Provisionally accepted for publication

CASE REPORT

Four-vessel umbilical cord with three arteries and one vein: a case report and literature review

Short title: Four vessel umbilical cord

Sara **Mari** [1,2], Mario **Polichetti** [2], Maria Antonietta **Castaldi** [2], Virginia **Gargano** [2], Elisabetta **Gragnano** [1,*], Gabriele **Saccone** [1], Mariavittoria **Locci** [1], Antonio **Mollo** [2]

[1] Department of Neuroscience, Reproductive Science and Dentistry, School of Medicine, University of Naples Federico II, Naples, Italy.

[2] Department of Advanced Biomedical Sciences, School of Medicine, University of Naples Federico II, Naples, Italy.

[3] Department of Medicine, Surgery and Dentistry "Schola Medica Salernitana", University of Salerno, Baronissi, Italy.

Doi: 10.36129/jog.2023.129

***Corresponding author**: Elisabetta **Gragnano**, RN. Department of Neuroscience, Reproductive Sciences and Dentistry, School of Medicine, University of Naples Federico II, via Sergio Pansini 5, Naples, Italy.
Email: elisabettagragnano@gmail.com

ORCID: 0000-0003-0078-2117.

ABSTRACT

Background. Four-vessel umbilical cord (FVUC) is a uncommon embryonic anomaly, characterized by the presence of an umbilical cord with 4 vessels, usually 2 arteries and 2 veins

Case presentation. Here we report a rare case of FVUC with three arteries and one vein.

Conclusions. FVUC is an uncommon condition associated with major malformations and high risk of IUGR. Cases with three arteries and one vein seem to be associated with better outcomes.

Key words

Embryology; FVCU; vascular biology.

INTRODUCTION

Four-vessel umbilical cord (FVUC) is a rare embryonic anomaly, characterized by the presence of an umbilical cord with 4 vessels, usually 2 arteries and 2 veins. In early embryonic life, at 4th week, three pairs of major veins (vitellins veins drain the yolk sac, cardinal veins drain fetal body, and umbilical veins from the placenta) are connected to the primitive fetal heart at the sinus venosus.

By the 6th week, a “critical anastomosis” between left umbilical vein and the hepatic sinusoid are formed and resulting in the normal drainage pattern of placenta through will be the ductus venosus [1,2]. Failure of this normal process reults in an uncommon anomaly of a persistent right umbilical vein (PRUV), and in rarer situation persistence of both umbilical veins, defined as FVUC [3,4]. A multivessel cord has been associated with congenital anomalies, especially cardiac abnormalities [4], but also intrauterine growth restriction (IUGR). A more uncommon anomaly is when a FVUC is made by three arteris and one vein, with only two cases described in the literatures [5,6].

CASE PRESENTATION

A 38 years old pregnant woman was referred to our Gynecology and Obstetrics outclinic of San Giovanni Di Dio E Ruggi D’Aragona Hospital for a routine fetal scan at 20 weeks and 2 days of gestation. She had a history of two previous caesarean deliveries, reported un-complicated pregnancies and absence of genetic anomalies. The indications for cesarean sections were respectively post-term pregnancy and fetal macrosomia. During first trimester screening no congenital anomalies were detected.

The second trimester anatomy scan showed a male fetus with normal biometry. The evaluation of the umbilical cord showed a FVUC [Figure 1], with three arteries and one vein at Doppler. No other congenital abnormalities were identified.

Follow-up ultrasound scan at 30 weeks confirmed the FVUC and also revelead a large cyst of the umbilical cord (77 x 74 mm), with corpuscular content. Second follow-up was planned at 35 weeks of gestation and showed regular growth and normal Doppler of the umbilical cord [Figure 2].

The woman received emergent cesarean delivery at 36 weeks of gestation due to onset of preterm labor contractions. A male fetus of 3,200 grams was born with APGAR score at 1 and 5 minutes of 8 and 9, respectively. The placent, sent to histological examination, revelead a 15 cm umbilical cord with paracentral insertion, and presence of blood clots. The FVUC was confirmed, with three arteries and one vein.

DISCUSSION

A systematic review of the literature was performed including all studies reporting cases of FVUC. Searches were performed independently by authors (SM, GS) in Medline, OVID, Scopus, and Web of Science, with the use of a combination of keywords: “Four-vessel umbilical cord,” “fetal vein,” “vein varix” and “fetal” from inception of each database to December 2021. Only studies published in English were analyzed. References from relevant research articles and reviews were also reviewed.

