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Prenatal Diagnosis of Sirenomelia by Two-Dimensional and Three-Dimensional Skeletal Imaging Ultrasound

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Summary: This study sought to evaluate the contribution of two-dimensional ultrasound (2D-US) and three-dimensional skeletal imaging ultrasound (3D-SUIS) in the prenatal diagnosis of sirenomelia. Between September 2010 and April 2014, a prospective study was conducted in a single referral center using 3D-SUIS performed after 2D-US in 10 cases of sirenomelia. Diagnostic accuracy and detailed findings were compared with postnatal three-dimensional helical computed tomography (3D-HCT), radiological findings and autopsy. Pregnancy was terminated in all 10 sirenomelia cases, including 9 singletons and 1 conjoined twin pregnancy, for a total of 5 males and 5 females. These cases of sirenomelia were determined by autopsy and/or chromosomal examination. Initial 2D-US showed that there were 10 cases of oligohydramnios, bilateral renal agenesis, bladder agenesis, single umbilical artery, fusion of the lower limbs and spinal abnormalities; 8 cases of dipus or monopus; 2 cases of apus; and 8 cases of cardiac abnormalities. Subsequent 3D-SUIS showed that there were 9 cases of scoliosis, 10 cases of sacrococcygeal vertebra dysplasia, 3 cases of hemivertebra, 1 case of vertebral fusion, 3 cases of spina bifida, and 5 cases of rib abnormalities. 3D-SUIS identified significantly more skeletal abnormalities than did 2D-US, and its accuracy was 79.5% (70/88) compared with 3D-HCT and radiography. 3D-SUIS seems to be a useful complementary method to 2D-US and may improve the accuracy of identifying prenatal skeletal abnormalities related to sirenomelia.
Key words: sirenomelia; three-dimensional skeletal imaging ultrasound; three-dimensional helical computed tomography

Sirenomelia, also known as "mermaid syndrome", is a very rare congenital malformation. Sirenomelia is characterized by single or fused lower limbs associated with other abnormalities, such as bilateral renal agenesis, bladder agenesis and anal atresia[1–4].

Due to renal agenesis, sirenomelia is often associated with oligohydramnios[4, 5], which makes prenatal diagnosis of skeletal abnormalities using two-dimensional ultrasound (2D-US) or traditional three-dimensional ultrasound (3D-US) challenging. Compared with 2D- and 3D-US, three-dimensional helical computed tomography (3D-HCT) has greater accuracy and detail, although radiation exposure limits its application in prenatal diagnosis[4, 6]. Recently, three-dimensional skeletal imaging ultrasound (3D-SUIS) technology developed by Siemens was shown to delineate skeletal spatial relations by subtracting soft tissue and reconstructing skeletal features in different views. In our study, we applied 3D-SUIS to 10 sirenomelia cases after 2D-US, and we compared the results of 3D-SUIS with 3D-HCT, radiography and autopsy.

1 SUBJECTS AND METHODS

Between September 2010 and April 2014, 10 pregnant women whose fetuses had suspected or confirmed sirenomelia consented to undergo 3D-SUIS examination following conventional 2D-US. All enrolled pregnant women were elected to have an abortion. Postnatal radiography, 3D-HCT and autopsy of the fetuses were performed. During the first trimester, one case received nuchal translucency (NT) and villus chromosomal examination. Nine cases were examined in the second trimester, 8 of which received umbilical cord blood chromosomal examination.

2D-US and 3D-SUIS were performed with a Siemens S2000 (Siemens, Erlangen, Germany) ultrasound machine using 6C2 (2−6 MHz) and C7F2 transducers (2−7 MHz). After the pregnant women were examined using 2D-US, we changed to the C7F2 transducer and used three-dimensional sampling to acquire a volumetric image. At the same time, we rotated in the X, Y, and Z axes by defining an arbitrary point as the center of planes A, B, and C. To obtain the best image, we modified the dynamic range, brightness and contrast gradient and then stored the volume image. At the end, we selected and activated the 3D skeletal mode and adjusted the skeleton enhanced setting (range 0%–100%, high setting for enhanced bone tissue, low setting for reduced bone tissue). We adjusted the brightness and contrast gradient to optimize the best visual skeletal structure and then stored the image.

3D-HCT volume acquisitions were obtained with a multislice 64-detector computed tomography scanner

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(GE Healthcare, USA), with 64 slices per rotation, a pitch of 0.625 mm and slice thickness of 10 mm. For all examinations, we obtained agreement and consent from the pregnant women or their family members.

