |
| Case 7 | 29 | F – 6; H – 6; T – 8; U – 6 | – | – | TOP | Achondroplasia (yes) |
| Case 8 | 31 | F – 10; H – 7; T – 10 | Small chest | – | TOP | Spondylo-epiphyseal D (Platyspondylisis seen on foetal radiographs only) (no) |
| Case 9 | 33 | F – 22; thickened long bones | CD – 22; short ribs; underossified calvaria | Oligohydramnios | TOP | Hypophosphatasia (no) |
| Case 10 | 34 | F – 4 | Hyperlordosis | Asymmetrical hydrocephalus; polyhydramnios | Normal birth | Achondroplasia (yes) |
| Case 11 | 34 | F – 22; T – 15; H – 16; thickened long bones | – | Hydramnios | Perinatal death | Diastrophic D (no) |
| Case 12 | 36 | F – 14; T – 11; wavy, curved long bones (Fig. 5 a) | Foot/femur ratio 0.74 (Fig. 5 a, b); globular normal-sized head; hyperlordosis | – | Normal birth | Achondroplasia (yes) |

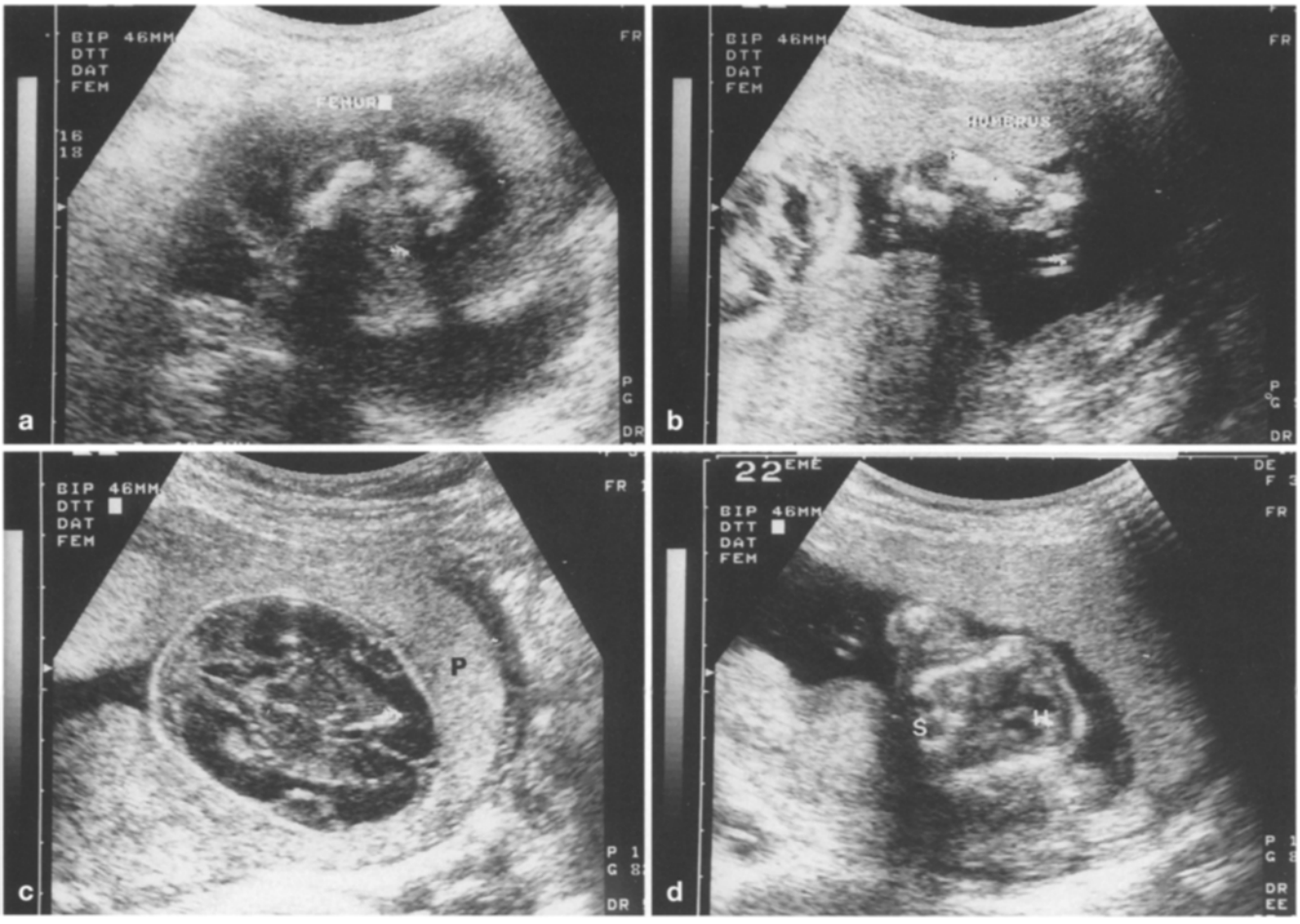



**Fig. 1a–e** Case 1: osteogenesis imperfecta type II 22nd week after last menstrual period *(LMP)*. **a** Foetal femur (18 mm between *crosses*) showing irregular, thickened bone (2 SD – 8 mm). **b** Foetal humerus (16 mm between *crosses*) showing irregular, thickened bone (2 SD – 13 mm). **c** Foetal head on a transverse scan showing markedly thinned calvaria bones; the cerebral anatomy is too well delineated (*P* placenta). **d** Foetal chest (transverse scan): the heart *(H)* occupies most of the chest, which displays an unusual square shape (*S* spine). **e** Foetogram: fractures with callus formation are obvious at the level of the long bones