The systematic review identified and included 15 relevant studies [5-15] for a total of 16 cases [Table 1]. Study period ranged from 1966 to 2019. Out of the 16 cases, only 7 were diagnosed prenatally with ultrasound, while most were diagnosed post-natally following umbilical cord catheterization. Gestational age at pretanatal diagnosis of FVUC ranged from 22 to 36 weeks. No cases of first trimester diagnosis were identified. Only two cases were FVUC with three arteries and one vein, while 14/16 were FVUC with two arteries and two veins [Table 1]. Amniocenteses were performed in 5 cases, and there were one thrisomy 18, and four normal karyo. Mode of deliveries reported were 7 vaginal deliveries, 6 cesarean deliveries, while in three cases mode of delivery was not reported. Four cases (4/16, 25%) had associated malformations, and there were 6/16 (37.5%) cases of IUGR.

CONCLUSIONS

In this study we reported a case of a FVUC with no associated malformations, no IUGR, and favorable outcome of the baby. We also reported a literature review of 16 cases. The rate of associated malformations was 25%, and the rate of IUGR was 37.5%. The literature review

confirmed that the cases with no associated complications have a favorable outcome. Notably, the two prior cases with three arteries and one vein had a normal outcome raises the question of the better outcome of this subtype of FVUC compared to the subtype of three veins and one artery.

In summary, FVUC is an uncommon condition associated with major malformations and high risk of IUGR. In case of prenatal diagnosis of FVUC we recommend detail examination of the fetus, including fetal echocardiography, and growth scan. Cases with three arteries and one vein seem to be associated with better outcomes.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

SM: Conceptualization, drafting. MP: Data revision. MC: Drafting. VG: Conceptualization. EG: Literature review. GS: Final approval. ML: Literature review, final approval. AM: Final approval

Funding

No funding was recieved for this study

Study registration

Not applicable

Disclosure of interests

No conflict of interest to disclose

Ethical approval

Not applicable

Informed Consent Statement

Subject gave informed consent and patient anonymity was preserved.

Data sharing

Not applicable

REFERENCES

1. Yagel S, Kivilevitch Z, Cohen SM, Valsky DV, Messing B, Shen O, Achiron R. The fetal venous system, part I: normal embryology, anatomy, hemodynamics, ultrasound evaluation and Doppler investigation. Ultrasound Obstet Gynecol.2010 Jun 35(6):741-50. doi: 10.1002/uog.7618.
2. Yagel S, Kivilevitch Z, Cohen SM, Valsky DV, Messing B, Shen O, Achiron R. The fetal venous system, Part II: ultrasound evaluation of the fetus with congenital venous system malformation or developing circulatory compromise. Ultrasound Obstet Gynecol.2010 Jul 36(1):93-111. doi: 10.1002/uog.7622.
3. Hill LM, Mills A, Peterson C, Boyles D. Persistent right umbilical vein: sonographic detection and subsequent neonatal outcome. Obstet Gynecol.1994 Dec 84(6):923-5.
4. Puvabanditsin S, Garrow E, Bhatt M, Kathiravan S, Gowda S, Wong R, Nagar M. Four-vessel umbilical cord associated with multiple congenital anomalies: a case report and

literature review. Fetal Pediatr Pathol.2011 30(2):98-105. doi: 10.3109/15513815.2010.524687.

