Case Report

A Case Report on the Antenatal Three Dimensional Sonographic Features of Thanatophoric Dysplasia

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Thanatophoric dysplasia (TD) is a well-known fatal skeletal dysplasia in fetal life. It can be usually diagnosed by two-dimensional (2D) ultrasonography. However, three-dimensional (3D) ultrasonography, a new rapidly available technique, can be a useful addition to 2D ultrasonography for improving the visualization of the abnormalities and giving help when providing counseling to a family regarding the diagnosis and future recurrences. Here, the authors present the first experience in Songklanagarind Hospital in applying 3D ultrasonography in the diagnosis of fetal thanatophoric dysplasia.

Keywords: *Imaging, Three-dimensional, Prenatal diagnosis, Thanatophoric dysplasia, Ultrasonography, Prenatal*

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A 41-year-old Thai primigravida woman was sent to the Fetal Maternal Medicine Unit at 30 weeks' gestation for detailed ultrasonography because of inappropriate uterine size (size more than date) with suspicion of polyhydramnios. The parents themselves appeared healthy, with an unexceptional medical history and there was no apparent congenital malformation in the family background visible in any living relatives. The paternal age was 43 years old. The pregnancy had been conceived by intrauterine insemination (IUI) due to primary infertility from an unknown cause. A fetal study at the second trimester during an amniocentesis test, due to advanced maternal age, showed a normal male (46XY) chromosome. At 17 weeks' gestation, ultrasonographic examination was normal. Conventional two-dimensional ultrasound identified polyhydramnios, macrocephaly with clover-leaf skull, shortening of all long bones with normal echogenicity, a narrow chest, and a protuberant abdomen. TD was suspected after completion of the 2D ultrasonographic examinations. It was decided to acquire 3D ultrasound volume data to raise more details. Using an annular-array volume transducer real time 3D ultrasonography in surface rendering mode (Voluson 730Expert; GE Medical Systems, Kretztechnik, Zipf, Austria), frontal bossing, a depressed nasal bridge, short limbs, and increased subcutaneous tissues in the digits and limbs (Fig. 1A-D) were all observed. This constellation grouping of features is strongly indicative of thanatophoric dysplasia. After being appraised of the fetal prognosis and subsequently given counseling and guidance, the parents decided to terminate the pregnancy. The parent chose a cesarean section because of over-distended uterus. A male baby was delivered with a body weight of 1560 g. No neonatal resuscitation was attempted. The features identified from the 3D imaging were confirmed macroscopically (Fig. 2). A radiograph taken of the dead baby showed platyspondyly, a narrow chest, shortness femurs, and short of all long bones (Fig. 3A-C). However, the parents withheld their permission to allow any autopsy and histological examination.

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Discussion

Thanatophoric dysplasia (TD) is a fatal skeletal dysplasia first described by Marateaux and Lamy[1]. The incidence of this condition has been estimated to be approximately 1/10,000 livebirths[1]. It