2 RESULTS

The age of the 10 pregnant women ranged from 23–26 years (24.5 years on average), and the time of prenatal ultrasound diagnosis ranged from 13.3–26.6 weeks (22 weeks on average). Of the 10 cases, 9 were singletons and 1 case involved conjoined twins. One case was in the first trimester [crown-rump length of 7.3 mm, age of 13.3 weeks and NT thickness of 1.8 mm], and the rest 9 cases were in the second trimester. The sex of the fetuses was determined by autopsy and/or chromosomal examination, with the results showing 5 males and 5 females. All 10 cases were associated with oligohydramnios, bilateral renal agenesis with absence of the bladder, single umbilical artery and spine abnormalities. Additionally, 8 cases showed cardiac abnormalities, 1 case had Dandy-walker syndrome, and 1 case showed congenital cystic adenomatoid malformation.

Detailed fetal skeletal abnormalities, as identified using 3D-SUIS, 3D-HCT and radiography, are shown in table 1. The accuracy and details related to lower limb abnormalities associated with sirenomelia were identical between 3D-SUIS, 3D-HCT and radiography (fig. 1).

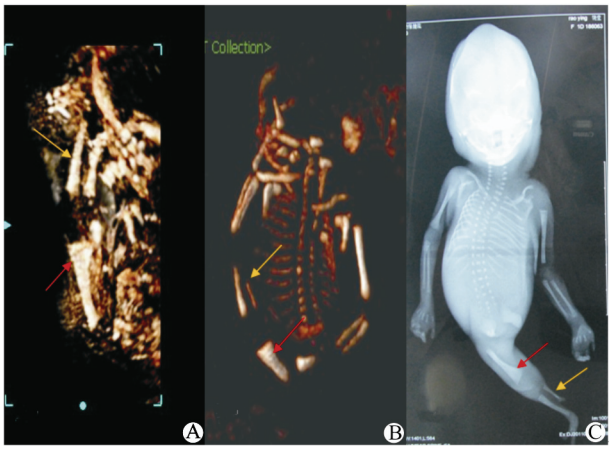

Fig. 1 Evaluation of the lower limbs in one case using 3D-SUIS (A), 3D-HCT (B) and radiography (C)
The images show a single femur with broad distal metaphysis (red arrow) and two tibias (yellow arrow).

Table 1 Details of fetal skeletal abnormalities detected on 3D-SUIS, 3D-HCT and radiography

Position of skeletal abnormalities		3D-SUS (*n*)	3D-HCT (*n*)	Radiography (*n*)
Lower limbs	Femur	10	10	10
	Tibia	10	10	10
	Fibula	10	10	10
Foot	Dipus or monopus	8	8	8
	Apus	2	2	2
Spine	Scoliosis	9	9	9
	Sacrococcygeal vertebra dysplasia	10	10	10
	Hemivertebra	4	4	4
	Butterfly vertebra	0	5	5
	Vertebra fusion	1	1	1
	Spina bifida	3	3	3
Rib	Absence	5	5	5
	Fusion	2	3	3
	Abnormal number of ribs	1	1	1
Pelvic	Ilium	0	3	3
	Ischium	0	9	9
Upper limbs	Ulna or radius	3	3	3
	Finger	2	2	2

For cases in the second trimester with normal amniotic fluid or oligohydramnios, 3D-SUIS could clearly detect abnormalities of the ribs, such as absence, fusion and an abnormal number of ribs (fig. 2). However, 3D-SUIS was not ideal for the diagnosis of rib abnormalities during the first trimester and failed to detect left rib fusion in one case.

3D-SUIS identified 9 cases of scoliosis, 10 cases of sacrococcygeal vertebra dysplasia, 3 cases of hemivertebra, 1 case of vertebra fusion, and 3 cases of spine bifida. These findings were consistent with those of 3D-HCT and radiography. However, for pelvic and spine imaging, 3D-SUIS was not as accurate as 3D-HCT or radiography in detecting abnormalities, such as butterfly vertebra and abnormalities of the ischium, pubis and symphysis pubis.

3 DISCUSSION

Sirenomelia is a rare congenital abnormality with an incidence between 1/60 000 and 1/100 000 births[4, 5, 7]. We diagnosed 10 cases of sirenomelia in 510 145 prenatal ultrasounds performed between September 2010 and April 2014 at our center (1.96/100 000). However, this number does not convey the actual incidence of sirenomelia in China, as our center is one of the most important prenatal diagnosis centers in central China and accepts many referral cases from other centers each year. All 10 cases of sirenomelia in our study came from five different regions of the Hubei province (approximately 180 000 square kilometers), including 4 cases from Wuhan city and 6 other cases from Hanchuan, Xiantao, Huangpi, Macheng, Honghu and Qichun. Although 80%

of pregnant women undergoing prenatal diagnosis in our center come from Wuhan city, the relationship between region and morbidity associated with sirenomelia requires further study.

