Clinical experience of Umbilical Cord cysts from a Chinese single centre

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Research article

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Abstract

Background

The aim of this series was to guide the prenatal management of umbilical cord cysts by summarizing their clinical datas.

Methods

A retrospected study from Jan 2012 to May 2019 was conducted in our centre from Women's Hospital, School of Medicine, Zhejiang University. Clinical datas and pregnancy outcomes of women with umbilical cord cysts were reviewed from the hospital's electronic record and descriptive information about the umbilical cord cysts were depicted from both the sonograms and macrography.

Results

Twenty-eight women were diagnosed with umbilical cord cysts during the last six years,of whom only three had therapeutic abortion for fetal malformations and twenty-three were diagnosed between 12 + and 38 + gestational week(GW). Eight had only maternal serum screening, six had non-invasive prenatal testing (NIPT) directly and six had both tests. Three had karyotype analysis while five cases had no record.With maternal serum screening,one had high risk and the other one had middle risk and they both further had NIPT low risk.Still another one had a HCG multiple of median (MoM) up to 2.9 whose fetal had left kidney cyst.Except umbilical cord cysts, six fetus had other sructural defects including multiple malformation,single umbilical artery,acromphalus and kidney absence or cyst.There were still two cases had fetal arrhythmia and atrial premature beats.The mean delivery week was 39 + GW, six women had successful vaginal delivery and the remaing had cesarean section. The mean birth weight was 3120 g and the majority had a good pregnancy outcome.

Conclusions

Umbilical cord cysts were rare but might warn fetal structural defects or chromosomal abnormality. Systematic ultrasound assessment and karyotype analysis or NIPT at least should be suggested in their prenatal counseling. More attention should be paid to fetal distress during pregnancy and vaginal delivery could be a choose unless they had other contraindication.

Background

Umbilical cord cysts were a rare entity, defined as an echolucent area within the umbilical cord. They were classified as true cysts and pseudocysts, with the former orignated from embryonic remnants including the allantoic duct and omphalomesenteric duct while the latter represented only localized edema or degeneration of the Wharton's jelly.That is, the essential difference between true cysts and pseudocysts was whether to have an epithelial lining inside the cyst wall or not,thus it was difficult to distinguish them prenataly[1].

Regardless of true cysts or pseudocysts,they both presented a challenge to obstetrician due to their association with adverse pregnancy outcoms. A number of cases indicated that umbilical cord cysts had no clinical significance when they were detected as early as 8-9 weeks menstrual age[2].However, multiple cycsts while not single detected in first trimesters had been reported to be associated with miscarriage and aneuploidy[3] and cycsts detected in the 2nd and 3rd trimesters were associated with fetal abdominal wall defects or chromosomal anomalies especially trisomy 13 and 18[1]. Their relation with obstructive uropathy had also been observed in some cases[4, 5]. It was very necessary to exclude fetal malformation and chromosomal anomalies for these pregnant women. In this series we summarized twenty-eight cases of umbilical cord cysts detected during the 2nd and 3rd trimester. The prenatal datas and pregnancy outcomes were also reviewed from the hospital's electronic record.

Methods

This was a retrospective study involved 28 pregnancy women with umbilical cord cysts delivered in our department during the period of September 2012 to March 2019. The diagnosis of umbilical cord cysts was made by routine B-mode ultrasound examinations. Pathological examination or macrography of the placentas ultimately confirmed the ultrasound diagnosis for all cases.The data were collected by searching on medical records and department of pathology databases.

This research conformed to the provisions of the Declaration of Helsinki and was approved by the ethics committee of Women's hospital Zhejiang University.The patients were informed and provided their written informed consent.

