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Taiwanese Journal of Obstetrics & Gynecology 52 (2013) 90–96

www.tjog-online.com

Short Communication

Prenatal diagnosis of fetal congenital cystic adenomatoid malformation of the lung using three-dimensional ultrasound: Comparison between the 20th and 21st centuries

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Accepted 12 October 2012

Abstract

Objective: Congenital cystic adenomatoid malformation of the lung (CCAML) is one of the most common lung lesions diagnosed prenatally. In order to compare the trends and improvements of prenatal diagnosis of CCAML, we herein retrospectively reviewed our cases of fetal CCAML detected by three-dimensional ultrasound (3-D US) between two centuries.

Materials and Methods: We reviewed our computer database of prenatal diagnosis of CCAML in National Cheng Kung University Hospital from October 1994 to November 2011. All of the fetuses were initially scanned by two-dimensional (2-D) US to locate the region-of-interest (ROI). Then, the 3-D probe was used to scan all of the ROI systematically and mechanically, and the images were stored in the laser discs for further 3-D visualization and reconstruction. To compare the characteristics at prenatal diagnosis of CCAML between the 20th and 21st centuries in our hospital, Chi-square tests were undertaken. A p value <0.05 was considered as statistically significant.

Results: In total, 58 fetuses with CCAML were depicted by 3-D US *in utero* (12 cases were diagnosed in the 20th century and 46 cases in the 21st century). The ranges of gestational age at prenatal diagnosis of CCAML by 3-D US in the 20th century were between 15 and 36 weeks (mean = 24 weeks), and were between 16 and 31 weeks (mean = 22 weeks) in the 21st century. Moreover, nine cases (75%) were diagnosed at the second trimester in the 20th century, whereas 44 cases (96%) were diagnosed at the second trimester in the 21st century.

Conclusion: The advancement of 3-D US has remarkable advantages in adding novel visual depiction of a 3-D lesion of a 3-D fetus in 3-D US after reconstruction, and thus assists substantially in the prenatal diagnosis and genetic consultation of CCAML. Furthermore, the trend analysis in this series showed a significantly earlier gestational age at prenatal diagnosis of CCAML in the 21st century than that in the 20th century.

Keywords: fetal congenital cystic adenomatoid malformation of the lung (CCAML); prenatal diagnosis; three-dimensional ultrasound

Introduction

Congenital cystic adenomatoid malformation of the lung (CCAML) is one of the most common lung lesions diagnosed prenatally, although the prevalence of CCAML is relatively low (around 0.003–0.004%) [1,2]. CCAML is a developmental malformation of the lower respiratory tract, which results from abnormalities of branching morphogenesis of the lung. The different types of CCAML are considered to originate at different levels of the tracheobronchial tree and at different stages of fetal lung development *in utero* [3–5].

CCAML is classified as macrocystic or microcystic, based on prenatal ultrasound appearance, and these masses are most commonly identified in the second trimester [6]. Macrocysts

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1028-4559/$ - see front matter
http://dx.doi.org/10.1016/j.tjog.2012.10.004

(type I) are anechoic and usually surrounded by hyperechogenic lung parenchyma. Microcysts (type III) appear as a homogeneous and solid mass that is hyper-echogenic compared to the adjacent normal lung parenchyma. Mixed lesions also occur (type II). Some studies find that lesions regress during the course of gestation in as many as 59% of cases [7–11]. Furthermore, complete spontaneous resolution in the postnatal period has been reported in a small number of cases [6,10–13].

To date, three-dimensional ultrasound (3-D US) has been applied in many fields. 3-D US can assess fetal organ volumes and diagnose congenital anomalies *in utero* [19–30]. With recent advancements of 3-D US, multiplanar orthogonal view, as well as reconstruction of surface-rendering modes, become feasible and have advantages in the differential diagnosis of fetal chest masses [19–30]. In order to compare the trends and improvements of prenatal diagnosis of CCAML, we herein retrospectively reviewed our computer database of fetal CCAML detected by 3-D US from 1994 to 2011.

