Taiwanese Journal of Obstetrics & Gynecology 56 (2017) 622–627

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Prenatal diagnosis of umbilical cord cyst: Clinical significance and prognosis

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ARTICLE INFO

Article history:
Accepted 30 June 2016

Keywords:
Gestation
Pregnancy outcome
Ultrasound
Umbilical cord
Umbilical cyst

ABSTRACT

Objective: Clarify the prognosis of the prenatal ultrasound diagnosis of umbilical cord cysts at any gestation trimester and to assess the ultrasound findings and chromosomal alterations associated to this entity.

Materials and methods: Between 2003 and 2015 a multicenter study was carried out, collecting, in five centers in Spain, the associated findings and perinatal outcomes of 27 cases of umbilical cord cysts, regardless of gestational age of diagnosis. A bibliographic review was conducted to identify previous studies in order to compare them with our data.

Results: In our sample, the prognosis of this finding and the neonatal outcome, when isolated, is favorable, regardless of gestational age at diagnosis, multiple or unique presentation or vanishing or persistent cysts.

Conclusions: It is important to properly assess the umbilical cord cyst and when is diagnosed, it is recommended to conduct a meticulous ultrasound examination searching for other associated malformations. In our study the prognosis of this finding seems to be favorable when isolated. Also, there is no relation between prognosis and gestation weeks at diagnosis. On the other hand, when we find this entity with associated anomalies, it is recommended to assess the need to carry out a karyotype.

Introduction

Although umbilical cord cysts are a relatively common, they cannot be considered a non-pathological ultrasound finding. Some reviews indicate that small cysts can be found in up to 3% of pregnancies in the first trimester. Sometimes are associated with other structural and/or chromosomal malformations (even up to 20%), [1–7]. If they are persistent and progressive in size, they can compromise the fetus by restricting blood flow through the umbilical cord, either by compression or thrombosis [1,8].

With the widespread use of the ultrasound for prenatal control (for example, in Spain for low-risk pregnancies, three ultrasound scans are performed during pregnancy), intrauterine abnormalities involving the umbilical cord are routinely diagnosed, being umbilical cysts the second most frequent disorder founded [9].

This is the first work published so far in which data has been collected and compared from cases diagnosed in any of the gestation trimesters, trying to clarify the prognosis associated to prenatal diagnosis of this entity. Also, the ultrasound findings more frequently associated to this entity and related to chromosomal alterations are described for a better management during pregnancy.

Material and methods

IRB: CP03/2015. The study was conducted between 2003 and 2015 involving five Spanish centers. Three public hospitals, Miguel Servet University Hospital in Zaragoza and Gregorio Marañón

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http://dx.doi.org/10.1016/j.tjog.2017.08.008

University hospital in Madrid (both referral center for high-risk obstetrics) and Puerta de Hierro University Hospital (first level general hospital) in Madrid. Also, two private hospitals joined the study (Nuevo Belén Universitario Hospital and Alcorcón South Hospital). Data and findings were collected from 27 fetuses diagnosed with umbilical cord cysts, regardless gestational age. Ultrasounds were performed as part of the routine prenatal pregnancy program. High-resolution equipment with transabdominal or transvaginal ultrasound probe – depending on the time of diagnosis – was used.

The presence of a single or multiple well defined anechoic images, well delineated and with a hyperechoic limit at umbilical cord level, was considered as umbilical cyst cord diagnosis. Color Doppler was used in all cases to rule out the presence of flow and to help assess the relationship with the umbilical vessels and their location. Figs. 1,2 and 3.

For each pregnant woman included in the sample, a range of data was collected according to:

- Maternal epidemiological characteristics.
- Gestational history.
- Ultrasonographic variables related to the cysts.
- Other ultrasonographic findings of prenatal diagnosis.
- Perinatal data in those pregnancies that achieved full term.

A bibliographic review in MEDLINE was conducted in order to identify previous studies of umbilical cord cysts diagnosed at any gestational trimester since 1980–2014, and to compare them with data obtained in our cohort.

