Second-trimester miscarriage and umbilical cord knot. Case report and review of the literature

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Summary

Purpose of investigation: The present study presents a case with an umbilical cord knot along with extensive literature review. *Materials and Methods:* Presentation of a rare case of second-trimester abortion which was attributed to a tight umbilical cord knot. Furthermore the authors reviewed the literature from 1952 to 2012 in order to compare impact of knots on intrapartum and perinatal outcomes. *Results:* Four large retrospective studies assessed several predisposing factors. Long umbilical cords, male embryos, and multiparity were correlated with knots in three of these studies. Data regarding perinatal effects of true knots from three studies were summarized and compared. *Conclusion:* Umbilical cord true knots during the second trimester could be a very rare cause of abortion. The presence of knots during the third trimester and labor do not seem to be associated with increased perinatal and intrapartum morbidity and mortality, although there is still some controversy in the literature on this topic.

Key words: Knot; Umbilical cord; Cord knot; Pregnancy outcome; Miscarriage; Abortion.

Introduction

To present a second-trimester miscarriage where a true knot was the more probable cause of fetal demise and to review the literature on umbilical cord knots. Objective of the present review was to gather and compare the data on important aspects of knotted pregnancies, such as predisposing factors, ultrasound diagnosis, and effects of knots on pregnancy outcome.

A review of the literature took place on Medline Pubmed, and Embase from 1952 to April 2011. The words included in the search were: "umbilical cord knots" and "true knots". From 1952 to date the search yielded 64 articles. The authors included in this review only large retrospective studies, interesting case reports, and general articles. Hence, data from nine retrospective studies, nine case reports, and four general articles were studied. An attempt was made to compare the results of retrospective studies, the aspects of the studies were assessed with similar parameters.

Case Report

A 34-year-old woman, gravida 2 para 1, had a second-trimester miscarriage at 16+1 weeks of gestation. Her first pregnancy, at the age of 30, was terminated at 32 weeks of gestation (preterm birth history). She had been diagnosed with an intrauterine growth restriction (IUGR) embryo and the pregnancy was terminated at the 32nd week, when she delivered by cesarean section a female baby weighing 1,450 g. Due to this incident, the patient was tested and resulted negative for inherited or acquired thrombophilia. Her remaining medical and family histories were clear. She was a non-smoker with a 22 body mass index (BMI) score.

At the 12th week of the present gestation, she underwent a first-trimester screening (nuchal translucency + first-trimester serum markers) and was found to have a low-risk gestation for chromosomal defects. She had a singleton pregnancy, with an appropriate fetal gestation age and the pulsatility index (PI) values of the uterine arteries were within normal range. Her blood and urine tests during the pregnancy were normal.

At the 16th week of gestation she was submitted to a routine scan where no fetal heart function was detected and an arrest of fetal development was documented. Thus a second-trimester miscarriage was diagnosed.

The following day she was introduced to the Hospital and received 400 mg of vaginal misoprostole and a vacuum aspiration completed the emptying of the uterus several hours later. At the time of abortion a tight knot was noted in the umbilical cord (Figure 1), while the fetus and the placenta were morphologically normal.

Her postoperative recovery was uneventful and she was discharged home the next day. Both the dead embryo and the placenta were histopathologically examined. No anatomical malformations were found in the organs of the dead female fetus. The placenta weighted 65 g with no anomalies found.

The only pathological finding was a true knot of the umbilical cord at 7.6 cm distance from the cord's placental outgrowth. The knot of the umbilical cord was found with venous distention at the knot's location (placental side) and a mural thrombosis in the umbilical vein.

Discussion

True umbilical cord knots occur in approximately one percent of singleton pregnancies. While single umbilical artery is the more frequent abnormality of the umbilical cord, true knots represent approximately four percent of cord complications [1]. In a recent retrospective study of gross cord abnormalities, a much higher incidence (20.6%) of knots was found among single cord abnormalities [2].

A study of spontaneous abortion specimens by Javert and Barton found 35% (104 out of 297) of the analyzed cords to be abnormal. The percentage of knotted cords among these abnormal cords was 0.9% (one out of 104). The afore-

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Figure 1. — Photograph showing a tight knot in the umbilical cord.