Materials and methods

Patients and setting

From October 1994 to November 2011, the records of patients with fetal CCAML by 3-D US were reviewed. In general, the patients were referred from local practitioners or from the Antenatal Care Clinic of National Cheng Kung University Hospital. The setting was at the Prenatal Ultrasound Lab of the Department of Obstetrics and Gynecology, National Cheng Kung University Hospital, which is the largest national tertiary medical center in Southern Taiwan. All of the fetuses were followed to the end of pregnancy to confirm the diagnosis of CCAML. Informed consent was given by the patients. The study was approved by the Institutional Review Board, National Cheng Kung University Hospital (IRB, ER-99-011).

Equipment

We used conventional 3-D US scanners for prenatal screening. The 3-D US machines were Voluson 530D (Kretz, Zipf, Austria), or Voluson 730 (GE, Milwaukee, WI, USA) and Accuvix V20 (Medison, Seoul, Korea). The details of 3-D US scanning have been described elsewhere [19–30]. In brief, the fetus with CCAML was initially scanned by two-dimensional (2-D) US to locate the region-of-interest (ROI). Then, the 3-D probe was used to scan all of the ROI systematically and mechanically and the images were stored in the laser discs for further 3-D visualization and reconstruction. Subsequently, the 3-D images were demonstrated on the screen. First, the multiplanar orthogonal view was illustrated. Second, reconstructions of various modes were depicted, including the surface-rendering mode, the transparent mode and the maximal intensity mode.

Statistics

In order to compare the clinical characteristics at prenatal diagnosis of CCAML between the 20th and 21st centuries in National Cheng Kung University Hospital, Chi-square tests were undertaken. A p value <0.05 was considered as statistically significant.

Results

During the study period between October 1994 and November 2011, 58 fetuses with CCAML were depicted by 3-D US *in utero* (Tables 1 and 2). Table 1 shows the cases (total = 12 cases) diagnosed before January 2000, and Table 2 lists the cases (total = 46 cases) diagnosed from January 2000 to November 2011. The ranges of gestational age at prenatal diagnosis of CCAML by 3-D US in the 20th century were between 15 and 36 weeks (mean = 24 weeks), and were between 16 and 31 weeks (mean = 22 weeks) in the 21st century. Notably, all of the cases were diagnosed after the first trimester. However, nine cases (75%) were diagnosed at the second trimester in the 20th century, but 44 cases (96%) were diagnosed at the second trimester in the 21st century.

Furthermore, a total of 17 cases were complicated with other additional abnormalities. As listed in Table 1, three cases

Table 1
Prenatal diagnosis of fetal congenital cystic adenomatoid malformation of the lung (CCAML) using 3-D US in the 20th century.

Case no.	Maternal age (y)	Pregnancy history	Gestational age (wk)	US diagnosis	Outcome	Karyotype	Associated conditions
1	29	G1P0	15	CCAML type I	VD	46,XX	—
2	31	G2P1	20	CCAML type III	TOP	ND	EIF
3	27	G3P2	21	CCAML type II	TOP	ND	Heart deviation, hydrops
4	21	G2P1	21	CCAML type III	Follow-up	ND	—
5	25	G1P0	21	CCAML type III	TOP	ND	Heart deviation, CPC, EIF
6	23	G1P0	22	CCAML type III	Follow-up	ND	—
7	31	G1P0	23	CCAML type II	TOP	45,X/46,XX	—
8	29	G3P1A1	24	CCAML type I	VD	46,XX	—
9	32	G2P1	26	CCAML type I	PTL	ND	Fetal death
10	32	G1P0	28	CCAML type III	VD	ND	—
11	34	G1P0	28	CCAML type III	Follow-up	ND	—
12	22	G2P1	36	CCAML type III	VBAC	ND	—

CPC = choroid plexus cyst; EIF = echogenic intracardiac focus; Follow-up = follow-up at outside clinics; ND = not done; PTL = preterm labor; TOP = termination of pregnancy; VBAC = vaginal birth after cesarean section; VD = vaginal delivery.

Table 2
Prenatal diagnosis of fetal congenital cystic adenomatoid malformation of the lung (CCAML) using 3-D US in the 21st century.