Results

A total of 27 cases were diagnosed by ultrasound examination within the normal gestation control protocol (Tables 1 and 2). The

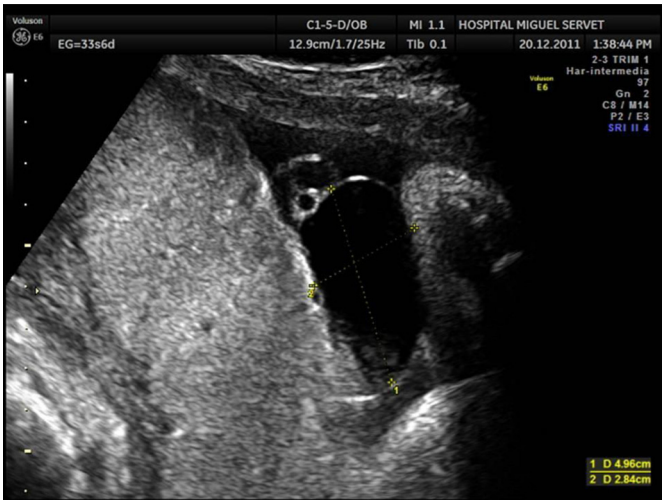

Fig. 2. Umbilical cord cysts in the third trimester.

average maternal age of the total sample at the time of diagnosis was 32.5 years (22–39). The inclusion of cases was carried out at the time of diagnosis in any trimester of the pregnancy. 11 of them (40.7%) were diagnosed during the first trimester, and the other 16 (59.3%) correspond to ultrasound findings in the 2nd or 3rd trimester, 8 in the second trimester (29.6%) (14–28wk.) and 8 in the third trimester (29.6%) (>28wk). The median of the weeks at diagnosis was 16 weeks.

In 21 cases there was a single umbilical cord cyst and in the remaining 6 cases there were multiple cord cysts. The persistence of cord cysts is influenced by the time of diagnosis in our sample, since those cysts diagnosed in the first trimester are more likely to disappear during the rest of the pregnancy (out of the eleven cases

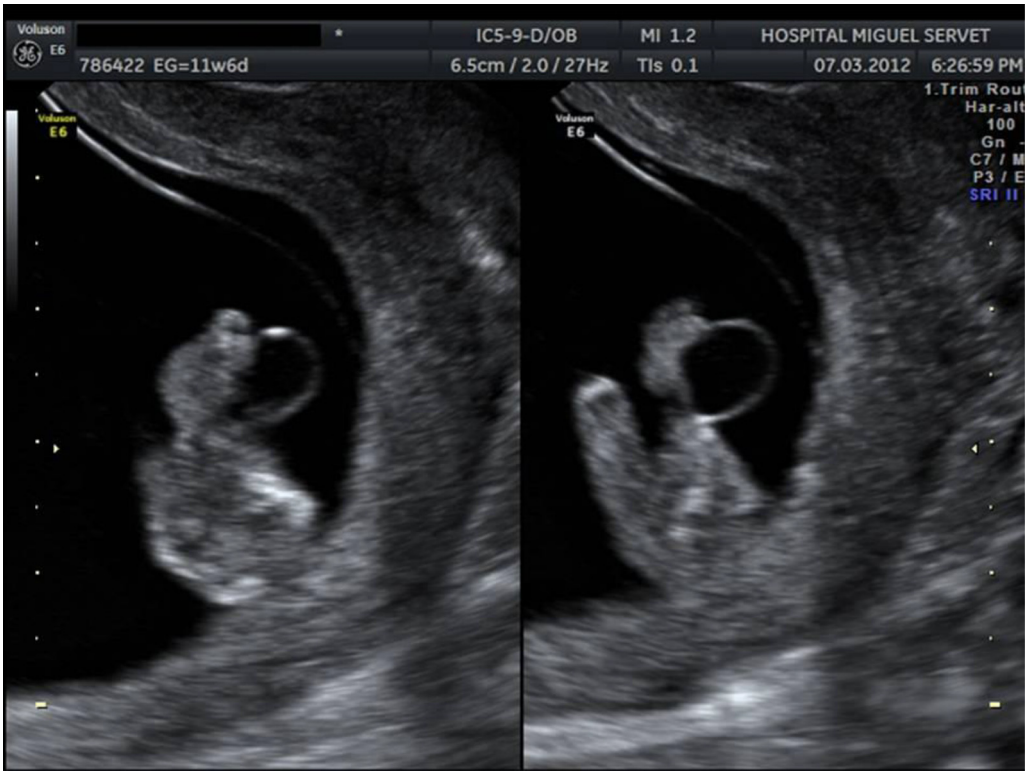

Fig. 1. Umbilical cord cyst in the first trimester near placental insertion.