Table 1. — *Predisposing factors for development of umbilical cord knot during pregnancy.*

Studies / Predisposing Factors	Airas *et al.* /2002/Am. J. Peritonal/ 23,215 deliveries	Blickstein *et al.* /1987/Int. J Gynaecol Obstet/ 4,650 deliveries	Hershkovitx *et al.* /2001/Eur J Obstet Gynecol Reprod Biol/ 69,139 deliveries	Spellacy *et al.* 1966/Am J Obstet Gynecol/ 17,190 deliberies
Long cords	√	√	?	√
Polyhydramnios	(-)	(-)	√	?
Small fetuses	(-)	(-)	(-)	(-)
MC/MA* twins	?	?	X	?
Multiparity	√	√	√	(-)
Male fetuses	√	√	√	?
Obesity	√	?	?	?
Maternal anemia	√	?	?	?
Maternal age	√	(-)	√	(-)
Previous miscarriages	√	?	√	?
Amniocentesis	?	?	√	?
Chronic hypertension	?	?	√	?

√: correlation found, (-): no correlation, X: excluded from this study, ?: not assessed in this study, *: monochorionic/monoamniotic

mentioned study showed the rare presence of umbilical cord knots associated to fetal demise that occurred until the 20th week of gestation [3]. A knot is formed when the embryo passes through a loop of the umbilical cord. This is apparently easier for a small embryo or when the cord is long enough. Conditions that ease fetal movements (e.g. long cords, more amniotic fluid) or provide a larger uterus (multiparity), could be contributing factors to knot formation. Long umbilical cords and polyhydramnios had been correlated with true knots [2, 4-7].

Several factors are considered to predispose to knot formation. Table 1 summarizes the results of four retrospective studies [1, 4, 5, 8] which assessed the correlation between various factors and knot presence in a large series of births. In three out of four studies male sex appears as a predisposing factor in knot formation. The fourth did not assess this parameter. By combining the fact that three out of four studies discuss long umbilical cords as a predisposing factor and the well-documented fact in the literature that male fetuses have longer cords [7, 9], an explanation could be postulated for this gender differentiation among knotted fetuses. Male fetuses due to their longer umbilical cords, which allows greater mobility, may form knots more easily than female fetuses. Also, three out of four studies [4, 5, 9] agree on multiparity as a predisposing factor. The larger uterus in this case, which enables fetal mobility, may explain this finding.

An interesting conclusion is that none of these four large studies found any correlation among small fetuses and knots. Although theoretically speaking small fetuses could pass easier through cord loops, giving rise to knots, this assumption was not confirmed by either of the studies. Furthermore, it appears that the presence of knots is not associated with uteroplacental insufficiency. Previous miscarriages and maternal age were considered predisposing factors in two studies [5, 9]. Only one study (5) correlated polyhydramanios with umbilical knots. Hershkovitz *et al.* were the first who assessed amniocentesis and chronic hypertension and found a statistical significant correlation. The same researchers did not find any correlation between mild or severe pregnancy-induced hypertension and umbilical cord knots. In the present case, there was none of the above predisposing factors.

Monochorionic monoamniotic twins, although frequently referred to as high-risk population for knots, were either excluded or not assessed in these studies.

Several opinions have been expressed on the gestational age at which knot formation takes place. Blickstein *et al.* [4] proposed the period between nine and 28 weeks as the more probable for knot formation.

The prenatal diagnosis of knots through ultrasound examination is rare and difficult. A specific sonographic finding has been reported by Ramón y Cajal and Martinez [10], and called it the "hanging noose sign". In this sign, by using power Doppler imaging, a transverse section of the umbilical cord is surrounded by a loop of umbilical cord. The use of 3D/4D imaging may confirm these sonographic signs, as has been mentioned by several reports [11-13].

Another specific sonographic feature is the "four-leaf clover". Two parts of the umbilical cord crossing each other may give rise to the sonographic appearance of this sign, which however lacks specificity and cannot contribute to the differential diagnosis between true and false knots [14, 15].