Case no.	Maternal age (y)	Pregnancy history	Gestational age (wk)	US diagnosis	Outcome	Karyotype	Associated conditions
1	28	G1P0	16	CCAML type III	TOP	ND	Heart deviation
2	29	G1P0	17	CCAML type III	TOP	ND	Heart deviation
3	35	G2P1	18	CCAML type III	Follow-up	ND	—
4	28	G1P0	19	CCAML type II	Follow-up	ND	—
5	31	G2P0A1	19	CCAML type II	Follow-up	ND	—
6	28	G3P2	20	CCAML type III	Follow-up	ND	—
7	24	G2P1	20	CCAML type II	Follow-up	ND	—
8	34	G1P0	20	CCAML type II	Follow-up	ND	EIF
9	19	G1P0	20	CCAML type III	Follow-up	ND	—
10	21	G2P0A1	20	CCAML type III	C/S	46,XY	Twin pregnancy, EIF
11	28	G1P0	21	CCAML type III	VD	ND	Poly-hydramnios
12	27	G1P0	21	CCAML type I	VD	46,XX	—
13	25	G1P0	21	CCAML type III	Follow-up	ND	—
14	32	G1P0	21	CCAML type II	VD	46,XX	—
15	32	G2P1	21	CCAML type III	Follow-up	ND	—
16	36	G1P0	21	CCAML type II	Follow-up	46,XX	—
17	30	G1P0	21	CCAML type III	Follow-up	46,XX	Triplet pregnancy
18	26	G3P2	21	CCAML type III	Follow-up	ND	Heart deviation
19	27	G2P1	21	CCAML type II	Follow-up	ND	EIF
20	29	G1P0	21	CCAML type III	TOP	ND	—
21	25	G1P0	22	CCAML type I	Follow-up	46,XX	Oligo-hydramnios, IUGR
22	31	G1P0	22	CCAML type III	Follow-up	ND	—
23	30	G1P0	22	CCAML type III	VD	ND	—
24	23	G1P0	22	CCAML type III	TOP	ND	—
25	32	G2P1	22	CCAML type II	Follow-up	ND	—
26	36	G1P0	23	CCAML type III	TOP	46,XY	—
27	36	G3P0A2	23	CCAML type III	Follow-up	46,XY	—
28	30	G1P0	23	CCAML type II	TOP	ND	Heart deviation
29	30	G2P1	23	CCAML type III	Follow-up	ND	—
30	29	G2P1	23	CCAML type III	VD	46,XX	—
31	21	G3P2	23	CCAML type III	Follow-up	ND	—
32	23	G2P1	23	CCAML type I	Follow-up	ND	—
33	29	G1P0	23	CCAML type III	Follow-up	ND	—
34	29	G3P2	24	CCAML type III	VD	ND	—
35	23	G1P0	24	CCAML type III	TOP	ND	Heart deviation
36	21	G3P1A1	24	CCAML type II	TOP	ND	Heart deviation
37	37	G2P1	24	CCAML type III	C/S	46,XX	—
38	31	G1P0	24	CCAML type III	TOP	ND	MCM EIF
39	26	G2P0A1	24	CCAML type III	Follow-up	46,XY	—
40	25	G2P1	25	CCAML type III	Follow-up	ND	—
41	28	G1P0	25	CCAML type II	TOP	ND	Hydrops
42	25	G1P0	26	CCAML type I	Follow-up	ND	—
43	30	G2P1	27	CCAML type III	Follow-up	ND	—
44	32	G4P3	27	CCAML type II	Follow-up	ND	Hydrops
45	36	G2P1	31	CCAML type III	C/S	ND	—
46	33	G1P0	31	CCAML type III	Follow-up	ND	—

C/S = cesarean section; EIF = echogenic intracardiac focus; Follow-up = follow-up at outside clinics; IUGR = intrauterine growth retardation; MGM = mega cisterna magna; ND = not done; TOP = termination of pregnancy; VD = vaginal delivery.

(25%) in the 20th century, with associated anomalies, were as follows: heart deviation (2 cases), echogenic intracardiac focus (2 cases), choroid plexus cyst (1 case), and hydrops fetalis (1 case). As listed in Table 2, 14 cases (30%) in the 21st century, with associated anomalies, were as follows: heart deviation (6 cases), echogenic intracardiac focus (4 cases), polyhydramnios (1 case), oligohydramnios (1 case), intrauterine growth retardation (1 case), mega cisterna magna (1 case), and hydrops fetalis (2 cases). Moreover, in a total of 14 fetuses with karyotyping, only one case (7%) had chromosomal abnormalities (45, X/46, XX).