Results

During the six years period, twenty-three cases were diagnosed with umbilical cord cysts by ultrasound at mid-late pregnancy(range,12+W-38+W) and five cases were found during delivery. Among the total twenty-eight cases, twenty-five patients successfully delivered at last and three had induced abortion for fetal malformations. The average age was thirty-one years old (range,24-38years)with 10 primipara and 18 multipara,of whom 4 primipara fertilized by IVF. As gestation proceeded,five cases had cysts diameter increased significanly and the largest one was 15cm in diameter. 7 cases were more than 5 cm when diagnosed while increased to that diameter at delivery. As to cycst location,placenta, fetal and central occurred equally and cycst were seen more(showed in Table 1 and 2).

Almost all cases had at least one type of prenatal screening except 5 cases with no record. 11 patients had maternal serum screening low risk and 5 had NIPT low risk as well. 1 had middle and the other had high risk

but both had NIPT low risk eventually while there was still 1 had high HCG mom 2.9 though with biochemical screening low risk. 6 cases had NIPT test directly. Of the 3 cases having karyotype analysis, 1 had 46XN,15S+ and the other two had normal karyotype(shown in Table 3). Except umbilical cord

cysts,eight cases had other fetal abnormality. One fetal was diagnosed with multiple malformation especially multiple cardiac anomalites at 16+GW while the other one was diagnosed with lobular whole forebrain. The third one was diagnosed with 4cm umbilical cord cysts at 25+GW but the cycst enlarged to 10 cm at 32+W and the fetal had multiple malformation. The forth case had single umbilical artery and acromphalus and the remaining two had left kidney absence or cyst.There were still two cases had fetal arrhythmia and atrial premature beats inspite inspite of no sructural defects(showed in Table 4). The mean delivery week was 39+W, six women had successful vaginal delivery and no fetal distress happened including the case with cycst diameter up to fifteen centimeter. Seven had emergency cesarean section for higher S/D, fetal distress or breech position while the other twelve had selective cesarean section for scarred uterus, intrauterine infection, or IVF. The birth weight ranged from 1420g to 4220g with the average 3120g and only one fetal's weight was lower than the 10 percentage. All these datas were summarized in Table 1,2 and 3.

Discussion

Umbilical cord cysts were usually detected incidentally on routine obstetric ultrasongraphy with the reported occurrence rate 0.4-3.4%[1, 6]. Our department was one of the largest top three specialized hospitals in China and the total number of birth was about two million per year,while only twenty-eight pregnancy women were diagnosed with umbilical cord cysts during the past six years. This, to some extent, explained umbilical cord cysts were really rare.As being detected accidently and no large scale reports, proper prenatal management was difficult to be established.The existing literature had reported that the gestational week of beening diagnosed, number,type and location of umbilical cord cysts were associated with poor fetal outcome.Umbilical cord cysts which occurred in first trimester and completely resolved before 20 weeks usually had a good outcome[7, 8]. However, the percentage of fetal structural defects might increased remarkably to 50% when they persisted to or were diagnosed in second and third trimester[9]. The association of umbilical cord cysts with abdominal wall defect[10] and urinary tract such as omphalocele[11-13] had been well documented previously and rare ones including cardiac malformation[14] and single umbilical artery[15] were also reported. Of our case series, six fetus had structural defects and the ratio was about 21%. Besides the above defects,other complicated abnormalities such as lobular whole forebrain,kidney absence or kidney cyst had yet not been reported. we suggested that women diagnosed with umbilical cord cysts should be given a systematic and comprehensive ultrasound assessment to exclude potential structural defects[16].

Literature also reported that it was the umbilical cord pseudocysts,rather than true cysts that had a higher risk of fetal trisomy 13 and 18[12].Though classied into true cysts and pseudocysts, it was difficult to distinguish them by prenatal ultrasound and it was very important to choose a relialbe prenatal method to screen fetal chromosomal abnormality for these women.There were three screening methods including maternal serum screening,NIPT and karyotype analysis of amniocentesis at present.The results of serum biochemical markers(AFP,free β-HCG ,PAPP-A) could just be used in general population to screen trisomy 21and 18. Meantime,the maternal serum AFP and free β-HCG levels tended to be significantly low in pregnant women with trisomy 18 fetus[17, 18] while fetus with abdominal defects,the two levels tend to