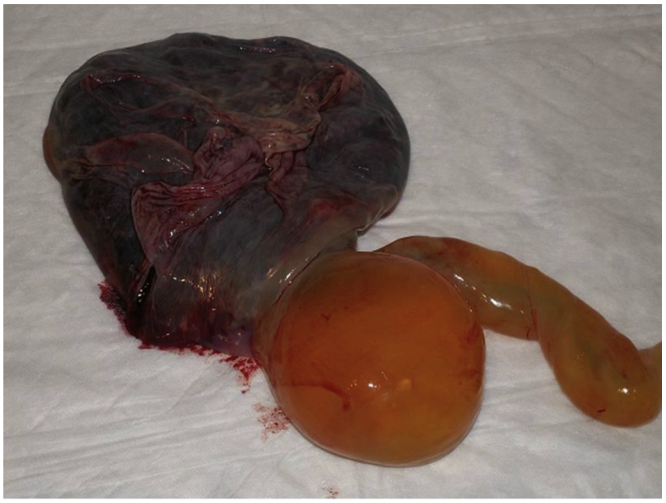

Fig. 3. Umbilical cord cyst after delivery.

five disappeared, 45%), while those which are diagnosed above week 14 usually remain until birth (14 out of 16, 87.5%).

In almost half of the sample (13 cases) the finding of umbilical cord cyst was isolated, and there were no other ultrasound or chromosomal anomalies.

Fetal karyotyping by invasive technique was offered to those patients presenting an additional ultrasound anomaly. One case, showed high risk in the first trimester screening, so an invasive test was done in spite of not having other sonographic findings, resulting the fetal karyotype in a triploid. Five cases of chromosomal abnormality (18.5%) following a fetal karyotype were confirmed. All of them showed severe abnormalities by ultrasound examination. The most frequent chromosomopathy was Edwards Syndrome (Trisomy 18), which was observed in two fetuses. Two other fetuses were diagnosed with partial mole, with subsequent confirmation on pathological examination. In two cases with additional sonographic findings the couple decides not to undergo an invasive test.

In the group of patients with associated ultrasound abnormalities (14 cases), omphalocele was the most common alteration, being present in 4 of them. One case was diagnosed with aberrant right subclavian artery (ARSA), which is considered to be a variant of normality when no other defects are associated.

Of the remaining three cases with normal genetic testing and karyotype 46XY, one was associated a single umbilical artery (SUA) and pyelectasis bilateral. At week 16 it was diagnosed of anhydramnios so the couple decided termination of pregnancy (TOP). The second fetus without chromosomal abnormality had megabladder so it was ended electively with a TOP. The third was a fetus with multiple structural anomalies and a stillbirth at 35 weeks.

In the 13 cases showing umbilical cord cysts isolated, every single one had a good perinatal outcome, regardless of the trimester in which the diagnosis was made. The rate of normal delivery was 77% for this group, with 2 cesarean sections and 1 instrumental delivery. The average gestational age at the time of delivery was 38 weeks (range 31–41). One of the two pregnancies, which ended prematurely, was a multiple pregnancy with triplets with an umbilical cord cyst on one of the monochorionic twins. In singleton pregnancies with the finding of a single umbilical cord cyst, no case was recorded with low birth weight (less than p10) [10].

In pregnancies where a chromosomal defect was confirmed, and in the two cases of partial mole, completion was by a early TOP. Only a fetus diagnosed with Edwards syndrome reached a viable gestational age, with death in perinatal period. This fetus associated multiple ultrasound findings such as: omphalocele, claw hands, double outlet in right ventricle, ventricular septal defect, aortic subvalvular obstruction, suspected dysplasia tricuspid valve and moderate aortic insufficiency.