Both the accuracy rate of prenatal diagnosis of CCAML by 2-D and 3-D US were 100%, but 3-D US can provide additional illustrations in 3-D after various modes of reconstruction, and thus can depict additional abnormalities more easily and evaluate fetal volume more precisely. Nevertheless, the pictures of 3-D US can reveal three orthogonal planes, including coronal, sagittal and axial views, of a fetus with CCAML, that allow the parents to have a better understanding of the fetal malformation. Besides, the additional illustrations in 3-D US can reduce the discrepancy in decision making and prenatal consultation between patients and obstetricians (Figs. 1–4).

As listed in Table 3, the trend analysis showed that the gestational age at prenatal diagnosis of CCAML in the 21st century was significantly earlier than that in the 20th century ($p < 0.05$). The mean gestational age at prenatal diagnosis in the 21st century was 22 weeks of gestation, while the mean gestational age in the 20th century was 24 weeks of gestation. Of interest, nine cases (75%) were diagnosed at the second trimester in the 20th century, but 44 cases (96%) were diagnosed at the second trimester in the 21st century.

Discussion

Comparison of gestational age at prenatal diagnosis

With the development of clinical use and improvement of reconstruction technology in 3-D US over the past decade, we investigate if there are any differences in timing and accuracy of the diagnosis of fetal CCAML by 3-D US between the centuries. Therefore, we compared the cases of CCAML in the 20th century with those in the 21st century (Table 3), and the results confirmed that the gestational age at prenatal diagnosis of CCAML in the 21st century was significantly earlier than that in the 20th century ($p < 0.05$). The possible reasons for the phenomenon of earlier diagnosis of CCAML may be due to the following factors: (1) the improvement of 3-D US machines [19–30]; and (2) the improved technique and elevated awareness of physicians. As mentioned in previous studies [19–30], 3-D US has advantages in adding novel a visual depiction of a 3-D lesion of a 3-D fetus in 3-D US after reconstruction, and thus substantially assists in the prenatal consultation and genetic screening. Besides, 3-D US is also helpful in the diagnosis of fetal malformation and fetal dysmorphology, and has an important impact on the fetal outcome and delivery management [19–30]. From this series, we further validated the clinical use of 3-D US in the prenatal diagnosis of CCAML.

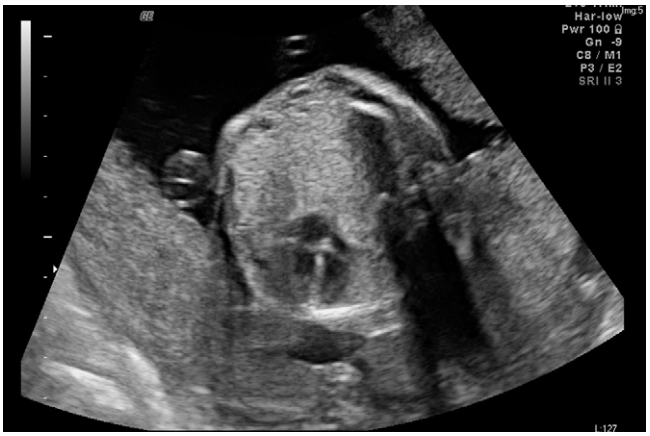

Fig. 2. Prenatal 2-D ultrasound of CCAML type III at 21 weeks of gestation with heart deviation (the same case as in Fig. 1).

Comparison of maternal age

In the 20th century, only one case (8%) had advanced maternal age, while seven cases (15%) with advanced maternal age were observed in the 21st century. In the 20th century, the mean maternal age with CCAML fetuses was 28 years, while the mean maternal age was 28.7 years in the 21st century. From these comparisons, the maternal age did not change significantly between the two centuries.

Comparison of associated anomalies

There are studies which mention that microcystic lesions may be associated with hydrops and a poor prognosis, while fetuses with macrocystic lesions usually do not have hydrops and are more likely to survive [14]. Nevertheless, some reports find that the combination of polyhydramnios, fetal hydrops,