be significantly high[19],then when the two coincidenced,the two levels might be in the normal range. NIPT had been widely used in prenatal screening for trisomy 21,18 and 13 both in high risk and general pupulation[20].In our present series,twenty had maternal serum screening and/or NIPT and three had karyotype analysis while five cases had no record (showed in Table 3).Of the twenty cases, eight had only maternal serum screening, six had NIPT directly and six had both tests.With maternal serum screening,one had high risk and the other one had middle risk while they both further had NIPT low risk.Still another one had a HCG MoM up to 2.9 whose fetal had left kidney cyst. One fetal had abnormal karyotype of our three karyotype analysis, and fetal mosaic tetrasomy 10p was also reported[21], thus karyotype analysis or NIPT at least was more recommended in these high risk population though half of our cases had low risk of serum screening.

Poor fetal outcomes were also reported to be related with larger ,multiple cysts or cysts located near to the placenta and fetus because of the compression of umbilical vessels or umbilical cord rupture. Limited cases reminded that umbilical cord cystic masses such as hematoma lead to intrauterine fetal death at any stage of pregnancy[22, 23], and some authors recommended cesarean section to prevent intrauterine vascular compression of umbilical cord during labor[13]. But so far there was no general consensus whether these women should choose vaginial delivery or elective cesarean section. In the present case series, the majority cases were located to near either placenta or fetus, twelve had the cycst diameter more than 5cm at delivery with the largest up to15cm, five had multiple cysts. However, all had a relative good outcome.The mean delivery week was 39+W, six women had successful vaginal delivery without fetal distress including the one with cycst diameter up to 15cm. Seven had emergency cesarean section duo to high S/D, fetal distress or breech position while the other twelve also had selective cesarean section for scarred uterus,intrauterine infection, or IVF. So experience from our case series was that more attention should be paid to fetal distress during pregnancy and vaginal delivery could be a choose unless they had other contraindication which was in accordance with Leyre Ruiz Campo's view[24].We also paid close attention to the fetal birth weight and sex,only one fetal's birth weight was lower than the 10 percentage and the femail:mail was 17:11, we still agreed to the view that umbilical cord cysts did not influence fetal growth while we did not note a male dominance[24].As prenatal ultrasound could not distinguish true cysts from pseudocysts, the pathological examination should be performed after delivery in each case. Unfortunately,only five cases had pathological examination, among whom 1 was pseudocysts and the remaining 23 cases could not be distinguished.So a limitation of our study was that the low rate of pathological examination.

Conclusions

Umbilical cord cysts were rare but might warn fetal structural defects or chromosomal abnormality. Systematic ultrasound assessment and karyotype analysis or NIPT at least should be suggested in their prenatal counseling. More attention should be paid to fetal distress during pregnancy and vaginal delivery could be a choose unless they had other contraindication.

Abbreviations

IVF:in-vitrofertilization;NIPT:no-invasive prenatal testing;AFI:amniotic fluid index;AFP:alpha fetoprotein

Declarations

Acknowledgements

No.

Authors' contributions

Wu zaigui collected the clinical data, analysis these data and drafted the manuscript. Dong minyue helped to revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The deta-sets used and /or analyzed during the current study are available from the authors on reasonable request.

Ethical approval and consent to participate

This research conformed to the provisions of the Declaration of Helsinki and was approved by the ethics committee of Women's hospital Zhejiang University(No:2019027).The patients were informed and provided her written informed consent.

Consent for publication

Not applicable

Competing interests.

The authors declare that they have no competing interests.

References

1. Ross JA, Jurkovic D, Zosmer N, Jauniaux E, Hacket E. K.H. Nicolaides. Umbilical cord cysts in early pregnancy. OBSTET GYNECOL. 1997;89:442–5.