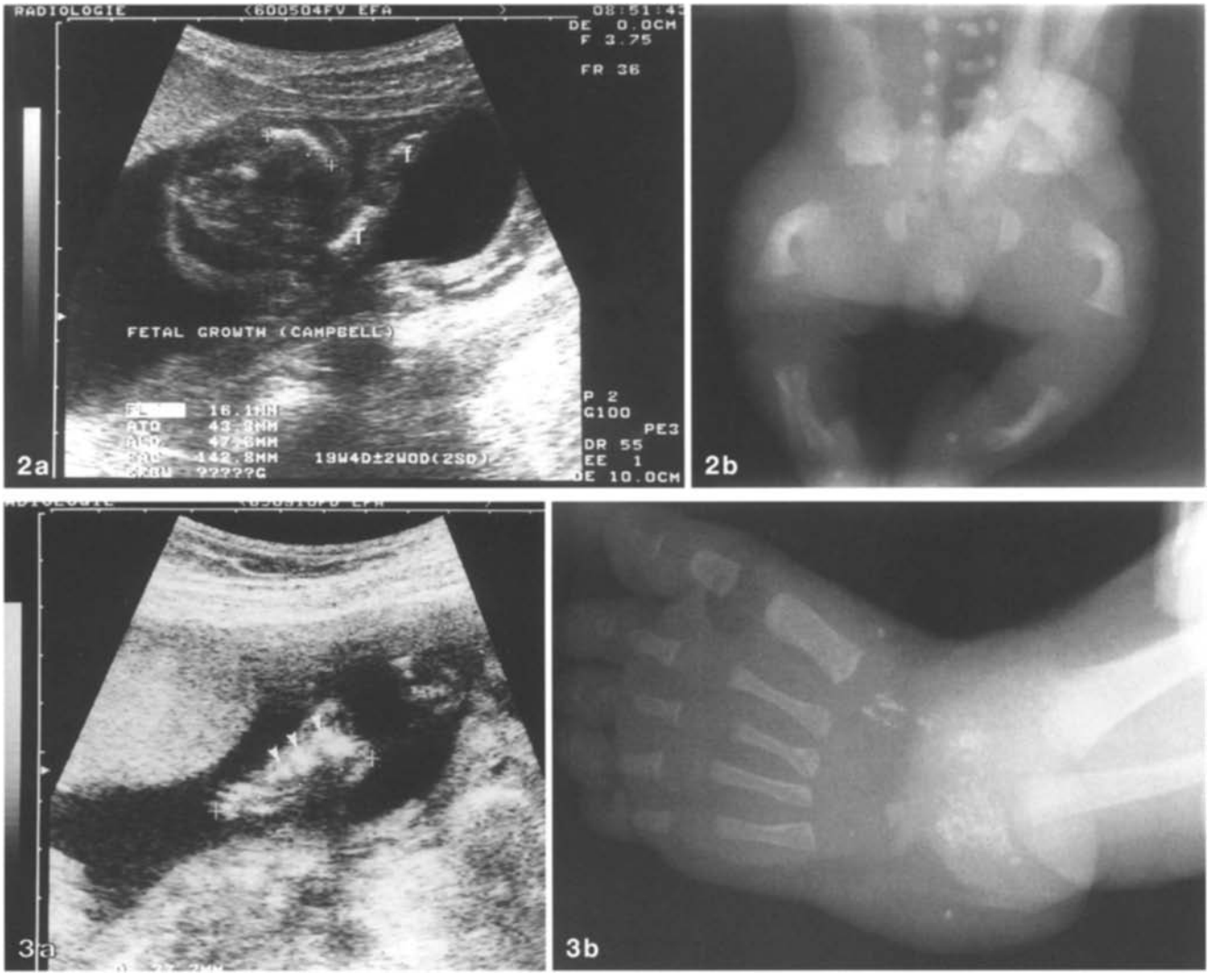



**Fig. 2 a, b** Case 3: camptomelic dwarfism (with Down syndrome). **a** In utero 22 weeks LMP: the scan through the foetal legs shows a shortened bowed femur (2 SD – 16 mm) marked by the *crosses*. The contralateral shortened tibia *(T*; 2 SD – 13 mm) and foot *(f)* are also visible. **b** Foetogram: the pelvic girdle and lower extremities are suggestive of camptomelic dwarfism

**Fig. 3 a, b** Case 4: Conradi-Hünermann syndrome. **a** In utero 22 weeks LMP: the hyperechoic foci *(arrowheads)* at the level of the foot (between *crosses*) correspond to stippled epiphysis (compare with Fig. 5 b). **b** Radiograph of the foot at birth showing typical stippled epiphysis

tory and thus confirm the dominant transmission of Conradi-Hünermann syndrome [13, 14]. If possible the hands and feet should also be studied in order to find any associated malformation [13, 14] (Fig. 3 a, b).

The foetal spine is the second skeletal area that can help in narrowing the differential diagnosis: the presence of all ossification centres, the size of each vertebra and the degree of ossification of all vertebral segments have to be checked. In case 5, the lack of ossification of segments of the cervical and lumbo-sacral spine facilitated the diagnosis of achondrogenesis of type I (Fig. 4 a, b) [15]. Platyspondylisis is less easy to appreciate and can be missed on in utero US.

Undermineralisation of bones, another important feature, is best demonstrated at the level of the calvaria bones and may be suspected when the brain structures appear too clearly delineated and when the skull appears thin or even absent on the biparietal view. Such findings are of utmost importance in confirming dysplasias like OI of type II (Fig. 1 c) or hypophosphatasia; in contrast normal ossification of the skull helps to exclude such syndromes [10–12]. Furthermore, the skull is an important landmark in case of thanatophoric dwarfism, one of the most frequent lethal forms of dysplasia detected in utero, and in which