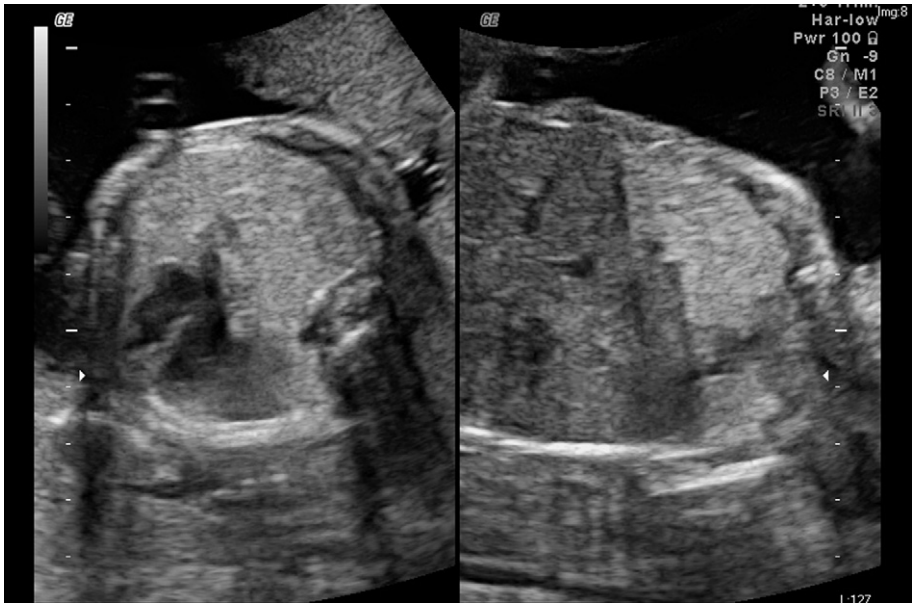

Fig. 1. Prenatal 2-D ultrasound of congenital cystic adenomatoid malformation of the lung (CCAML) type III at 21 weeks of gestation.

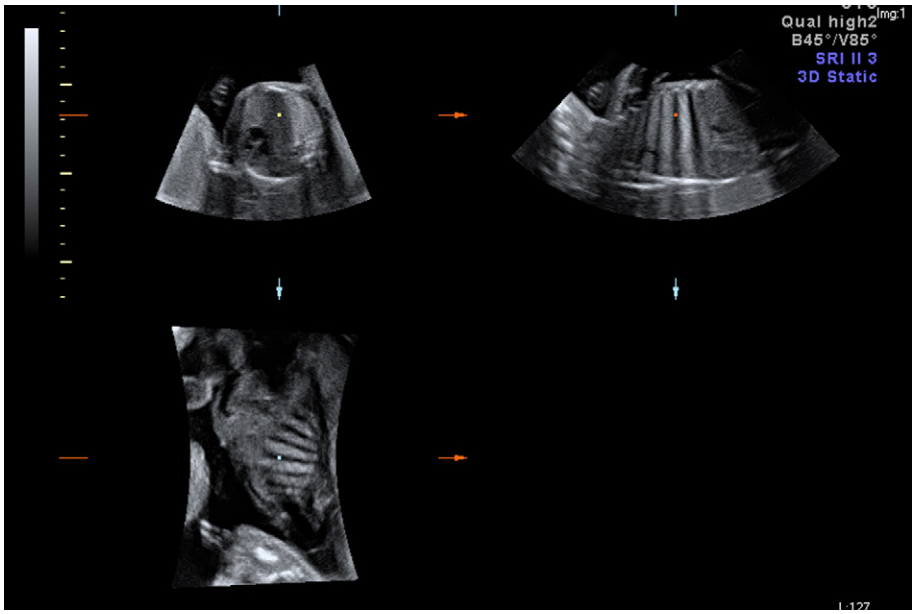

Fig. 3. Prenatal 3-D ultrasound (multiplanar orthogonal view) of CCAML type III at 21 weeks of gestation (the same case as in Fig. 1).

and a small lung to thorax transverse area ratio, was predictive of increased mortality and severe respiratory compromise [15]. Moreover, 10–20% of patients with CCAML have associated congenital abnormalities, such as esophageal atresia with tracheoesophageal fistula, bilateral renal agenesis or dysgenesis, intestinal atresia, other pulmonary malformations, and diaphragmatic, cardiac, central nervous system, and bony anomalies [16,17].

