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Letters to the Editor

Three-dimensional sonographic aspects in the antenatal diagnosis of achondroplasia

We describe two cases of achondroplasia diagnosed prenatally with the help of three-dimensional (3D) ultrasound.

Case 1

A 38-year-old woman, gravida 10 para 5, was referred to the Centre Femme Mere Enfant, Hopital de L'Archet in Nice, France at 32 weeks' gestation following the diagnosis of short fetal limbs. She had no family history of skeletal anomalies.

Level II ultrasound examinations with 3D surface and volume rendering revealed a characteristic craniofacial appearance with brachycephaly (biparietal diameter, 93 mm; i.e. 97.5th centile of the normal range) and a prominent forehead. The midface was small with a flat nasal bridge (Figure 1a).

Shortening of the long bones was particularly marked in the proximal segments. The right and left femurs measured 50 mm (equivalent to 27 weeks) and the humeri 44 mm (equivalent to 26 weeks). The spine presented a caudal narrowing of the lumbar interpediculate distance, rather than the normal caudal widening (Figure 1b). The thorax exhibited mild hypoplasia and achondroplasia was diagnosed.

A female baby was delivered with a body weight of 3020 g and a body length of 45 cm. Radiographs confirmed the diagnosis of achondroplasia.

Case 2

A 29-year-old woman, gravida 3 para 2, was referred to the Centre d'Échographie in Grasse, France at 30 weeks' gestation following the diagnosis of short fetal limbs. She had two healthy children and no family history of skeletal anomalies.

Level II ultrasound examinations with 3D surface and volume rendering revealed a normal amniotic fluid volume, an abnormal craniofacial appearance with brachycephaly (biparietal diameter, 85 mm; 97.5th centile) and the characteristic facial features included a large head with a prominent forehead as in Case 1.

Shortening of the long bones was observed particularly in the proximal (rhizomelic) segments. The right and left femurs measured 42 mm (equivalent to 23 weeks), the tibias 42 mm, the humeri 36 mm (equivalent to 22 weeks) and the ulnae 36 mm. The thorax was mildly hypoplastic.

The hands were podgy and had fingers of similar length (Figure 2a) and in 3D multiplanar view the upper extremity of the femur was shown to have a pointed aspect typical of achondroplasia (Figure 2b).