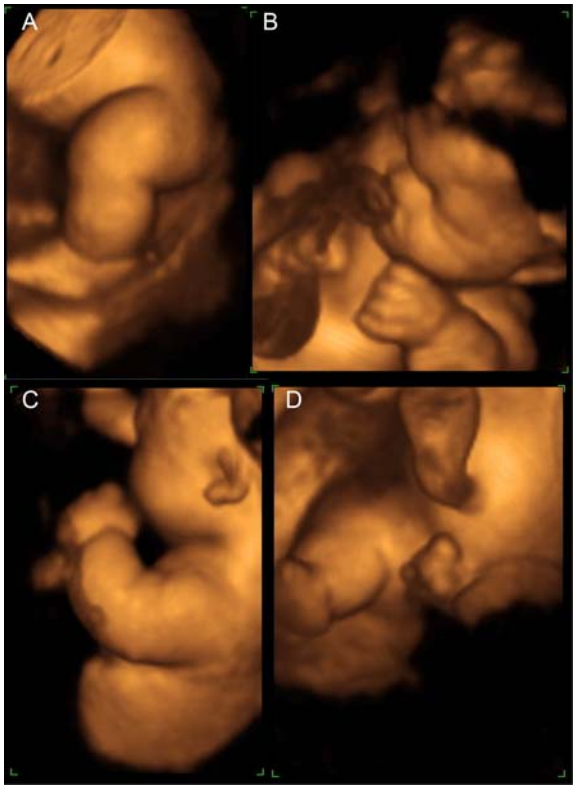

Fig. 1 Three-dimensional ultrasound images at 30 weeks of gestation images showing (A) increased subcutaneous tissues in the lower limbs, (B) frontal bossing and a depressed nasal bridge, (C) short upper limbs, (D) short lower limbs

Fig. 2 The Stillborn male infant with generally shortened extremities

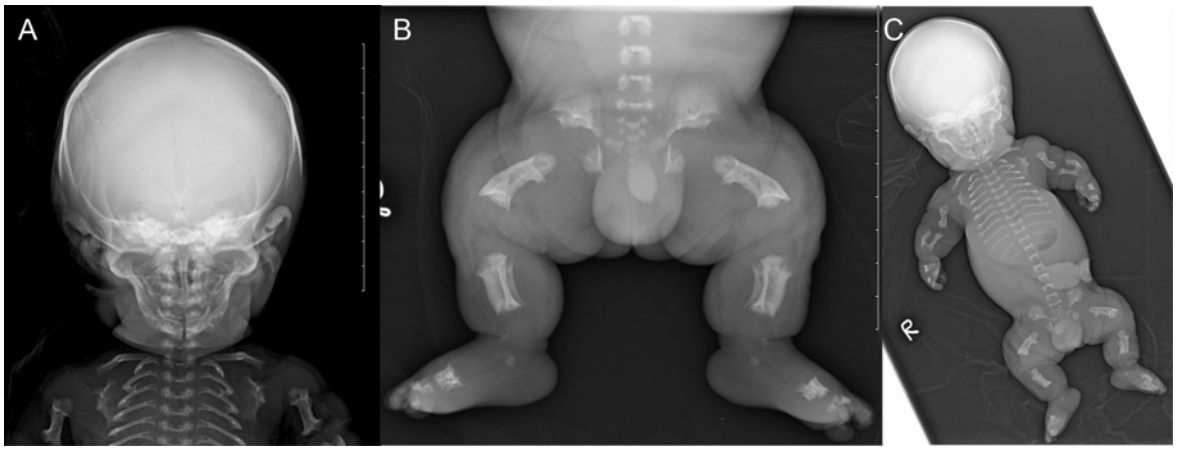

Fig. 3 Full postmortem body X-ray of the fetus showing (A) macrocephaly and short upper limbs, (B) very short and shaped like " French telephone receiver" (C) platyspondylia, narrowed thorax and generally shortened long bones

is caused by specific fibroblast growth factor receptor 3 (FGFR3) mutations[2].A fetus affected with TD is characterized by extreme shortening of the limbs, relative macrocephaly with frontal bossing, flattened vertebrae, disorganized chondrocytes and trabeculae in the growth plates of the long bones, and shortened ribs resulting in a reduced thorax and a bell-shaped abdomen[3]. The disease is classified according to the presence of curved (type I) as opposed to straight femurs (type II)[3]. An affected baby usually dies shortly after birth and death is often secondary to pulmonary hypoplasia caused by the small thoracic cavity, or necrosis of the cervical spine due to foramen magnum stenosis and resultant failure of respiratory control[1]. A definite diagnosis confirmed by pathological examination, a full postmortem body X- ray, histologic examination of affected bones, and molecular analysis of FGFR3[1-3].