However, in our series, three cases (25%) were complicated with other associated abnormalities in the 20th century, including heart deviation (2 cases), echogenic intracardiac focus (2 cases), choroid plexus cyst (1 case), and hydrops fetalis (1 case). In the 21st century, 14 cases (30%) were complicated with other abnormalities, namely, heart deviation (6 cases), echogenic intracardiac focus (4 cases), polyhydramnios (1 case), oligohydramnios (1 case), intrauterine growth retardation (1 case), mega cisterna magna (1 case), and hydrops fetalis (2 cases). From these comparisons, the incidence of hydrops fetalis and associated anomalies did not change significantly between the two centuries.

On prenatal consultation of the prognosis of CCAML, the prenatal course of CCAML depends on the gestational age, size of the mass, amount of mediastinal shift, fetal hemodynamics, and associated anomalies. The risk of chromosomal

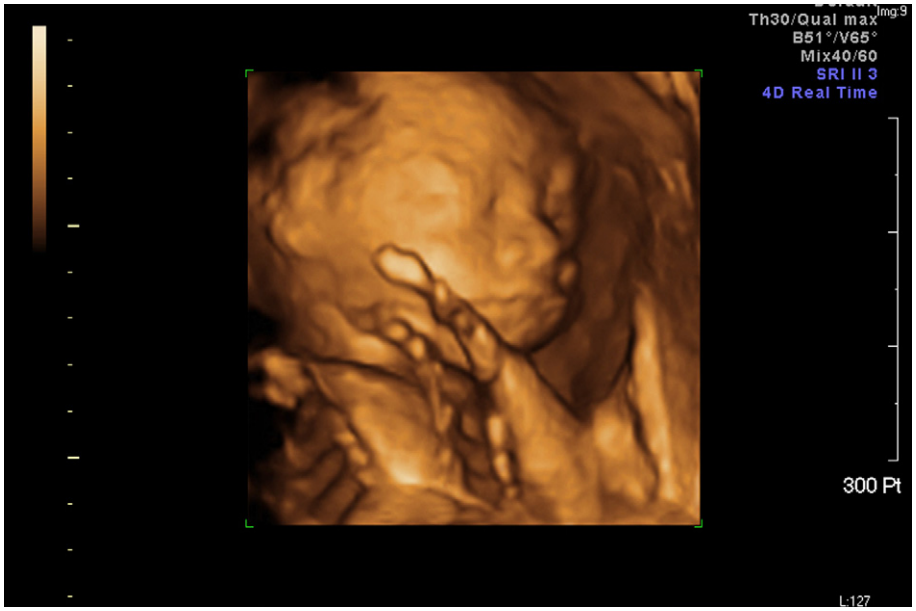

Fig. 4. Prenatal 3-D ultrasound (surface render mode) of CCAML type III at 21 weeks of gestation (the same case as in Fig. 1).

Table 3
Comparison of gestational age at diagnosis of fetal congenital cystic adenomatoid malformation of the lung (CCAML) by 3-D US.

	Mean maternal age (y)	Second trimester (15–28 wk)	Third trimester (≥28 wk)	Total cases
20th century (1994–2000)	28.0	9 (75%)	3 (25%)	12 (100%)
21st century (2000–2011)	28.7	44 (96%)	2 (4%)	46 (100%)

$p = 0.02$ by Chi-square test.

abnormalities is increased in fetuses with additional anomalies or nonimmune hydrops [2–18]. In addition, various effects of maternal–placental complications and fetal aneuploidy have to be considered on prenatal diagnosis of a congenital anomaly [31–37]. Moreover, the impacts of fetal biometry and amniotic fluid amount have to be comprehensively deciphered on the prenatal diagnosis of a congenital anomaly [38,39]. CCAML is not an exception. Therefore, it is very important for prenatal consultation to precisely depict fetal CCAML, with or without associated anomalies, abnormal karyotyping, or fetal hydrops as well, as to predict fetal prognosis.

In conclusion, more cases of CCAML were detected in the 21st century, and the gestational age at prenatal diagnosis of CCAML in the 21st century was significantly earlier that in the last century. Over the past decades, we have engaged in the development of the clinical use of 3-D US in fetal medicine [19–29]. From this series, we further prove that 3-D US can be applied in the antenatal diagnosis of a fetal congenital anomaly, and thus has substantial advantages in clinical medicine.

Acknowledgments

We are grateful to the staff of the Prenatal Ultrasound Lab of the Department of Obstetrics and Gynecology, National Cheng Kung University Hospital. This series was supported in part by a grant from the National Science Council, Executive Yuan, Taipei, Taiwan.

