

# Two Cases With Dichorionic Diamniotic Triplet Pregnancy and Early Cord Entanglement

Ashley E.R. Meri en<sup>1,2</sup>, Jim van Eyck<sup>1, 2</sup>, Birgit Arabin<sup>1,2</sup>

<sup>1</sup> Department of Perinatology, Isala (Sophia) Hospital 8025 AB Zwolle, The Netherlands

<sup>2</sup> Clara Angela Foundation, Institute of Research & Development, 58455 Witten, Germany

Within a period of 6 years (1994–99) we registered 29 triplet deliveries out of a total of 13,969 hospital deliveries (0.02%). Since there is limited information about specific problems of chorionicity in triplet pregnancies, we analysed the 29 cases according to origin of pregnancy and chorionicity. We here report on two cases with a high risk according to chorionicity with dichorionic (DC) diamniotic (DA) triplet pregnancies. Out of the two cases, one pregnancy was spontaneous and one originated after in-vitro fertilization. In both pregnancies, cord entanglement was detected early in pregnancy (at 10 and 15 weeks) by color Doppler velocimetry demonstrating different heart rates within the segment of the entangled umbilical branches. The pregnancies were followed by documenting fetal behavior and color Doppler velocimetry of umbilical and fetal arteries at weekly intervals. In both cases, a primary Cesarean section was performed after detection of lung maturity. In the first case, one of the MA triplets had a transposition of the great arteries and abnormal lung vein drainage, which was the reason for neonatal death three weeks postnatally. Although early cord entanglement has been described in MA twins, this series demonstrates that it can as well be demonstrated in MA triplets. The early detection allows for extensive surveillance of the a priori high risk triplet pregnancy.

Monoamniotic (MA) multiple pregnancies are rare and occur when one fertilized ovum divides between day 7 and 13 after fertilization (Annan & Hutson, 1990). The incidence of monozygotic (MZ) twins, which is world wide fairly constant, is approximately 4 in 1000 pregnancies (0.4%). About 1% of the MZ twins is MA (Quigley, 1935). The incidence of MA twin pregnancies varies in the literature from 1: 6,500 (Simonsen, 1966) to 1: 93,734 (Colburn & Pasquale, 1982) and is approximately 1: 25–30,000 of pregnancies (Salerno, 1959; Tessen & Zlatnik, 1991). Chorionicity is influenced by infertility techniques (Blickstein et al., 1999).

Cord entanglement has been reported in up to 70% of MA twins at birth (Salerno, 1959). Perinatal mortality in MA twins ranges between 30–70% (Benirschke & Kaufmann, 1990; Quigley, 1935; Rodis et al., 1987; Timmons & DeAlvarez, 1963) with up to 50% due to cord entanglement (Baldwin, 1994). However, this rate may even be higher when cord entanglement is detected prenatally (Arabin et al., 1999; Sebire et al., 2000;

Shahabi et al., 1997) because there is an unknown rate of early intrauterine death.

Up to now, most authors describing cases or series with cord entanglement have concentrated on risks of fetal demise and death in MA twin pregnancies. In triplet pregnancies, cord entanglement might even be more harmful since antenatal surveillance is more complex. Since there are up to now no large studies about the prognosis of triplets considering the risks of different chorionicity, we here describe the course of two DC DA triplet pregnancies which were characterized by an additional risk: cord entanglement between two of the triplets diagnosed early in pregnancy.

## Chorionicity and Origin of Pregnancy in 29 Triplet Pregnancies

During 1994–1999 out of a total of 13969 deliveries at our unit, 526 twin and 29 triplet deliveries were registered. The rate of prenatally detected and postnatally confirmed MA twins was 5/526 (ca.1%). The rate of DC DA triplet pregnancies with two MA triplets in each pregnancy was 2/29 (7%).

The chorionicity of all our triplet pregnancies related to the origin of pregnancy was analyzed (Table 1). Within the total group of triplets, there were 8 spontaneous triplet pregnancies (1 DC DA, 6 DC TA, 1 TC TA) 4 after ovulation induction (4 TC), 14 after in-vitro fertilization (1 DC DA, 3 DC TA, 10 TC TA) and 3 after in-vitro-fertilization combined with intra-cellular sperm injection (ICSI) (3 TCTA). 7/8 of the spontaneous triplet pregnancies were DC, only 1/8 trichorionic (TC). All triplet pregnancies after ovulation induction ( $n = 4$ ) were TC. Among the triplets after in vitro fertilization (IVF) ( $n = 14$ ), 10 were TC, all of them after replacement of three “embryos”, 3 were DC triamniotic (TA) and 1 was DC DA. All 4 of these DC triplet pregnancies originated after replacement of two “embryos”. The 3 triplet pregnancies

Address for correspondence: Birgit Arabin, MD PhD, Isala Klinieken, location Sophia 8025 AB Zwolle, The Netherlands. Email: clara-angela@wxs.nl

after intracellular sperm injection (ICSI) were all TC, after replacement of three “embryos”.