Diagnosis obtained from prenatal screening is usually confirmed by 2D ultrasonographic findings. Typical 2D ultrasonographic finding are characterized by the detection of megacephaly with a cloverleaf-shaped skull, progressive hydrocephaly, polyhydramnios, a hypoplastic thorax that is disproportionately small in relation to the abdomen, short ribs and bones of the extremities, excess skin, and flattened vertebrae with diminution of the intervertebral spaces[4]. However, it is very difficult to describe this condition to the parents. Therefore, the additional 3D ultrasonography to accompany the 2D form can help the parents visualize the affected baby and easily comprehend the condition. The advantage of 3D ultrasonography for counseling has been acknowledged in many reports[5,6]. Using the surface-rendering tool of 3D ultrasonography is an ideal choice with this condition. This feature of the 3D package only receives signals from the surface of the region of interest. The data is electronically extracted, and the image is displayed on a monitor have a plastic-like appearance. The 3D ultrasonographic images do give more clarity of information than does the 2D ultrasonography. Using 2D ultrasonography, macrocephaly and shortness of long bones can be easily diagnosed by measurement the biparietal diameter (BPD), head circumference (HC), frontooccipital diameter (OFD), and bone length. The relation of chest and abdomen in the sagittal is used to diagnose the protuberant abdomen condition. However, 2D does not clearly reveal the characteristics of frontal bossing, depressed nasal bridge, and excess skin. Fortunately, the characteristic of frontal bossing, a depressed nasal bridge, and excess skin were obviously shown in the 3D plastic images of the presented patient (Fig. 3A-C). The 3D ultrasonographic image presents the facial TD profile better than 2D ultrasonographic image. Not only that, the 3D ultrasonographic technique can aid the physician in obtaining a better view of the baby when the fetal position is not good by allowing axial rotation of the image[7].

An association of TD, intrauterine insemination, and infertility has never previously been reviewed but the correlation of TD and high parental age has, and it shows the mean paternal age is slightly elevated when compared with a control population[8, 9]. Therefore, the recurrence may be possible in the presented patient. From the literature review, a useful method for early prenatal TD diagnosis is to measure the fetal nuchal translucency thickness (NT)[10,11]. This useful tool shows that the prevalence of TD is greater in fetuses with an increased NT and normal karyotype. The association between increased NT and TD may be the result of mediastinal compression by a narrow thorax and altered cutaneous composition.

The authors have presented a TD fetus diagnosed by 2D and 3D enhanced ultrasonography. The extra visualization from the 3D ultrasonography is a useful adjunct to the conventional 2D image in the prenatal diagnosis and subsequent counseling of TD. From our review, the authors suggest that NT screening in the first trimester should be advised for couples with a probability of a high recurrence.

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ลักษณะการตรวจวินิจฉัยก่อนคลอดด้วยคลื่นเสียงความถี่สูงสามมิติของทารกในครรภ์ที่เป็นโรคทารกพิการ แขนขาสั้นชนิดธานาโทโฟลิค

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โรคทารกพิการแขนขาสั้นชนิดธานาโทโฟลิคเป็นโรคในกลุ่มกระดูกแขนขาทารกผิดปกติที่พบบ่อย โดยทั่วไปสามารถให้การวินิจฉัยได้ด้วยการตรวจด้วยคลื่นเสียงความถี่สูงสองมิติสามารถให้การวินิจฉัยได้ แต่ในปัจจุบันการพัฒนาการตรวจด้วยคลื่นเสียงความถี่สูงสามมิติ สามารถช่วยเพิ่มความแม่นยำในการวินิจฉัยได้มากขึ้น เนื่องจากการตรวจด้วยคลื่นเสียงความถี่สูงสามมิติจะสามารถมองเห็นความผิดปกติของทารกได้ชัดเจนมากขึ้น นอกจากนี้ยังช่วยในการให้คำแนะนำในการรักษาหลังการวินิจฉัยได้ง่ายขึ้นเพราะหญิงตั้งครรภ์เข้าใจความพิการมากขึ้น ด้วยการมองเห็นภาพของทารกเสมือนลักษณะจริง ในรายงานฉบับนี้ผู้นิพนธ์นำเสนอถึงการวินิจฉัยทารกพิการ โรคทารกพิการแขนขาสั้นชนิดธานาโทโฟลิคด้วยคลื่นเสียงความถี่สูง สามมิติครั้งแรกของโรงพยาบาลสงขลานครินทร์