Fetal short femurs: interest of three-dimensional computed tomography in prenatal management

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Purpose

Osteochondrodysplasias (OCD) gather anomalies of the growth or the structure of the bones or the cartilages that precede them. Their prevalence in newborn is estimated between 2,3-4/10000 [1-3] and their frequency among perinatal death is 9/10000. A precise diagnosis is often difficult (60-65% by 2D ultrasonography [2-5]) whereas the evaluation of prognosis is accurate in more than 96% [5, 6]. Short femurs are frequent anomalies that can be observed in multiple conditions including OCD.

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The objective of our study is to estimate the performances of fetal bone computed tomography in management of short femur, to discriminate OCD and other etiologies (IUGR, constitutional short stature).

Methods and materials

We retrospectively analyzed 59 consecutives fetal bone scans performed at our center from 2006 to 2012. Only scans realized for short femurs were included.

All patients underwent referral ultrasound examination by high-frequency probes for transabdominal (4-8 MHz) and transvaginal (5-9 MHz) way (GE Voluson E8, GE Medical Systems, Ultrasound and Primary Care Diagnostic, Gif sur Yvette, France). The indication of CT scan was a multidisciplinary decision. The acquisition of images was performed by a 40-MDCT (Philips, 2005), until January 2011 and 64-MDCT until 2012 (General Electric, 2011).

The acquisition protocol was: no scout-view, from the pubis, 32-40 cm height, tube voltage: 80-140 kV, tube currents: 20-90 mAs, collimation : 0.9 mm, pitch : 0.6 mm.

The fetal irradiation: fetal effective dose was estimated by the CTDI (Computed Tomography Dose Index).

A pediatric radiologist conducted image reconstruction (MIP, 3D-VR) and analysis. A multidisciplinary team evaluated the images and proposed a diagnosis.

Monitoring of patients:

- Biological prenatal analysis were studied: karyotype, array CGH, FGFR3 mutation

- In case of suspected fetal affection of particular gravity and judged incurable at diagnosis, termination of pregnancy could be accepted, at parental request, in
accordance with the French law [7], and the results of the fetal post-mortem examination including standard X-rays were listed.

- In case of continuation of pregnancy: weight and height at birth, histological examination of placenta, pediatric examination at, at least, 6 months and if possible post natal X-rays were analyzed.

All these data defined the gold standard.

Statistical analysis: diagnostic performance of fetal bone scans to diagnose an OCD was evaluated as well as the ability of the association CT scan/ultrasonography to obtain an accurate diagnosis (sensitivity, specificity, positive predictive value, negative predictive value, the significance level was 0.05).

The radiological diagnosis was compared to postnatal or post-mortem radiographs.

**Results**

Over the period of the study 40 fetal bone scans were realized for short femur, 27/40 (59%) were isolated. The mean gestational age was 32 weeks (21-35+6).

The mean fetal effective dose estimated by CTDI was 2.5 mGy (0.49-12, # : 2.47).

Termination of pregnancy was accepted for 6 patients (15%).

The final diagnosis was: 10/40 (25%) OCD, 18/40 (45%) constitutional short statures, 12/40 (30%) IUGR.

The OCD were: 2 achondroplasias, 1 hypochondroplasia, 1 Spondyloepiphyseal dysplasia congenital, 1 Diastrophic dysplasia, 1 Asphyxiating thoracic dysplasia, 1 Chondroectodermal dysplasia, 1 Thanatophoric dysplasia, 1 Osteogenesis imperfect and 1 VACTERL association.

In management of fetal short femurs, CT had a sensitivity of 90 %, a specificity of 99.6 %, a PPV of 90% and a NPV of 99.6%, to differentiate OCD from other etiologies: 1 achondroplasia was not diagnose by imaging but by molecular analysis, and 1 fetal bone scan showed short femurs <1 percentile with anomalies of the lumbar interpedicular distance and large hipbone, that could not eliminate an hypochondroplasia.

The association ultrasound/computed tomography made an accurate diagnosis in 70% of cases. CT provided additional evidence in 60% of the cases: in one case of Thanatophoric
dysplasia it confirmed the diagnosis (Fig.1), in 3 cases made an accurate diagnosis without ultrasound diagnosis (Fig. 2), and corrected the diagnosis in 2 cases (Fig. 3).

CT alone was better than ultrasonography to diagnose abnormalities of the spine and hipbone. Conversely, CT was less accurate for the study of hands feet and skull.

There was a statistically significant difference between the OCD and non-OCD population when short femurs were not isolated and when all long bones were shortened.

These parameters were equivalent or superior to those of the study performed by Mace et al. [8] that were on their entire cohort (67 CT scans): sensitivity 82%, specificity 91%, PPV 90% and NPV 83 %.

Scanners made for short femurs have uncovered in 60 % additional signs and in 50 % of cases changed the diagnosis, close to the results of the study performed by Miyazaki et al. [9] with a change of diagnosis in 59% (10/17) against 15% (10/67 ) in the study performed by Mace et al. [8].

The threshold < 1 percentile seems accurate to avoid unnecessary irradiation of the fetus having no OCD.

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The disadvantages of the techniques are mainly the irradiation, which is in our study lower than the recommendations [10, 11], the motion artifacts of the fetus, and the poor analysis of bone mineralization.

Images for this section:
Fig. 1: Thanatophoric dysplasia: fetal bone scan MIP reconstruction, post-mortem X-ray: macrocrania, very short "twisted" long bones, platyspondyly, square iliac wings and medial and lateral osseous spurs, elongated narrow thorax.
**Fig. 2:** Asphyxiating thoracic dysplasia: fetal bone scan and post mortem X ray: narrow thorax, square iliac wings horizontal acetabular roofs, lateral osseous spurs.
Fig. 3: Chondroectodermal dysplasia: 3D ultrasound: short long bones right ectrodactyly; Fetal bone scan and post-mortem X-ray: bilateral polydactyly, L1 vertebra rostrum, square iliac wings, medial osseous spurs.
Conclusion

Our study confirms the importance of fetal bone scan in prenatal diagnosis of OCD including the indication of short femurs. A threshold < 1 percentile seems relevant to perform CT when short femurs are isolated.

Limitations:

There are several limitations of this study. First this is a retrospective study. Second there wasn't a blind study of the fetal bone scans by two radiologists, and a blind analysis of the scan from the results of the ultrasonography. Third, the short post-natal monitoring, as several OCD may reveal later, and finally the low number of OCD in our population.

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Bew ICRP recommendations, review.
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