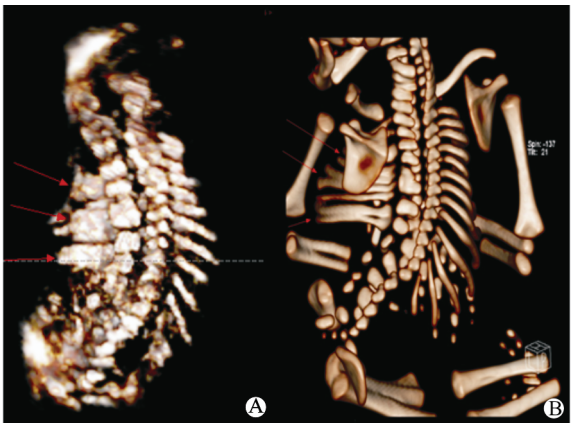

Fig. 2 Rib abnormalities detected using 3D-SUIS (A) and 3D-HCT (B) showing left rib fusion (red arrow)

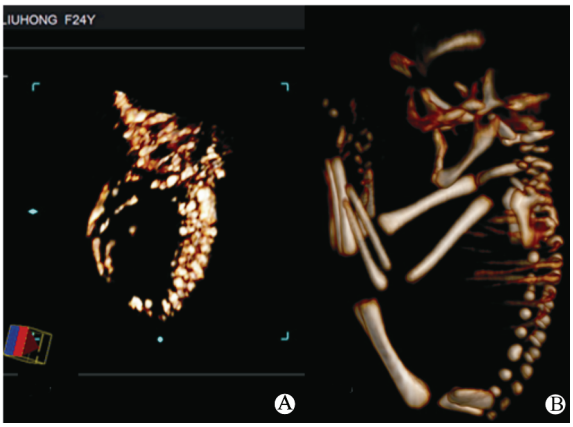

Fig. 3 Whole skeletal images of a first-trimester case using 3D-SUIS (A) and 3D-HCT (B)

As previously reported, sirenomelia is more common in identical twins and shows a male to female ratio of 2.7 to 1[1, 7]. Our study included 9 cases of singleton fetuses and one case of conjoined twins, and we identified 5 males and 5 females via chromosomal examination and/or autopsy without finding any chromosomal abnormalities. Approximately 22% of pregnant women were reported to have diabetes[7–9]; however, we did not find similar histories in this study. Based on the literature, sirenomelia is more common in pregnant women younger than the age of 20[3, 10], although in our study, the age of the pregnant women ranged from 23–26 years (24.5 years on average).

The causes of sirenomelia remain unclear, although vitelline artery steal syndrome has been proposed by some authors[5, 7, 11]. This hypothesis is based on the presumption that a large artery, which is likely a derivative of the vitelline artery, arises from the aorta high in the abdominal cavity beyond which the aorta and its branches are hypoplastic. The "vascular steal theory" proposes that a single large artery assumes the function of the umbilical arteries, thus diverting blood flow from the caudal portion of the embryo to the placenta. Moreover, the vitelline umbilical artery is thought to "steal" blood and nutrition from the lower body and divert it to the placenta, which results in a small aorta and variable absence of the arteries that supply the kidneys, large intestine, and genitalia. These changes result in maldevelopment of the terminal bowel, kidneys, bladder, genital organs and pelvic bones. In our study, all 10 cases had a single umbilical artery, and we found several small branches off the iliac artery in 6 cases with prenatal ultrasound and similar branches in 7 cases via autopsy; these results are consistent with a prior report[12].

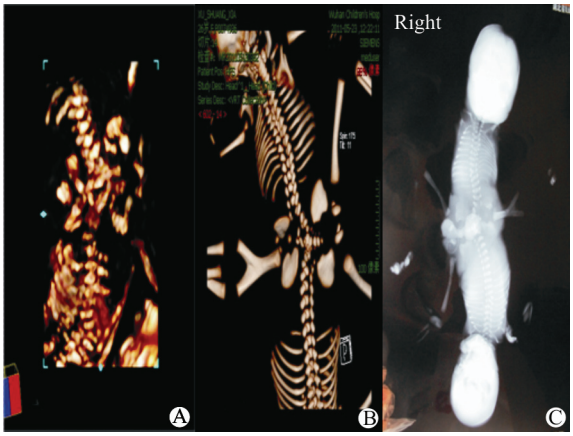

Fig. 4 Spine fusion of conjoined twins detected using 3D-SUIS (A), 3D-HCT (B) and radiography (C)
3D-SUIS could present distinct fused imaging of the ilium and ischium in conjoined twins. However, 3D-SUIS is not as effective at indicating pelvic abnormalities as 3D-HCT.