References

[1] Curran PF, Jelin EB, Rand L, Hirose S, Feldstein VA, Goldstein RB, et al. Prenatal steroids for microcystic congenital cystic adenomatoid malformations. J Pediatr Surg 2010;45:145–50.
[2] Daltro P, Werner H, Gasparetto TD, Domingues RC, Rodrigues L, Marchiori E, et al. Congenital chest malformations: a multimodality approach with emphasis on fetal MR imaging. Radiographics 2010;30:385–95.
[3] Priest JR, Williams GM, Hill DA, Dehner LP, Jaffé A. Pulmonary cysts in early childhood and the risk of malignancy. Pediatr Pulmonol 2009;44:14–30.
[4] Kunisaki SM, Fauza DO, Nemes LP, Barnewolt CE, Estroff JA, Kozakewich HP, et al. Bronchial atresia: the hidden pathology within a spectrum of prenatally diagnosed lung masses. J Pediatr Surg 2006;41:61–5.
[5] Riedlinger WF, Vargas SO, Jennings RW, Estroff JA, Barnewolt CE, Lillehei CW, et al. Bronchial atresia is common to extralobar sequestration, intralobar sequestration, congenital cystic adenomatoid malformation, and lobar emphysema. Pediatr Dev Pathol 2006;9:361–73.
[6] Adzick NS, Harrison MR, Crombleholme TM, Flake AW, Howell LJ. Fetal lung lesions: management and outcome. Am J Obstet Gynecol 1998;179:884–9.
[7] Hsu KF, Wu MH, Chang CH, Yao BL, Chang FM. Complete intrauterine resolution of fetal congenital cystic adenomatoid malformation of the lung type III. J Ultrasound Med 1995;14:871–5.
[8] Duncombe GJ, Dickinson JE, Kikiros CS. Prenatal diagnosis and management of congenital cystic adenomatoid malformation of the lung. Am J Obstet Gynecol 2002;187:950–4.
[9] Laberge JM, Flageole H, Pugash D, Khalife S, Blair G, Filiatrault D, et al. Outcome of the prenatally diagnosed congenital cystic adenomatoid lung malformation: a Canadian experience. Fetal Diagn Ther 2001;16:178–86.
[10] Sauvat F, Michel JL, Benachi A, Emond S, Revillon Y. Management of asymptomatic neonatal cystic adenomatoid malformations. J Pediatr Surg 2003;38:548–52.
[11] Revillon Y, Jan D, Plattner V, Sonigo P, Dommergues M, Mandelbrot L, et al. Congenital cystic adenomatoid malformation of the lung: prenatal management and prognosis. J Pediatr Surg 1993;28:1009–11.
[12] Ankermann T, Oppermann HC, Engler S, Leuschner I, Von Kaisenberg CS. Congenital masses of the lung, cystic adenomatoid malformation versus congenital lobar emphysema: prenatal diagnosis and implications for postnatal treatment. J Ultrasound Med 2004;23:1379–84.
[13] Maas KL, Feldstein VA, Goldstein RB, Filly RA. Sonographic detection of bilateral fetal chest masses: report of three cases. J Ultrasound Med 1997;16:647–52.
[14] Azizkhan RG, Crombleholme TM. Congenital cystic lung disease: contemporary antenatal and postnatal management. Pediatr Surg Int 2008;24:643–57.
[15] Adzick NS, Harrison MR, Glick PL, Golbus MS, Anderson RL, Mahony BS, et al. Fetal cystic adenomatoid malformation: prenatal diagnosis and natural history. J Pediatr Surg 1985;20:483–8.
[16] Usui N, Kamata S, Sawai T, Kamiyama M, Okuyama H, Kubota A, et al. Outcome predictors for infants with cystic lung disease. J Pediatr Surg 2004;39:603–6.
[17] Schott S, Mackensen-Haen S, Wallwiener M, Meyberg-Solomayer G, Kagan KO. Cystic adenomatoid malformation of the lung causing hydrops fetalis: case report and review of the literature. Arch Gynecol Obstet 2009;280:293–6.
[18] Hubbard AM, Adzick NS, Crombleholme TM, Coleman BG, Howell LJ, Haselgrove JC, et al. Congenital chest lesions: diagnosis and characterization with prenatal MR imaging. Radiology 1999;212:43–8.
[19] Lai TH, Chang CH, Yu CH, Kuo PL, Chang FM. Prenatal diagnosis of alobar holoprosencephaly by two-dimensional and three-dimensional ultrasound. Prenat Diagn 2000;20:400–3.
[20] Chuang L, Chang CH, Yu CH, Chang FM. Three-dimensional sonographic visualization of a fetal omphalocele at 14 weeks of gestation. Prenat Diagn 2000;20:523–4.
[21] Bega G, Lev-Toaff A, Kuhlman K, Kurtz A, Goldberg B, Wapner R. Three-dimensional ultrasonographic imaging in obstetrics: present and future applications. J Ultrasound Med 2001;20:391–408.
[22] Pretorius DH, Nelson TR. Fetal three-dimensional ultrasonography: today or tomorrow. J Ultrasound Med 2001;20:283–6.
[23] Shih JC, Chen CP, Hsieh FJ. Three-dimensional ultrasonography in genetic screening and counseling. Ultrasound Rev Obstet Gynecol 2001;1:120–7.
[24] Kang L, Chang CH, Yu CH, Chang FM. Prenatal depiction of cystic hygroma using three-dimensional ultrasound. Ultrasound Med Biol 2002;28:719–23.
[25] Chang CH, Chang FM, Yu CH, Liang RI, Ko HC, Chen HY. Systemic assessment of fetal hemodynamics by Doppler ultrasound. Ultrasound Med Biol 2000;26:777–85.
[26] Chang CH, Chang FM, Yu CH, Liang RI, Ko HC, Chen HY. Fetal ear assessment and prenatal detection of aneuploidy by the quantitative three-dimensional ultrasonography. Ultrasound Med Biol 2000;26:743–9.
[27] Merz E. 3-D ultrasound in prenatal diagnosis. Curr Obstet Gynecol 1999;9:93–100.