2. Sepulveda W, Leible S, Ulloa A, Ivankovic M, Schnapp C. Clinical significance of first trimester umbilical cord cysts. J Ultrasound Med. 1999;18:95–9.
3. Ghezzi F, Raio L, Di Naro E, Franchi M, Cromi A. P. Durig. Single and multiple umbilical cord cysts in early gestation: two different entities. Ultrasound Obstet Gynecol. 2003;21:215–9.
4. Pal K, Ashri H, Al-Ghazal FA. Allantoic cyst and patent urachus. INDIAN J PEDIATR. 2009;76:221–3.
5. Zimmer EZ, Bronshtein M. Fetal intra-abdominal cysts detected in the first and early second trimester by transvaginal sonography. J CLIN ULTRASOUND. 1991;19:564–7.
6. Skibo LK, Lyons EA, Levi CS. First-trimester umbilical cord cysts. RADIOLOGY. 1992;182:719–22.
7. Hannaford K, Reeves S, Wegner E. Umbilical cord cysts in the first trimester: are they associated with pregnancy complications? J Ultrasound Med. 2013;32:801–6.
8. Gilboa Y, Kivilevitch Z, Katorza E, Leshem Y, Borokovski T, Spira M, Achiron R. Outcomes of fetuses with umbilical cord cysts diagnosed during nuchal translucency examination. J Ultrasound Med. 2011;30:1547–51.
9. Zangen R, Boldes R, Yaffe H, Schwed P, Weiner Z. Umbilical cord cysts in the second and third trimesters: significance and prenatal approach. Ultrasound Obstet Gynecol. 2010;36:296–301.
10. Chen CP, Liu FF, Jan SW, Sheu JC, Huang SH, Lan CC. Prenatal diagnosis and perinatal aspects of abdominal wall defects. Am J Perinatol. 1996;13:355–61.
11. Suzuki T, Yamamoto Y, Nakamura H, Sei-Okawa K, Maruyama Y, Takeda J, Makino S, Yamataka A. A. Itakura. Fetal umbilical cord cyst may evolve to omphalocele during pregnancy. J CLIN ULTRASOUND. 2020;48:181–3.
12. Emura T, Kanamori Y, Ito M, Tanaka Y, Hashizume K, Marumo G. K. Goishi. Omphalocele associated with a large multilobular umbilical cord pseudocyst. PEDIATR SURG INT. 2004;20:636–9.
13. Chen CP, Jan SW, Liu FF, Chiang S, Huang SH, Sheu JC, Wang KG, Lan CC. Prenatal diagnosis of omphalocele associated with umbilical cord cyst. Acta Obstet Gynecol Scand. 1995;74:832–5.
14. Tongsong T, Khunamornpong S, Piyamongkol W, Chanprapaph P. Prenatal sonographic delineation of the complex cardiac anatomy of thoraco-omphalopagus twins. Ultrasound Obstet Gynecol. 2005;25:189–92.
15. Haino K, Serikawa T, Itsukaichi M, Numata M, Kikuchi A, Kojima K, Matsunaga M, Takakuwa K, K. Tanaka. Large pseudocyst of the umbilical cord detected in the second trimester. J Med Ultrason (2001). 37 (2010), 213–215.
16. Bonilla FJ, Raga F, Villalaiz E, Osborne N, Castillo JC. F. Bonilla-Musoles. Umbilical cord cysts: evaluation with different 3-dimensional sonographic modes. J Ultrasound Med. 2010;29:281–5.
17. Canick JA, Palomaki GE, Osathanondh R. Prenatal screening for trisomy 18 in the second trimester. Prenat Diagn. 1990;10:546–8.
18. Spencer K, Macri JN, Aitken DA, Connor JM. Free beta-hCG as first-trimester marker for fetal trisomy. LANCET. 1992;339:1480.

