CASE REPORT

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

Short title: Four vessel umbilical cord

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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 results 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 arteries 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 outpatient clinic 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 identified.

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 revealed 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 placenta, sent to histological examination, revealed 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 prenatal 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 trisomy 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 received 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


Table 1. Characteristics of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Maternal age (years)</th>
<th>Risk factors</th>
<th>Associated malformations</th>
<th>Diagnosis of FVUC</th>
<th>Type of FVUC</th>
<th>Fetal karyotype</th>
<th>Baby sex</th>
<th>Intrauterine growth restriction</th>
<th>Mode of delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murdoch 1966</td>
<td>16</td>
<td>N/R</td>
<td>None</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>male</td>
<td>Yes</td>
<td>Vaginal</td>
</tr>
<tr>
<td>Painter 1977</td>
<td>32</td>
<td>N/R</td>
<td>Ectopic cordis, cleft lip and palate, bifid liver, pulmunar stenosis</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>male</td>
<td>Yes</td>
<td>Vaginal</td>
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<tr>
<td>Rodriguez 1984</td>
<td>30</td>
<td>N/R</td>
<td>None</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>female</td>
<td>No</td>
<td>CS</td>
</tr>
<tr>
<td>Aoki 1997 #1</td>
<td>N/R</td>
<td>N/R</td>
<td>None</td>
<td>29 weeks</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>female</td>
<td>No</td>
<td>Vaginal</td>
</tr>
<tr>
<td>Aoki 1997 #2</td>
<td>N/R</td>
<td>N/R</td>
<td>None</td>
<td>23 weeks</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>female</td>
<td>No</td>
<td>Vaginal</td>
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<tr>
<td>Schimmel 1998</td>
<td>N/R</td>
<td>Invitro fertilisation</td>
<td>None</td>
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<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>male</td>
<td>Yes</td>
<td>NR</td>
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<tr>
<td>Paize 2006</td>
<td>N/R</td>
<td>N/R</td>
<td>None</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>male</td>
<td>No</td>
<td>Vaginal</td>
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<tr>
<td>Perez-Cosio 2008</td>
<td>37</td>
<td>SLE</td>
<td>None</td>
<td>33 weeks</td>
<td>Two arteries Two veins</td>
<td>Not performed</td>
<td>male</td>
<td>No</td>
<td>CS</td>
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<tr>
<td>Authors</td>
<td>Year</td>
<td>Cases</td>
<td>Sex</td>
<td>Gestation</td>
<td>Arteries</td>
<td>Veins</td>
<td>Age</td>
<td>Sex</td>
<td>CS</td>
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<tr>
<td>Avnet 2011</td>
<td>33</td>
<td>N/R</td>
<td>None</td>
<td>22 weeks</td>
<td>Two arteries Two veins</td>
<td>Regular, XX fema le</td>
<td>No</td>
<td>CS</td>
<td></td>
</tr>
<tr>
<td>Karatza 2011</td>
<td>16</td>
<td>N/R</td>
<td>Hydropic neonate with hypertrophic cardiomyopathy</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Regular, XX female</td>
<td>No</td>
<td>CS</td>
<td></td>
</tr>
<tr>
<td>Puvabanditsin 2011</td>
<td>20</td>
<td>N/R</td>
<td>Heterotaxy syndrome, interrupted IVC, common atrium, CAVC, HLV, malrotation of the small bowel</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Regular, XX female</td>
<td>Yes</td>
<td>CS</td>
<td></td>
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<tr>
<td>Degirmencioglu 2012</td>
<td>22</td>
<td>N/R</td>
<td>Esophageal atresia</td>
<td>Postpartum</td>
<td>Two arteries Two veins</td>
<td>Trisomy 18 N/R</td>
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<td>Du 2015</td>
<td>28</td>
<td>N/R</td>
<td>None</td>
<td>Postpartum</td>
<td>Three umbilical arteries and one vein</td>
<td>Not performed N/R</td>
<td>No</td>
<td>NR</td>
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<tr>
<td>Hoh 2015</td>
<td>N/R</td>
<td>N/R</td>
<td>None</td>
<td>22 weeks</td>
<td>Three umbilical arteries and one vein</td>
<td>Not performed male</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Lei 2017</td>
<td>31</td>
<td>N/R</td>
<td>None</td>
<td>35 weeks</td>
<td>Two arteries Two veins</td>
<td>Regular, XY mal e</td>
<td>Yes</td>
<td>Vaginal</td>
<td></td>
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<tr>
<td>Kurakazu 2019</td>
<td>37</td>
<td>N/R</td>
<td>None</td>
<td>36 weeks</td>
<td>Two arteries Two veins</td>
<td>Not performed female</td>
<td>No</td>
<td>Vaginal</td>
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</tr>
</tbody>
</table>
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