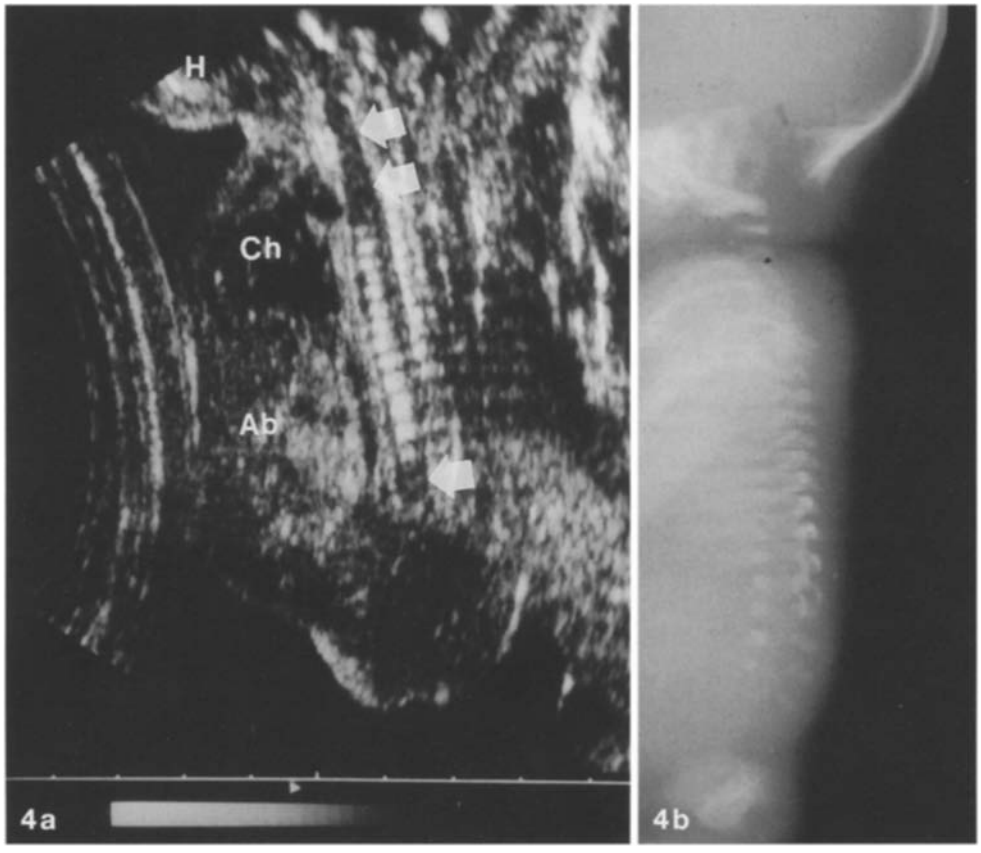
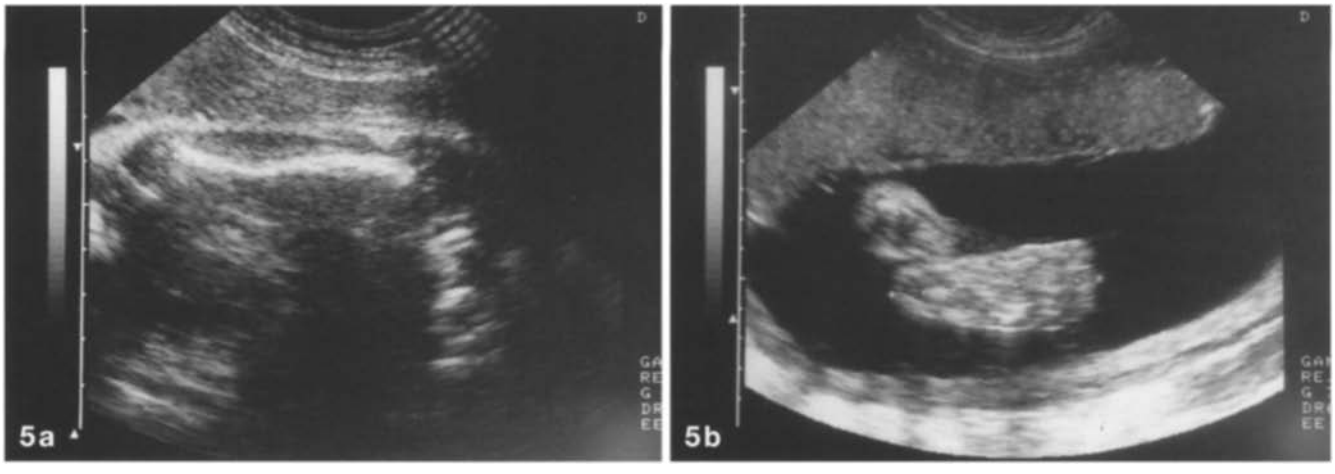



**Fig. 4a, b** Case 5: achondrogenesis type I. **a** In utero 22 weeks LMP: sagittal scan of the foetal spine showing absence of vertebral body ossifications at the level of the cervico-thoracic and lumbo-sacral junctions *(arrows; Ab* foetal abdomen, *Ch* foetal chest, *H* foetal head). **b** Foetogram: the radiograph confirms the lack of vertebral ossification

**Fig. 5a, b** Case 12: achondroplasia, 36 weeks LMP. **a** Foetal femur: 52 mm between the *crosses* (2 SD – 14 mm); the femur has a curved appearance. **b** Foetal foot: at same age, the foot (between the *crosses*) measures 68 mm and the femur/foot ratio is 0.74




kleeblattschädel deformity may be present; in this dwarfism and in various other dysplasias (achondroplasia and achondrogenesis in our series), hydrocephalus or other brain malformations may be associated findings [5, 6]. As mentioned, many of the dysplasias detected during the second trimester are lethal, and most foetuses die at birth from associated lung hypoplasia with respiratory failure; this can be predicted already in utero by measuring the chest diameter or circumference (Fig. 1 d) [16].