Although radiography and 3D-HCT represent gold standards for the diagnosis of skeletal diseases, both are rarely used in pregnancy due to radiation exposure, which is the most significant challenge in the diagnosis of fetal skeletal diseases. Compared with 2D-US and 3D-US, 3D-SUIS can generate skeletal images similar to 3D-HCT by subtracting soft tissue and enhancing skeletal signals. Stocker classified sirenomelia into 7 types (type Ⅰ to type Ⅶ) according to the malformation grade of the lower extremities[13]. We identified 3 cases of type Ⅳ, 1 case of type Ⅴ, and 1 case of type Ⅵ using 3D-SUIS (table 2), and the remainder of cases could not be classified according to these criteria because they represented unusual forms of sirenomelia.

Sirenomelia is associated with multiple abnormalities, among which spine and rib abnormalities account for 21.4% of all cases[14]. In our study, we found that all cases were associated with spine abnormalities, including 9 cases of scoliosis, 10 cases of sacrococcygeal vertebral dysplasia, 3 cases of hemivertebra, 1 case of vertebra fusion, and 3 cases of spina bifida detected using 3D-SUIS, and we also clearly detected 5 cases of rib abnormalities (absence, fusion and abnormal number of ribs). In addition, in the first trimester, 3D-SUIS could display the whole skeleton almost as effectively as 3D-HCT (fig. 3). In addition to displaying the whole skeleton, 3D-SUIS could present fused imaging of the ilium and ischium in conjoined twins (fig. 4). However, 3D-SUIS is not as effective at indicating pelvic abnormalities as 3D-HCT.

Table 2 Details of lower limb anatomy in 10 cases of sirenomelia detected on 3D-SUIS according to the Stocker and Heifetz classification

Case	Femur	Tibia	Fibula	Foot	Classification
1	Single	Single	Absent	Apus	Ⅵ
2	Partially fused	Two	Single	Monopus	Ⅳ
3	Single	Two	Absent	Monopus	?
4	Single	Single	Absent	Monopus	?
5 (conjoined twins)	Partially fused	Two	Single	Monopus	Ⅳ
6	Partially fused	Two	Absent	Monopus	Ⅴ
7	Single	Two	Two	Monopus	?
8	Single	Two	Absent	Monopus	?
9	Single	Two	Absent	Apus	?
10	Partially fused	Two	Single	monopus	Ⅳ

Upper limb defects, including maldevelopment of the radius, shortened upper extremities, and lobster claw deformity, have been found in approximately one third of sirenomelia cases[14]. In the conjoined twins case in our study, we detected all of the above abnormalities; the fetus with normal lower limbs manifested the absence of a right radius and right polydactylism, while the other fetus with sirenomelia showed associated Dandy-Walker syndrome, left lobster claw deformity, and absence of the left upper extremity and right radius. This case demonstrated multiple complicated deformities associated with conjoined twins and sirenomelia.

Due to its association with fetal renal agenesis, sirenomelia is generally accompanied by oligohydramnios or anhydramnios[4, 5, 14]. However, in our study, the first-trimester case showed a normal amount of amniotic fluid, likely because in early pregnancy, amniotic fluid does not come from the fetal kidneys. Although approximately 10%–15% of sirenomelia occurs in twins (mainly monozygous)[1, 15, 16], sirenomelia has not been previously reported in conjoined twins. In our study, the conjoined twins showed normal amniotic fluid, although the sirenomelia fetus suffered from renal agenesis whereas the other fetus had normal bilateral kidneys.

Cardiac abnormalities are present in 20.6% of fetuses with sirenomelia[14], although 82% of cases in our study showed cardiac abnormalities, which is significantly higher than previously reported. This difference may be due to advances in imaging technology and emphasizes the importance of detecting cardiac abnormalities in sirenomelia.

In conclusion, combined with 2D-US, 3D-SUIS can provide accurate information for the diagnosis of sirenomelia and may also contribute to the prenatal diagnosis of other skeletal abnormalities.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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