19. Schmidt D, Rose E, Greenberg F. An association between fetal abdominal wall defects and elevated levels of human chorionic gonadotropin in mid-trimester. Prenat Diagn. 1993;13:9–12.
20. Rieder W, White S, McGillivray G, Hui L. Contemporary prenatal aneuploidy screening practice in Australia: Frequently asked questions in the cell-free DNA era. Aust N Z J Obstet Gynaecol. 2018;58:397–403.
21. Wu YC, Yu MT, Chen LC, Chen CL, Yang ML. Prenatal diagnosis of mosaic tetrasomy 10p associated with megacisterna magna, echogenic focus of left ventricle, umbilical cord cysts and distal arthrogryposis. AM J MED GENET A. 2003;117A:278–81.
22. Kalter CS, Williams MC, Vaughn V, Spellacy WN. Sonographic diagnosis of a large umbilical cord pseudocyst. J Ultrasound Med. 1994;13:487–9.
23. Sepulveda W, Pryde PG, Greb AE, Romero R, Evans MI. Prenatal diagnosis of umbilical cord pseudocyst. Ultrasound Obstet Gynecol. 1994;4:147–50.
24. Ruiz CL, Saviron CR, Gamez AF, Martinez-Payo C, Perez PP, Garrido FP, Lerma PD. Prenatal diagnosis of umbilical cord cyst: Clinical significance and prognosis. Taiwan J Obstet Gynecol. 2017;56:622–7.

Tables

Table1 Main characteristics of the study population(n=28)

Maternal/fetal characteristics	Median(range) or n(%)
Age(years)	30.9(24-38)
Multipara	17(60.7%)
Fertilization way	
natural	23(82.1%)
IVF-ET	4(14.3%)
IUI	1(3.6%)
Delivery week	37.3(29-40)
Delivery mode	
Vaginal	6(24%)
Emergency caesarean	7(28%)
Selective caesarean	12(48%)
Fetal sex	
Femail	17(60.7%)
Mail	11(39.3%)
Birth weight(g)	3099(1420-4220)

Table 2 Descriptive information about the umbilical cord cysts

Characteristics of cycsts	Median(range) or n(%)
Diagnosed week (GW)	
Second trimester	19.8(12-25);12(42.9%)
Third trimester	33.1(29-38);10(35.7%)
Delivery	37.7(36-40); 6(21.4%)
Cycsts diameter(cm)	
<5cm when diagnosed	2.5(1.5-4);15(53.6%)
≧5cm when diagnosed	7.2(5-10);8(28.6%)
No record	5(17.8%)
Enlarged significantly	6(21.4%)
Daignosed	4.6(1.9-9.6)
Delivery	8.5(5-15)
Location of cycsts	
Placenta	9(32.1%)
Fetal	9(32.1%)
Central	3(10.7%)
Fetal+central	1(3.6%)
Number of cycsts	
Single	16(57.2%)
Multiple	6(21.4%)
Not described	6(21.4%)
Complicated other abnormalitis	6(21.4%)

Table 3 Methods and results of prenatal screening

Methods /results of screening	n(%)
Maternal serum screening	14(50%)
Low risk	12
Middle risk	1
High risk	1
NIPT	12(42.6%)
Negative	12
Positive	0
Karyotype analysis	3(10.7%)
Normal	2
Abnormal	1(46XN,15S+)
No record	5(17.6%)

Note:six persons had both maternal serum screening tests and NIPT.

Table 4 Cases complicated with multiple malformation

Case	Multiple malformation
Case 1	nuchal translucency thickness 5.5mm, Fetal cardiac malformation Interrupted ventricular septum echogenicity about 2.3mm Aortic span Suspicious reversed flow within the ductus arteriosus with the main pulmonary artery not clear The mitral and tricuspid valves at the same level Endocardial pad defects not excluded
Case 2	Fetal cardiothoracic enlargement about 0.65 Hydropericardium 0.55cm The internal segment of the umbilical vein dialred with the thicker 1.0cm Small fetus kidney,left:2.0*0.8*0.9cm,right:2.0*1.3*1.9cm, cortex and medulla poorly demarcated Small bladder about 7.1*6.4cm Mixed signals in the gastric cavity Oligoamnios, AFI:2.7cm