European Journal of Obstetrics & Gynecology and Reproductive Biology 238 (2019) 100–103

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Is scanning for vasa previa important for singleton pregnancies that started as multiple conceptions?

Yaakov Melcer, Marina Pekar-Zlotin, Brian Wolf, Moshe Betser, Shira Dvash, Nataly Zilberman Sharon, Ron Maymon*

Department of Obstetrics and Gynecology, The Yitzhak Shamir Medical Center (formerly Assaf Harofeh Medical Center), Zerifin, Israel[1]

ARTICLE INFO

Article history:
Received 16 January 2019
Received in revised form 14 May 2019
Accepted 17 May 2019

Keywords:
Vasa previa
Ultrasound
Multiple gestation
Vanishing twin
Scanning
Risk factors

ABSTRACT

Objectives: Vasa previa (VP) is a congenital placentation disorder in which fetal vessels run across the internal os of the cervix under the fetal presentation. This rare condition is associated with a high rate of perinatal morbidity and mortality when undetected before delivery. Roughly 85% of all cases of VP can be associated with one or more identifiable risk factors including in-vitro fertilization (IVF), multiple gestations, bilobed, succenturiate or low-lying placentas, and velamentous cord insertion (VCI). Recent evidence indicates the need for standardized prenatal targeted scanning protocols of pregnancies at risk of VP. The present study reports on pregnancies that began with multiple gestations but ended with a single fetus diagnosed with VP.

Study design: We retrospectively collected and reviewed medical records from 2006 to 2018 of early multiple pregnancies that ended with a single fetus diagnosed with VP in our medical center, including three cases of twin gestation complicated by a vanishing twin and a case of multifetal reduction in triplet pregnancy. This retrospective cohort study was approved by our Institutional Clinical Research Committee.

Results: The database search identified 50 pregnancies that started as multiple gestations but continued as singletons. Of these, 4 pregnancies were diagnosed with VP, for a prevalence of 8.0%. For two of the four cases, the diagnosis was made during delivery as expressed by a low Apgar score at 1 and 5 min, a low cord blood pH value, newborn resuscitation, blood product transfusion, and NICU supervision. There was a statistically significant difference in the prevalence of VP in pregnancies that started as multiple gestations but continued later as singletons compared to multiple pregnancies (8.0% vs. 0.2% respectively, $p < 0.0001$). The OR for VP in pregnancies that started as multiple gestations but continued as singletons was 41.1 (95% CI, 12.77–131.94).

Conclusions: Our findings suggest there is an increased risk of VP in conceptions that started as viable multiple gestations but continued later as singletons. If our findings supported by others, it may be prudent to consider all twins at the beginning of pregnancy to be at risk for VP, irrespective of the actual number of life fetuses at later stages of gestation.

Introduction

In the last twenty years, there has been a dramatic increase in multiple gestation rates. This is considered to be primarily due to increasing maternal age at childbearing and the use of assisted reproductive technologies (ART) [1–4]; this has resulted in a higher incidence of perinatal risks for both mothers and fetuses compared to singleton pregnancies [5,6]. These risks could be related to placental or umbilical cord disorders including abnormalities of placental shape and abnormal vasculature [5–8].

Vasa previa (VP) is an aberrant fetal vessels run through the membranes across the internal os of the cervix under the fetal presentation. VP are divided into two types based on their anatomical features: in type I the free vessel is connected to a velamentous cord whereas in type II, it is attached to a succenturiate or accessory lobe of the main placenta [8–10]. Studies consider that 1 in 500 to 1 in 5000 pregnancies result in VP. In an overview published in 2016 on the risk factors associated with VP, roughly 85% of the cases were associated with 1 or more factors that included multiple gestations, placenta previa, bilobed

* Corresponding author at: Department of Obstetrics and Gynecology, Assaf Harofeh Medical Center, Zerifin, 70300, Israel.
E-mail address: maymonrb@bezeqint.net (R. Maymon).
[1] Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

https://doi.org/10.1016/j.ejogrb.2019.05.018
0301-2115/

placenta, succenturiate placental lobes, conception by assisted reproductive technology (ART) and velamentous cord insertion (VCI) [11]. The highest odds ratio (OR) was found for the presence of a VCI [OR, 6.72; 95% confidence interval (CI), 1.12–4.034] followed by placental morphological anomalies, conception by ART, second trimester low-lying placenta, and multiple gestations.