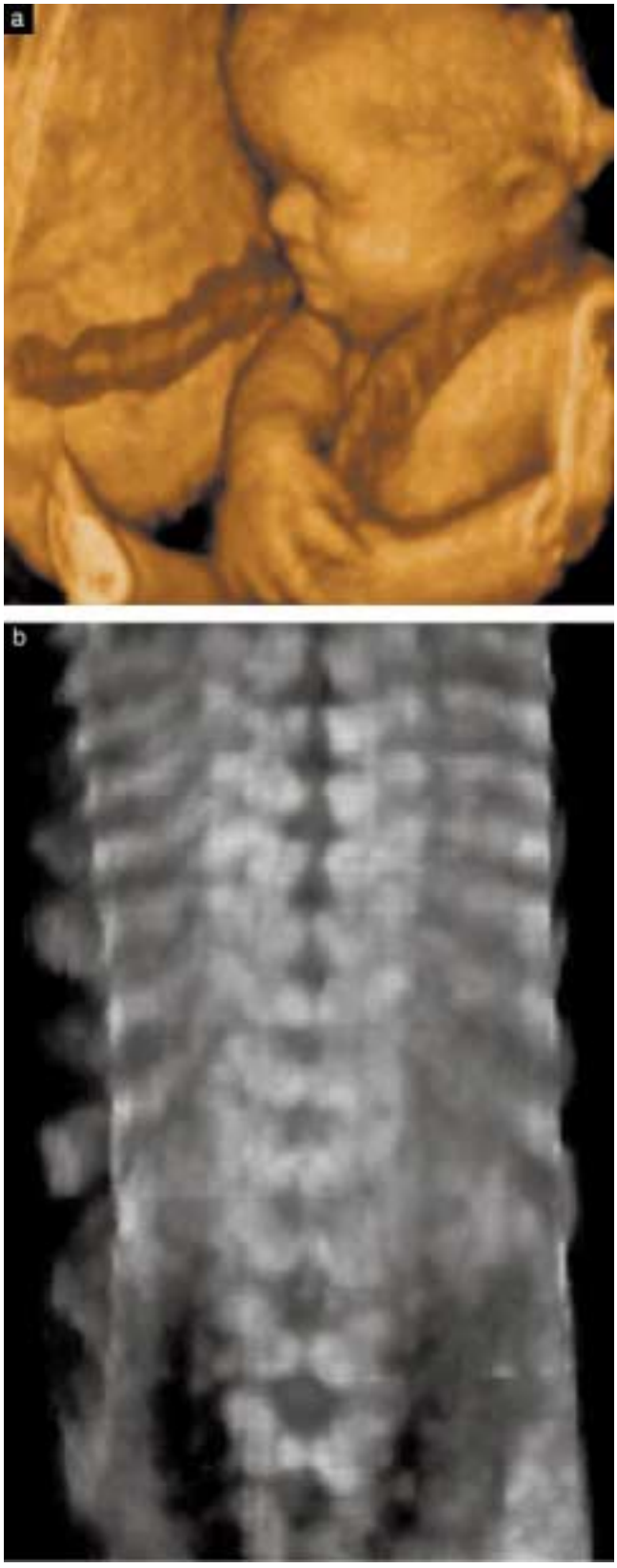

Figure 1 Case 1, showing the characteristic craniofacial appearance (a) and the caudal narrowing of the interpediculate distance (b).

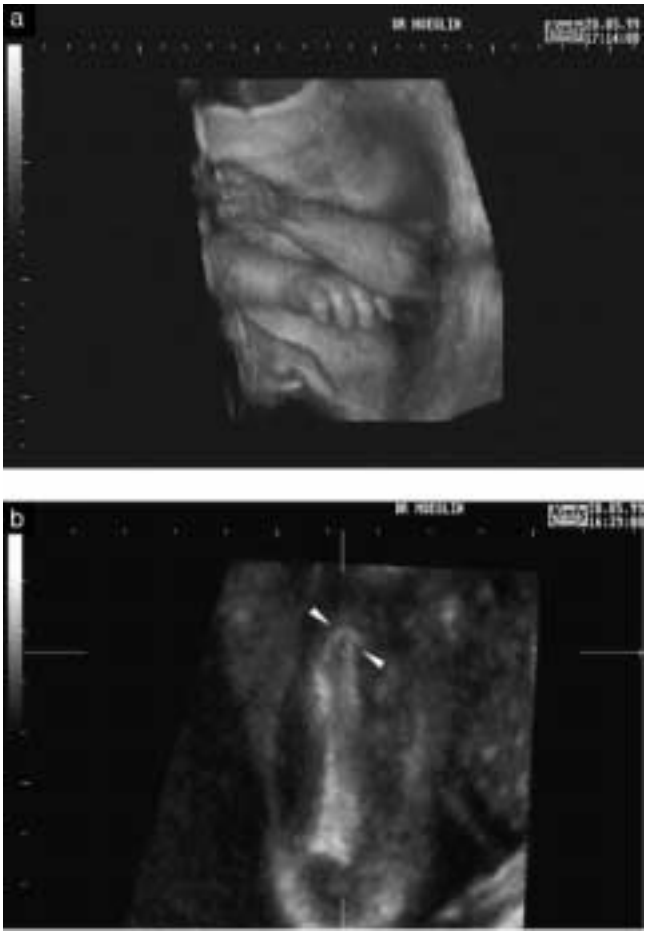

Figure 2 Case 2 showing podgy hands with fingers of similar length (a) and the pointed aspect of the upper extremity of the femur (b).

The mother opted to terminate the pregnancy and a female baby was delivered with a body weight of 1940 g and a body length of 41 cm. Postmortem examination and radiographs confirmed the diagnosis of achondroplasia.

Discussion

Achondroplasia is the most common form of short-limb dwarfism. Its prenatal sonographic diagnosis is possible[1–3] but difficult and often made late[4]. When this condition is suspected, molecular genetic testing can be used to detect a mutation in the *FGFR3* gene (chromosomal locus, 4p16)[5].