[28] Wang P, Chang FM, Chang CH, Yu CH, Jung YC, Huang CC. Prenatal diagnosis of Joubert syndrome complicated with encephalocele using two-dimensional and three-dimensional ultrasound. Ultrasound Obstet Gynecol 1999;14:360–2.
[29] Lin HH, Liang RI, Chang FM, Chang CH, Yu CH, Yang HB. Prenatal diagnosis of otocephaly using two-dimensional and three-dimensional ultrasonography. Ultrasound Obstet Gynecol 1998;11:361–3.
[30] Merz E, Bahlmann F, Weber G, Macchiella D. Three-dimensional ultrasonography in prenatal diagnosis. J Perinat Med 1995;23:213–22.
[31] Chen CP. Placental abnormalities and preeclampsia in trisomy 13 pregnancies. Taiwan J Obstet Gynecol 2009;48:3–8.
[32] Chen CP. Prenatal sonographic features of fetuses in trisomy 13 pregnancies (I). Taiwan J Obstet Gynecol 2009;48:210–7.
[33] Chen CP. Prenatal sonographic features of fetuses in trisomy 13 pregnancies (II). Taiwan J Obstet Gynecol 2009;48:218–24.
[34] Chen CP. Prenatal sonographic features of fetuses in trisomy 13 pregnancies (III). Taiwan J Obstet Gynecol 2009;48:342–9.
[35] Chen CP. Prenatal sonographic features of fetuses in trisomy 13 pregnancies (IV). Taiwan J Obstet Gynecol 2010;49:3–12.
[36] Chen CP. Prenatal diagnosis and genetic counseling for mosaic trisomy 13. Taiwan J Obstet Gynecol 2010;49:13–22.
[37] Hsieh TY, Yu CH, Kuo PL, Chang FM. Prenatal diagnosis of alobar holoprosencephaly with cystic hygroma. Taiwan J Obstet Gynecol 2006; 45:146–9.
[38] Lu SC, Chang CH, Yu CH, Kang L, Tsai PY, Chang FM. Reappraisal of fetal abdominal circumference in an Asian population: analysis of 50,131 records. Taiwan J Obstet Gynecol 2008;47:49–56.
[39] Lu SC, Chang CH, Yu CH, Chang FM. Reappraisal of normal amniotic fluid index in an Asian population: analysis of 27,088 records. Taiwan J Obstet Gynecol 2007;46:260–3.