Varication of the umbilical vein can be differentiated from a knot by ultrasound, due to the lack of cord's tortuosity at the level of the knot [16].

Three large retrospective studies [4, 8, 17] assessed the risks for fetal demise due to umbilical cord knots, by comparing knotted and unknotted pregnancies. Fetal death rates and other perinatal parameters from these studies are summarized in Table 2. Fetuses with true umbilical cords were found to be at a four- to ten-fold increased risk of stillbirth [8, 17].

As for the mode of delivery, cesarean section rates were found to be either similar [17] or unexpectedly lower [8] in the knotted pregnancies. Findings concern-

Table 2. — *Correlation of umbilical cord knot with perinatal and intrapartum outcome.*

	Knotted pregnancies/ percentage	Fetal death in knotted pregnancies/ percentage	Cesarian section in knotted pregnancies/ percemtage	Cesarian section in unknotted/ pregnancies	Vaginal operative deliveries in knotted pregnancies	Vaginal operative deliveries in unknotted pregnancies	Fetal heart rates pathologic/suspicious
Airas et al./ 2002/ Am J Perinatol/ 23,215 deliveries	288 1.25%	4 1.4%	34 11.8%	3,881 16.9%	34 11.8%	1,377 5.9%	Similar rates of pathologic FHR among knotted/ unknotted (16.7% vs 15.9%)
Sornes et al./ 2000/ Acta Obstet Gynecol Scand/ 22,012 deliveries	216 1%	6 2.7%	24 11.1%	2,304 10.6%	8 3.71%	1,310 6.9%	?
Blickstein et al./ 1987/Int J Gynaecol Obstet/ 4,650 deliberies	57 1.22%	2 3.7%	9.4%	?	?	?	Knotted: 12,9% pathologic or suspicious Unknotted: 4.8% suspicious

?: not assessed in the study. FHR: fetal heart rate.

ing vaginal operative delivery rates were also conflicting. Two of these studies [4, 9] assessed the Fetal Heart Rates (FHR) tracings. One found similar rates of pathologic FHR between knotted and unknotted fetuses [4], while the other recorded increased rates of pathologic or suspicious tracings [8].

Sornes *et al.* [17] found equal Apgar scores, while Airas *et al.* [9] recorded lower Apgar Scores at one min in the knotted group.

In a study that compared umbilical arterial and venous blood gas values (without FHR tracings recorded), the authors reported similar results between the knotted and the control population [18]. They concluded that umbilical cord knots lack clinical significance since no alterations were found on umbilical artery acidemia (lower pH values on the umbilical artery of the knotted pregnancies, but with no statistical significance). Therefore, perhaps the "degree" of tightness of the knot may play a key role, and together with the cord diameter, can represent the parameters which will increase the risk of fetal demise in a knotted pregnancy, which otherwise (without extreme knot-tightening and a decreased cord diameter) has no increased risk for negative outcomes [18]. Small umbilical cord diameter in knotted cords has been associated with an increased venous perfusion pressure in a study by Chasnoff and Fletcher that included fifty umbilical cords [19].

In an interesting paper by De Felice *et al.* [20], all infants with knots lacked inferior labial frenulum. Congenital oral mucosal changes (increased complexity and destructed randomness of oral vascular networks) were also recorded in these infants with an umbilical cord knot history. It has been speculated by the authors that a possible lower degree of extracellular matrix impairment may explain these findings [20].

As for any correlation between IUGR embryos and true knots, only a few case reports found a correlation between knots and IUGR fetuses [21, 22]. In none of the large retrospective studies that were reviewed was there any association among true knots and IUGR fetuses.

Conclusion

In conclusion, umbilical cord true knots during the second trimester could be a very rare cause of abortion. During the third trimester, knots seem to be a rare event and main predisposing factors for their formation are considered male sex and long umbilical cords. In addition, the presence of umbilical cords during the third trimester and labor do not seem to be associated with increased perinatal and intrapartum morbidity and mortality, although there is still some controversy on this topic in the literature. The use of ultrasonography could be helpful in specific cases.

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