Our two observations emphasize the benefit of 3D ultrasound[6,7] for the diagnosis of achondroplasia. Surface rendering allows the visualization of the specific facial features and the aspect of the extremities (Figures 1a and 2a)[8]. While multipanar visualization provides images that appear similar to conventional two-dimensional (2D) images, they can be viewed from any orientation in the volume. This improves the analysis of long bones, particularly their epiphyses and metaphyses[9–11]. Figure 2b shows the typical pointed appearance of the upper femoral extremity. This sharpened aspect of the upper femoral diaphysis is linked to a vertical metaphyseal slope which is characteristic of achondroplasia. Volume rendering in transparent mode visualizes the highest gray levels in the 3D matrix. With this method bony structures are prominently displayed (Figure 1b).

Categorization of skeletal dysplasia is based on radiological findings derived from neonates and infants. During the postnatal period triangulation is commonly used. Triangulation is obtained by identifying the major findings of an anomaly and comparing these defects with those described for the 'gamut' of classic syndromes[12]. Only some of these criteria can be derived from 2D sonography in a fetus[13,14].

Three-dimensional volume rendering allows sequential and systematic visualization of the different parts of the fetal skeleton:

- skull (frontal and profile);
- rachis (frontal and profile);
- thorax (ribs, scapulae and clavicles);
- pelvis (pubic bones, iliac bones and ischii);
- long bones (particularly epiphysis and metaphysis);
- extremities.

This systematic survey allows, for example, the determination of the interpediculate distance and measurement of the height of the vertebral bodies[15] (Figure 1b). Adopting the methodology of Garjian *et al.*[16], we have recently undertaken a retrospective study of fetal skeletal dysplasia from 3D volume data collected in four level II ultrasound centers[17] and are systematizing the sonographic criteria for triangulation of fetal osteochondrodysplasia. Our preliminary results combining multiplanar visualization and volume rendering are very encouraging. Most of the sonographic findings described in the 'radiological gamut' could be used in antenatal 3D exploration.

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Re: Trisomy 21: 91% detection rate using second-trimester ultrasound markers

DeVore's[1] very useful report providing likelihood ratios for positive and negative findings in the second-trimester anomaly scan unfortunately contains an error in the demonstration of the computation of the posterior risk in Table 7. The author states in the earlier discussion that the likelihood ratio should be multiplied by the prior risk to obtain the posterior risk. This is a common misunderstanding as the correct method is to multiply the likelihood ratio by the prior odds ratio in order to obtain the posterior odds ratio. With low risk the different methods have very similar results but with high risk there is a significant error (Table 1).

Table 1 Recalculation of likelihood ratio from DeVore's data

1 in risk x	*1: odds* x−*1*	*Likelihood ratio* y	*1: post odds* (x−*1*)/y	*1 in post risk* (x−*1*)/y + *1*
270	269	10.02	26.84630739	27.84630739
270	269	33.2785	8.083297024	9.08329702
270	269	182.582837	1.473303867	2.47330386
100	99	0.11	900	901
100	99	0.42	235.7142857	236.7142857

Although this is a common misunderstanding, I suspect that there could be an error in the transcription of the manuscript. Using the method shown:

1 1/risk
2 (1/risk) × LR – simplified this is the same as LR/risk
3 1/((1/risk) × LR) – simplified this is the same as risk/LR,

there is no need to go through the complications shown. Dividing risk by LR gives the same result.

The correct method[2] is:

1 1/(risk – 1)
2 (1/(risk – 1)) × LR
3 1/((1/(risk – 1)) × LR).

For those risks that are close to a decision threshold the different results could be critical and in any case it is important that the methods are correctly understood.

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Author's reply

I appreciate the comments expressed in this Letter to the Editor. In preparation of the manuscript and during the peer review process this issue was raised. At the present time there are three approaches that investigators have used when the risk is expressed as 1 in x. For discussion purposes we will use the risk of 1 in 100. One approach is to compute the decimal value for the risk by adding 1 to the denominator, i.e. 1/101. The second approach is to do as I did, and compute the decimal value by dividing 1 by 100. The third approach is the one expressed by

Table 1 Comparison of methods for calculating posterior risk

		New risk		
Maternal age (years)	*Maternal age risk (1 : x)*	*DeVore (1/x)*	*(1/(x + 1))*	*Hutchon (1/(x – 1))*
35	296	65	65	65
36	236	52	52	52
37	186	41	41	41
38	146	32	32	32
39	112	25	25	24
40	86	19	19	19
41	65	14	14	14
42	50	11	11	11
43	38	8	9	8
44	28	6	6	6
45	22	5	5	5
46	16	4	4	3
47	12	3	3	2