Out of the 7 patients presenting ultrasound anomalies without chromosomal alterations, 4 of them had a good perinatal outcome, with completion of gestation by vaginal delivery in all cases, and Apgar test and cord pH normal at birth. Of the other 3 cases, 2 were a TOP (anhydramnios and a multiple malformation's fetus) and 1 a stillbirth.

Discussion

It is very difficult to establish the real prevalence of this find in pregnancy, since it is estimated that during the first trimester it can reach 3.4% [1–4]. In the second and third trimesters this is unknown [5,6,11]. Most current literature corresponds to casual diagnoses in routine examinations during pregnancy, and it is difficult to establish the prognosis and possible neonatal outcome that will be found associated with this entity. A number of cases have been published with larger samples of pregnancies, which can

Table 1
Cases without ultrasonographic abnormalities.

Cases	GA (weeks)	Maternal age (years)	Cysts number	Persistent	Fetal karyotype	Additional sonographic findings	Delivery	GA at delivery (weeks)	Weight	Weight percentile	Apgar 1/5	pH
1	12	32	2	No	ND	None	Instrumental	39	2830	11	9/10	7,12
2	12	39	1	No	ND	None	Cesarean	38	3370	81	9/10	7,33
3	12	31	1	No	46XY	None	Eutocic	40	3930	91	9/10	7,28
4	12	33	1	No	ND	None	Eutocic	35	2640	72	9/10	7,33
5	16	31	1	No	46XY	None	Eutocic	39	3150	38	9/10	7,30
6	16	39	3	Yes	46XY	None	Eutocic	41	3440	34	9/10	7,31
7	19	34	1	Yes	46XY	None	Eutocic	36	2330	11	9/10	7,34
8	28	36	1	Yes	ND	None	Eutocic	40	3360	53	10/10	7,34
9	28	37	1	No	ND	None	Eutocic	38	3690	97	9/10	7,24
10	29	36	2	Yes	46XY	None	Eutocic	39	3420	68	9/10	7,28
11	33	23	1	Yes	ND	None	Eutocic	39	3100	32	8/10	7,23
12	34	33	1	Yes	ND	None	Eutocic	40	3760	88	9/10	7,43
13	35	37	1	Yes	ND	Triplets: pregnancy bichorial triamniotic (cyst in one of monochorials)	Cesarean	31	1571, 1400, 1100	56, 24, 1	9/10, 9/10, 6/9	7,44, 7,35, 7,22

GA: gestational age; ND: not done.

Table 2
Cases with ultrasonographic abnormalities.

Cases	GA (weeks)	Maternal age (years)	Cysts number	Persistent	Fetal karyotype	Additional sonographic findings	Delivery	GA at delivery	Weight	Apgar 1/5	pH
14	11	32	1	No	ND	Aberrant right subclavian artery (ARSA)	Eutocic	40	3670	10/10	7,37
15	12	39	2	Yes	ND	Omphalocele	Eutocic	40	4000	9/10	7,30
16	13	32	1	No	46XY	Little omphalocele that disappeared at 16 week	Eutocic	40	2790	9/10	7,25
17	35	38	1	Yes	46XX	Portosystemic shunt + single umbilical artery	Eutocic	39	3860	9/10	7,34
18	12	30	2		46 XX Partial hydatidiform mole	Hydrops fetalis without heartbeat	Miscarriage				
19	12	25	1		46XY	Right dysplastic pelvic kidney + single umbilical artery + anhydramnios 16 week.	TOP				
20	14	34	1		46XX	Megabladder	TOP				
21	20	32	1		Partial hydatidiform mole	Choroid plexus cyst >3 mm unilaterals	Miscarriage				
22	32	22	1	Yes	46XY	Multiple structural anomalies: spinal muscular atrophy, arthrogryposis, atrial septal, dysplastic hands, polyhydramnios, bilateral cryptorchidism, brachycephaly	Eutocic	35	1700	Intrauterine death	
23	12	30	1		45X	Body wall complex	TOP				
24	12	31	1	Yes	47XY + 18	Omphalocele + claw hands + Double outlet right ventricle + VSD + aortic subvalvular obstruction	Eutocic	38	1530	Intrauterine death	
25	14	26	1		Triploidy		TOP				
26	16	33	1		Trisomy 13	Holoprosencephaly semilobar, HLHS, Omphalocele, single umbilical artery, IUGR severe and early	TOP				
27	23	32	3		47XY + 18	Megabladder + holoprosencephaly + poorly positioned lower limbs	Miscarriage at 18 week.				