Prenatal diagnosis of VP is crucial to help avoid fetal death [4,12–15]. Even though there is not enough evidence currently to support universal mid-gestation ultrasound screening for VP [16,17] primarily because of the dearth of prospective data, recent findings underscore the need to establish standardized prenatal targeted screening protocols for pregnancies at risk of VP [4].

To the best of our knowledge there is no information in the literature on the association between pregnancies that begin with multiple gestations but end with a single live birth and VP. In the present study we report for the first time a series of singletons diagnosed with VP that resulted from multiple pregnancies.

The importance of this finding and its potential impact on the prenatal care is further discussed.

Material and methods

We reviewed our electronic medical records database for clinical cases of multiple pregnancies diagnosed with VP. The information included obstetrical history, modes of conception, sonographic scans and associated placental pathologies, mode of delivery and outcomes. The neonatal medical record data included the Apgar score, the cord blood gas pH, need for newborn resuscitation and intubation, blood products transfusion, admission to the NICU and perinatal mortality.

All ultrasound examinations in our department are conducted with standard ultrasound machines (GE Voluson E10) equipped with a transvaginal probe (5- to 9-MHz frequency with a focal range of 6 cm from the transducer tip) and a transabdominal probe (3.5- to 5-MHz frequency). The targeted scanning protocol for pregnancies at risk of VP, namely in cases of low-lying placenta, VCI, bilobate placenta, succenturiate lobed placenta, multiple pregnancies, and IVF conceptions have been implemented in our antenatal clinics since 2008 [4,13]. None of these patients had fetuses with abnormal karyotype, nor did they deliver infants with any malformations. The sonographic diagnoses of VP were all confirmed by transvaginal sonography combined with color Doppler imaging as previously described [13]. Briefly, the VPs were visualized in gray-scale sonography as parallel or circular echogenic lines within 2 cm from the internal cervical os, where color Doppler identified these structures as vessels, and pulsed Doppler indicated a fetal arterial or venous waveform.

All asymptomatic women presenting with VP were followed up with transvaginal ultrasound for cervical length and VP position every 2 weeks from the time of the first diagnosis of VP until delivery. The timing of delivery was scheduled as a function of cervical length and/or clinical symptoms (mainly uterine contractions and/or vaginal bleeding), subsequent to a course of corticosteroids. When the cervical remained stable with normal fetal development and there were no clinical symptoms, delivery was planned at 35–36 weeks' gestation.

This retrospective cohort study was approved by our Institutional Clinical Research Committee.

Statistical analysis

Calculations from the case series were analyzed using SPSS software (SPSS Inc., version 24 Chicago, IL, USA). Statistical analysis included Fisher's Exact Test for inter- group comparisons. A P value of less than 0.05 was considered statistically significant.

Results

Case series

Between 2006 to 2018, we managed 4156 multiple pregnancies. 2576 (62.0%) and 1589 (38.0%) were conceived after ART treatment or spontaneously, respectively. An institutional database search identified 50 pregnancies that started as multiple gestations with viable fetuses but continued as singletons. Of these, 4 pregnancies were diagnosed with VP, a prevalence of 8.0%. Three cases were twin gestations complicated by a vanishing twin and one case involved multifetal reduction in a triplet pregnancy (Table 1).

Case 1

A 36 year-old healthy woman, gravida 8, para 6, presented with an unremarkable medical history. The current pregnancy began with spontaneously-conceived dichorionic-diamniotic (DCDA) twins complicated by an intrauterine demise of 1 co-twin at 22 weeks of gestation. The fetal growth scan follow-up was normal. An emergency cesarean delivery was performed at 37 + 3 weeks because of a non-reassuring fetal heart rate trace and intrapartum vaginal bleeding. A girl weighing 2855 g was delivered with 1 and 5 min Apgar scores of 6 and 6, respectively, and a cord blood pH of 7.3. VP vessels were diagnosed after delivery of the placenta. At birth, the newborn exhibited hypovolemic shock requiring resuscitation, blood products transfusion and neonatal intensive care unit (NICU) supervision.

Case 2

A healthy 37 year-old healthy woman, gravida 2, para 1, presented with an unremarkable medical history with a previous cesarean delivery. The current pregnancy began as IVF-conceived triplets reduced to a singleton at 13 weeks of gestation. The mid-trimester examination and fetal growth scan follow-up were uneventful. A repeat emergency cesarean delivery was performed at 37 + 1 weeks because of a non-reassuring fetal heart rate trace and intrapartum vaginal bleeding. A boy weighing 2460 g was delivered with 1 and 5 min Apgar scores of 1 and 7, respectively,

Table 1
Characteristics of the four pregnancies that begin with multiple gestations but end with a single fetus diagnosed with VP.