5. Du X, Yuan Q, Li Z, Li Y. Three umbilical arteries resulting in a four-vessel umbilical cord in a stillbirth. Int J Clin Exp Med.2015 Mar 8(3):4682-5.
6. Hoh H, Boo E, Lee E, Seo M, et al. Four-vessel umbilical cord containing three arteries and one vein. Ultrasound in Ob Gyn. Volume46, IssueS1 Supplement: Abstracts of the 25th World Congress on Ultrasound in Obstetrics and Gynecology,2015 Montréal, Canada
7. Painter D, Russell P. Four-vessel umbilical cord associated with multiple congenital anomalies. Obstet Gynecol.1997 Oct 50(4):505-7.
8. Rodriguez MA. Four-vessel umbilical cord without congenital abnormalities. South Med J.1984 Apr 77(4):539. doi: 10.1097/00007611-198404000-00043.
9. Schimmel MS, Eidelman AI. Supernumerary umbilical vein resulting in a four-vessel umbilical cord. Am J Perinatol.1998 May 15(5):299-301. doi: 10.1055/s-2007-993947.
10. Paize F, Yoxall CW. Supernumerary umbilical vein demonstrated by radiography of a 27-week-gestation neonate. Pediatr Radiol.2006 Jun 36(6):570. doi: 10.1007/s00247-005-0106-x.
11. Pérez-Cosio C, Sheiner E, Abramowicz JS. Four-vessel umbilical cord: not always a dire prognosis. J Ultrasound Med.2008 Sep 27(9):1389-91. doi: 10.7863/jum.2008.27.9.1389.
12. Avnet H, Shen O, Mazaki E, Yagel S, Daniel-Spiegel E. Four-vessel umbilical cord. Ultrasound Obstet Gynecol.2011 Nov 38(5):604-6. doi: 10.1002/uog.9045.
13. Karatza A, Tsamandas A, Varvarigou A, Davlouros P, Pavlou V, Mantagos S. Supernumerary umbilical vein in a hydropic neonate with hypertrophic cardiomyopathy. Fetal Pediatr Pathol.2011 Feb 30(3):173-6. doi: 10.3109/15513815.2010.547557.
14. Puvabanditsin S, Garrow E, Bhatt M, Kathiravan S, Gowda S, Wong R, Nagar M. Four-vessel umbilical cord associated with multiple congenital anomalies: a case report and literature review. Fetal Pediatr Pathol.201130(2):98-105. doi: 10.3109/15513815.2010.524687.
15. Degirmencioglu H, Oncel MY, Yurttutan S, Calisici E, Erdeve O, Zergeroglu S, Dilmen U. A four-vessel umbilical cord with omphalomesenteric duct in trisomy 18.2012 Genet Couns 23(3):431-3.

Table 1. Characteristics of the included studies

	Maternal age (years)	Risk factors	Associated malformations	Diagnosis of FVUC	Type of FVUC	Fetal karyo	Baby sex	Intrauterine growth restriction	Mode of delivery
Murdoch 1966[7]	16	N/R	None	Postpartum	Two arteries Two veins	Not performed	male	Yes	Vaginal
Painter 1977[8]	32	N/R	Ectopic cordis, cleft lip and palate, bifid liver, pulmunar stenosis	Postpartum	Two arteries Two veins	Not performed	male	Yes	Vaginal
Rodriguez 1984[9]	30	N/R	None	Postpartum	Two arteries Two veins	Not performed	female	No	CS
Aoki 1997 #1[10]	N/R	N/R	None	29 weeks	Two arteries Two veins	Not performed	female	No	Vaginal
Aoki 1997 #2[10]	N/R	N/R	None	23 weeks	Two arteries Two veins	Not performed	female	No	Vaginal
Schimmel 1998[11]	N/R	Invitro fertilisation	None	Postpartum	Two arteries Two veins	Not performed	male	Yes	NR
Paize 2006[12]	N/R	N/R	None	Postpartum	Two arteries Two veins	Not performed	male	No	Vaginal
Perez-Cosio 2008[13]	37	SLE	None	33 weeks	Two arteries Two veins	Not performed	male	No	CS

Avnet 2011[14]	33	N/R	None	22 weeks	Two arteries Two veins	Regular, XX	female	No	CS
Karatza 2011[15]	16	N/R	Hydropic neonate with hypertrophic cardiomyopathy	Postpartum	Two arteries Two veins	Regular, XX	female	No	CS
Puvabanditsin 2011[16]	20	N/R	Heterotaxy syndrome, interrupted IVC, common atrium, CAVC, HLV, malrotation of the small bowel	Postpartum	Two arteries Two veins	Regular, XX	female	Yes	CS
Degirmencioglu 2012[17]	22	N/R	Esophageal atresia	Postpartum	Two arteries Two veins	Trisomy 18	N/R	Yes	CS
Du 2015[5]	28	N/R	None	Postpartum	Three umbilical arteries and one vein	Not performed	N/R	No	NR
Hoh 2015[6]	N/R	N/R	None	22 weeks	Three umbilical arteries and one vein	Not performed	male	NR	NR
Lei 2017[18]	31	N/R	None	35 weeks	Two arteries Two veins	Regular, XY	male	Yes	Vaginal
Kurakazu 2019[19]	37	N/R	None	36 weeks	Two arteries Two veins	Not performed	female	No	Vaginal

FVUC, four vessels umbilical cord; N/R, not reported; SLE, Systemic Lupus Erythematosus; CS, cesarean section; CAVC, complete atrioventricular canal; HLV, hypoplastic left ventricle IVC, inferior ven cava