GA: gestational age; ND: not done; TOP: termination of pregnancy; IUGR intrauterine growth restriction; VSD: ventricular septal defect; HLHS:hypoplastic left heart syndrome.

be helpful for proper handling. Table 3 shows a summary of the case series published in the literature.

The pathological classification of cord cysts is as true cysts or pseudocysts [5,11–15].

True cysts can derive either from the embryologic remaining part of the extra embryonic allantois or from the omphalomesenteric duct, and they are typically located near the fetal cord insertion. They are covered with epithelium [16]. Alan toids cysts resolve themselves but may be associated with omphalocele, persistent urachus and obstructive uropathy [4,13,17]. Cysts in the onfalomesenteric duct can be associated with defects in the abdominal wall and with Meckel's diverticulum. Besides, amniotic inclusion cysts (covered with amniotic epithelium) can be found inside true cysts. These are produced by amnion entrapment within the umbilical cord.

Pseudocysts are more common than true cysts and they also tend to be located near the fetal cord insertion. They are mainly caused by focal degeneration within Wharton's jelly or by its focal lack after degeneration, having no epithelial covering [16].

The differentiation between both entities at prenatal level is often difficult because their appearance is similar. The etiopathogenic is unknown and it is thought to be due to an alteration during embryogenesis in the process of umbilical cord formation.

Apparently the location of the cyst near the placenta or near the fetus abdominal wall is associated with increased risk of fetal abnormalities [1].

Although literature associates the presence of multiple cysts cord – instead of one isolated – with an increased risk of chromosomal abnormalities (mainly trisomy 18, and even more if these multiple cysts persist after the first trimester [2,9,18,19]) in our study we did not find that association with altered karyotype or poor gestational prognosis. Three cases with multiple cysts belong to the group of cases without ultrasound anomalies, and the other three belong to the group associated with ultrasound anomalies. Trisomy 18 was the chromosomal abnormality most commonly associated to this last group.

The gestational age at the time of diagnosis has been well documented previously. Most cysts that are diagnosed during the first trimester have no clinical impact, but up to 13% of cases have some kind of structural alteration, and if the cyst persists during pregnancy, this percentage is increased [1,5,20,21]. In this trimester it is important not take the yolk sac for a cord cyst. When the diagnosis take place at a later gestational age – during the second or third trimester – the percentage of abnormalities associated with these cases rises to 50% [12,14,18,22–25]. Our series of cases is the only published so far in which the data is collected at any time during pregnancy (first, second or third trimester). In our cohort, the moment of cyst diagnosis has no influence on the structural alterations or on the pregnancy outcome. When it comes to an isolated finding, gestational age has not influenced in a poor prognosis. Perinatal outcomes have been satisfactory in all cases collected in this study.

The persistence of umbilical cord cyst during pregnancy, as we have previously explained, has historically been associated with negative perinatal outcomes [5,18,19]. Our study shows that the time of diagnosis does influence the persistence or not of the finding, being more frequent that they persist when such cysts are detected in the second or third trimester. However, if it is an isolated finding, the fact that it is a persistent cyst does not imply a poorer prognosis, according to our data.

In the cases of pregnancies with persistent cysts which reached end of term, the percentile of infant weight at birth was higher than p10, except in the patient with multiple gestation, so it can be deduced that the presence of a persistent cyst by itself -being this the only finding- does not compromise fetal weight. At the same

Table 3
Published case series.