Case No.	Maternal age (yrs)	GP	Mode of conception	Other US findings	Diagnosis	Gestational age at delivery (wk + d)	Mode of delivery and birth weight (g)	Apgar score at 1 and 5 minute and Blood gas Ph	Newborn resuscitation, blood products transfusion and NICU admission
1	36	G8P6	Spontaneous	None	Intrapartum	37 + 3	EmCD; 2855	6,6; 7.3	Yes
2	37	G2P1	IVF	None	Intrapartum	37 + 1	EmCD; 2460	1,7; 6.9	Yes
3	32	G8P5	Spontaneous	VCI	Prenatal	33 + 6	EmCD; 2075	9,10; NA	No
4	33	G2P1	IVF	VCI and PP	Prenatal	Ongoing pregnancy	Ongoing pregnancy	Ongoing pregnancy	Ongoing pregnancy

G=gravity, P = parity, IVF = in vitro fertilization, US = ultrasound, VCI = velamentous cord insertion, PP = placenta previa, NA=not available, EmCD = emergency cesarean delivery.

and a cord blood pH of 6.9. The diagnosis of VP was based on the postpartum examination of the placenta and membranes. At birth, the newborn exhibited hypovolemic shock requiring resuscitation, blood products transfusion and NICU supervision.

Case 3

A 32 year-old healthy woman, gravida 8, para 5, presented with an unremarkable medical history. The current pregnancy began as spontaneously-conceived DCDA twins complicated by a vanishing twin at 12 weeks of gestation. A VCI was detected during the mid-trimester ultrasound examination and after implementation of the targeted scanning protocol [4]. VP was diagnosed at week 25 of gestation and glucocorticoids were administered to enhance fetal lung maturation. An emergency cesarean delivery was performed at 33 + 6 weeks because of spontaneous onset of labor. A girl weighing 2075 g was delivered with 1 and 5 min Apgar scores of 9 and 10, respectively. A VCI and VP were diagnosed upon postpartum examination of the placenta and membranes. The neonatal outcome was uneventful.

Case 4

A 33 year-old healthy woman, gravida 2, para 1, presented with an unremarkable medical history. The current pregnancy began as IVF-conceived DCDA twins complicated by a vanishing twin at 13 weeks of gestation. A VCI and placenta previa were detected during the mid-trimester ultrasound examination and after implementation of the targeted scanning protocol [4]. VP was diagnosed at 19 weeks of gestation. The patient is currently at 25 weeks of gestation and is being followed in our antenatal high risk clinic.

We found a significant difference in the prevalence of VP in pregnancies started as multiple gestations but which continued as singletons compared to multiple pregnancies (8.0% vs. 0.2% respectively, $P < 0.0001$, Fig. 1). The OR for VP in pregnancies starting as multiple gestations but progressing as singletons was 41.1 (95% CI, 12.77–131.94).

Discussion

The findings of the present study underscore the importance of prenatal diagnosis of VP [4,12–14] as seen in the low Apgar scores at 1 and 5 min, low cord blood pH value, newborn resuscitation, blood products transfusion, and NICU supervision in two of the four cases when the diagnosis was made during delivery.

Twin pregnancies are known to have a higher incidence of succenturiate lobes and other morphological placental abnormalities [5,8,18–20]. A VCI of one of the umbilical cords is eight times more frequent in twins than in singletons [19]. Our recent case series and systematic review has indicated that VCI was the most frequent additional ultrasound finding in twins presenting with VP [20]. Five of the 7 cases (71.4%) of our series and 5 of the 8 cases (62.5%) described in the literature presented with a VCI [20]. In pregnancies presenting with a bilobate placenta or a succenturiate lobe, the VP odds ratio was evaluated at 2.1 (95% confidence interval, 1.0–4.2) in twin pregnancies [19].

The pathogenesis of VCI is uncertain. One theory, called the 'trophotropism theory', was first introduced by Kouyoumdjian et al. [21] (to explain the preferential implantation and placentation at sites with optimal uterine perfusion). Placental development and remodeling are dependent on factors that determine the relative myometrial perfusion, the insertion of the umbilical cord modifying its initial position according to the placental pole migrating towards the more vascularized uterine area [22]. This could explain why velamentous cords are associated with an increased risk of other placental disorders such as placental abruption, placenta praevia, pre-eclampsia and intrauterine growth restriction and epidemiological data suggests shared genetic and environmental mechanisms associated with altered implantation, migration, invasion and transformation of the spiral arteries [23]. By contrast, marginal cord insertions is associated with decreased placental weight but not fetal weight suggesting a primary developmental disorder with increased utilization of placental reserve [24]. Our recent data indicate that the association of a VP with a velamentous cord is associated with a decrease in both placental and fetal growth [25].