It is noteworthy that in one case of our series a trisomy 21 was detected and therefore we recommend systematic chromosomal analysis in all cases of suspected bone dysplasia. Obviously it will not be possible to identify every dysplasia, since a certain percentage remains unclassified even with skeletal radiographs at birth and because for some the characteristic features will appear only later, sometimes in childhood [12, 13]. However, early detection will allow a long-term follow-up and a full work-up at birth.

The significance of a *short femur* (2 SD below the mean) detected during the second trimester appears less straightforward as it may correspond to various pathologies. In the study of Kurz et al. [1], patients included in group 1 had a more favourable outcome and no case of bone dysplasia was included in this group. Yet such a finding could suggest the progressive development of a dwarfism and successive control examinations are mandatory to monitor the growth curve of the long bones. For example, OI may have varying expression during successive pregnancies; the shortening appears sometimes early and sometimes late in the second trimester. Therefore in a family with previous history this finding indicates the recurrence of the disease and, consequently, one can reassure a family with a previous history of OI only if after 28 weeks' gestation the growth of long bones continues to be normal [10–12].

Most commonly the question raised by a short femur detected during the second trimester is that of a possible indicator of chromosomal anomaly. It has been shown that patients with Down syndrome may have a short femur and an expected femur/measured femur length ratio below 0.91. In our experience, it is never an isolated finding and we do not consider it an indication for amniocentesis when no other abnormality is present [17, 18]. Finally, a short femur could also indicate a growth-retarded fetus and follow-up examination will be necessary to follow its growth.

As shown by cases 9 and 11, during the third trimester a *very short femur* most probably corresponds to a short-limbed dwarfism too, and therefore the work-up should be the same as during the second trimester, checking the whole foetal skeletal system for associated anomalies. The significance of a *short femur* is much more difficult to appreciate than in the second trimester and various conditions, both normal and abnormal, have to be considered. It can correspond to a short-limbed dwarfism of late development, usually a non-lethal type. Heterozygous achondroplasia is typically detected during the third trimester after femoral growth has slowed down (Fig. 5 a) [2, 5]. More commonly a short femur detected during the third trimester expresses intrauterine growth retardation (IUGR) of asymmetrical type, where the growth of the biparietal bones is preserved but the femur is shortened [19]. A way of differentiating between bone dysplasia and IUGR is to use the femur/foot ratio with a value of $0.99 \pm 0.06$ in normal or growth-retarded foetuses but which is markedly decreased in dwarfism [20]. The value was 0.78 in our patient with achondroplasia (Fig. 5 a, b). Another important element of the differential diagnosis for a short femur detected during the last weeks of pregnancy is a constitutional shortness and a family inquiry may help [1].

Whatever the type of anomaly and the time of detection, it is mandatory to obtain confirmation of the sonographic findings either in utero by plain film of the mother's abdomen or after delivery by skeletal radiographs of the newborn (or stillborn) (Figs. 1 e, 2 b, 3 b, 4 b) [21]. Each case should be managed individually with the help of paediatric radiologists, foetologists and geneticists. Finally, one should be aware of possible error in measuring the long bones and therefore a control examination should be carried out in doubtful cases. An antenatal diagnosis of dwarfism carries many questions and much anxiety for parents and therefore, after a complete work-up has been achieved and if a precise diagnosis can be proposed, a multidisciplinary team should inform and counsel the parents so they can choose the most appropriate procedure.

In conclusion, many skeletal dysplasias may be accurately identified by US. A careful assessment of the foetal skeleton should be performed when the foetus is at risk or when the screening examination identifies a skeletal disorder. The main differential diagnosis for bone dysplasia is a growth-retarded foetus. Each case should be cautiously approached, focusing the analysis on the time of diagnosis, severity of shortness and associated findings. The more associated anomalies are detected, the easier it will be to make a precise diagnosis. Skeletal radiograph confirmation should always be obtained. This approach should provide sufficient information to counsel the family not only for the ongoing pregnancy but also for subsequent ones.

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