Reference	GA (weeks)	n	Normal infants (%)	Abnormal karyotype	n (%)	Sonographic findings	n (%)
Shipp et al. (1995)	14–37	13	8 (61,5%)	1 Trisomy 13	1 (8%)	Multiple vascular anomalies (n = 1), IUGR and umbilical hernia (n = 1), Patent urachus (n = 2)	4 (31%)
Smith et al. (1996)	15–39	23	4 (17,4%)	11 Trisomy 18, 2 Trisomy 13	13 (57%)	Isolated Omphalocele (n = 2), Multiple anomalies (n = 4)	6 (46%)
Ross et al. (1997)	7–13	29	20 (69%)	2 Trisomy 18	2 (7%)	Acrania (n = 1), Cystic hygroma (n = 1), Arthrogryposis (n = 1), Obstructive uropathy (n = 1), Omphalocele (n = 1)	5 (17%)
Sepulveda et al. (1999)	15–37	13	2 (15,4%)	5 Trisomy 18, 1 Trisomy 13, 1 Trisomy 21	7 (30%)	Isolated Omphalocele (n = 2), Multiple anomalies (n = 2)	4 (57%)
Ghezzi et al. (2003)	7–14	24	18 (75%)	2 Trisomy 18	2 (8%)	Obstructive uropathy	1 (4%)
Zangen et al. (2010)	16–34	10	8 (80%)	Trisomy 18	1 (10%)	IUGR, polyhydramnios, heart malformation, clenched hands (n = 1), Moderate polyhydramnios and suspected IUGR (n = 1), IUGR + VSD (n = 1)	3 (30%)
Gilboa et al. (2011)	11–14	8	5 (62,5%)	1 Trisomy 18	1 (12%)	Hypoplastic left heart (n = 1), Multiple anomalies (n = 1), Ectopic kidney and patent urachus (n = 1)	3 (37%)
Hannaford et al. (2013)	<12	45	43 (95,5%)	0	0	Choroid plexus cysts (n = 3), FOCI (n = 1), Area of localized edema over the lower thoracic/lumbar region (n = 1), IUGR (n = 2)	7 (16%)
Ruiz et al. (2015)	11–35	27	13 (48,15%)	2 Trisomy 18, 1 Triploidy, 1 45 X, 1 Trisomy 13	5 (18,5%)	ARSA (n = 1), Isolated Omphalocele (n = 2), Portosystemic shunt + single umbilical artery (n = 1),Isolated megabladder (n = 1), Choroid plexus cysts (n = 1), Right dysplastic pelvic kidney + single umbilical artery + anhydramnios (n = 1), Hydrops fetalis (n = 1), Multiple anomalies (n = 5)	14 (51,8%)
Total (1995–2015)	7–39	192	121 (63,02%)	24 Trisomy 18, 5 Trisomy 13, 1 Trisomy 21, 1 Triploidy, 1 45 X.	32 (16,7%)		47 (24,5%)

GA: gestational age; IUGR: intrauterine growth restriction; FOCI: Cardiac echogenic foci; ARSA: Aberrant right subclavian artery; VSD: ventricular septal defect.

time, it has not been observed in our cohort that there is any increased risk of fetal growth problems if the cysts were multiple.

There have not been any publications found in the bibliographic review that assess the relationship between this entity and fetal sex. However, in our sample is noteworthy that from a total of 20 infants born (out of the 18 pregnancies which reached end of term), only 3 were female and the remaining 17 were male.

Regarding the mode of delivery, if the gestational course has run normally without associated structural anomalies, there is no contraindication to vaginal delivery, which was the predominant delivery mode in the sample, with good neonatal outcomes regarding umbilical pH and Apgar test for these cases. It has never been previously documented in the literature which route of delivery is right, so we cannot compare our results in this regard.

Conclusions

Within the routine ultrasound pregnancy examination, it is important to properly assess the umbilical cord. In case of cord cyst diagnosis it is recommended to perform a comprehensive ultrasound examination looking for other abnormalities and, if these are founded, the need to carry out a fetal karyotype has to be considered. Within the chromosomal abnormalities that may appear associated with umbilical cord cysts, trisomy 18 is frequent, and the ultrasound anomaly that is most closely related is omphalocele.

In our sample the prognosis of this finding, – if it's isolated – is favorable, regardless of gestational age at diagnosis and if the cysts are multiple or unique, persistent or not.

Conflicts of interest

The authors declare no conflicts of interest.

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