VP has been reported to be as 1 in 200 pregnancies conceived after ART [11,26]. Two of the four cases (50%) included in the present study resulted from IVF. ART and more particularly in vitro fertilization (IVF) have been linked to a higher incidence of abnormally shaped placenta, placenta previa, and cord insertion outside the placental chorionic plate [11,26]. It has been hypothesized that these placental and cord anomalies are related to the inadequate orientation of the IVF blastocyst at the time of implantation or a higher incidence of vanishing twins in IVF than in spontaneous twins [6,26–30]. These data suggest that in the

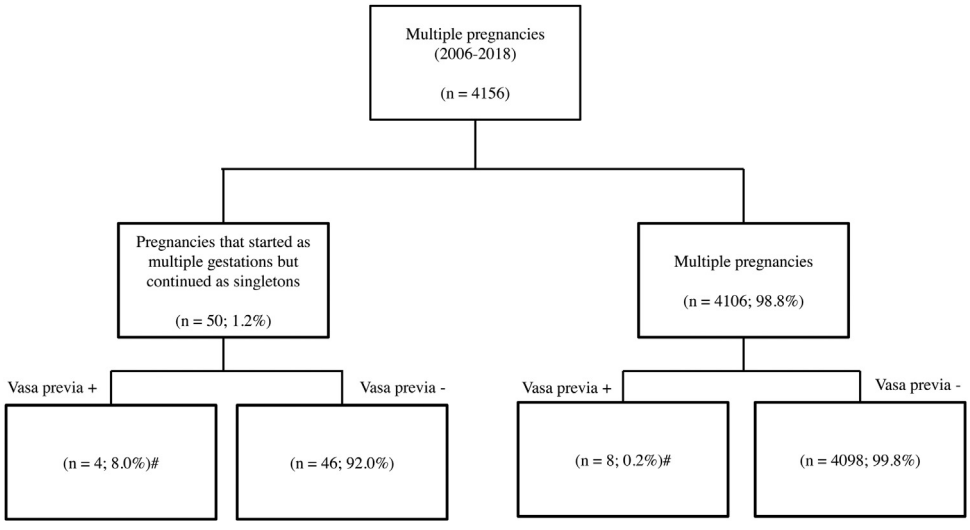

Fig. 1. Flow chart showing the distribution of multiple pregnancies in our institute. # = $p < 0.0001$, Fisher's Exact Test.

coming years the incidence of VP in both singleton and multiple pregnancy gestations is likely to increase with increased use of ART worldwide.

In two of the four cases (50%) included in the present study VCI was observed. We may speculate that same of the above mechanism that contributes to the etiology of vasa previa in twins may still persist even after in utero demise of one of the co-twins.

During the mid-gestation ultrasound examination to exclude a VCI or another main risk factor for VP, identification of the placental cord insertion is easy and accurate, takes less than 1 min, and requires no additional scanning skills for a trained sonographer. Currently however there are no guidelines for universal scanning for VP as part of a complete ultrasound examination. Recently, we showed that implementing standardized prenatal targeted scanning protocols for pregnant women with risk factors for VP improves prenatal diagnosis and hence the perinatal outcome [4]. Our study examined 51 cases with confirmed VP at delivery [4]. Importantly, the prenatal detection rate increased after implementation of the scanning protocol [nine of 18 cases (50%) vs. 29 of 33 cases (87.9%)] [4]. Accurate prenatal diagnosis can thus reduce the risks of perinatal complications as manifested primarily by low Apgar scores, and improve umbilical cord pH and hemoglobin levels for newborns with VP [4].

The current report is limited by its retrospective design and data analysis. In particular, our registry may not include information on all pregnancies that started with multiple viable gestations but ended with a single fetus. Thus, we may have underestimated the true incidence of these cases, which may not be a rare event.

Our findings suggest there is an increased risk of VP in conceptions that begin as viable multiple gestations but continue as singletons. If confirmed by other studies, it may be prudent to consider all twins at risk of VP at the beginning of pregnancy, irrespective of the actual number of live fetuses at later stages of gestation.

Conflicts of interest

None.

Funding and support

None.

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