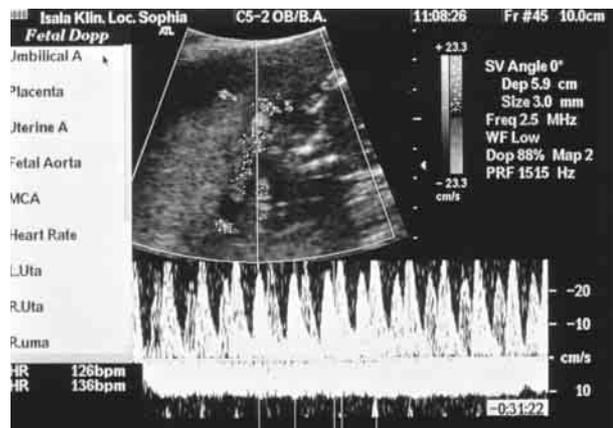
Out of the two cases with DC MA triplet pregnancies, one was originated after IVF and one was spontaneous. Cord entanglement was prenatally diagnosed in both cases.

**Case 1**

In a 34-year-old woman, gravida 2 para 0, a DC DA spontaneous triplet pregnancy was diagnosed at 12 weeks by ultrasound. Two chorionic sacs were visualized by transvaginal ultrasound without any inter-twin membrane between two of the triplets. Cord entanglement between the two MA triplets was observed from 15 weeks onwards by color Doppler which became more “severe” during the following weeks (Figure 1). Doppler velocimetry of the same segment revealed the different pulsatile waveforms with two different heart rates in the umbilical arteries (Figure 1b).

Weekly ultrasound examination demonstrated normal growth. However, in one of the MA triplets there was a suspicion of interventricular septal defect transposition of the great arteries and abnormal position. The Doppler waveform patterns in the umbilical and cerebral arteries, as well as in the ductus venosus remained normal during the whole pregnancy in all triplets. There was no sign of congestive heart failure and no sign of constriction of the umbilical cord by color Doppler velocimetry at any time of pregnancy. At 26 weeks, the mother was admitted due to increasing discomfort and premature contractions. Cesarean section was performed after lung maturity was confirmed by amniocentesis at 31 weeks and three girls were delivered with birth weights of 1880 g (DC girl), 1720 g and 1480 g (MA girls). The Apgar-values after 1, 5 and 10 minutes were of 5/8/9 (A), 2/3/5/ intubation (B) and 5/8/10 (C) and pH values in the umbilical arteries were 7.28 (A), 7.28 (B) and 7.25 (C).

Cord entanglement was confirmed between the two umbilical cords of the MA triplets. The distance of the two umbilical cord insertions at the chorionic plate was less than 1 cm (Figure 2). Computer angiography of the MC part of the placenta confirmed deep arteriovenous(AV) anastomoses between both MA twins in both directions and even the cord entanglement. Examination of the placenta by conventional color dye injection confirmed a DC



**Figure 1.**

Color Doppler of increasing cord entanglement at 24 gestational weeks (a) (Case 1), corresponding Doppler velocimetry of the segment of cord entanglement at 15 weeks showing two different heart rates within the segment (b) (Case 1 and 2).

DA placenta with 6 AV (1 from MA twin B to C/ 5 from MA twin C to B) and 1 arterioarterial (AA) anastomoses between the MA triplets. Postnatal echocardiography of the triplets revealed not only dextrocardia, an interventricular septal defect and a transposition of the great arteries but also abnormal lung-vein drainage in one of the MA triplets. Second opinion of neonatal cardiologists and heart surgeons was pessimistic about the prognosis due to extent of abnormal lung vein drainage and refused surgical correction. Unfortunately, this child died 3 weeks postnatally due to progressive decompensation.

Blood group analysis revealed that the single triplet had a different blood group compared with the MA triplets. This triplet was thus dizygotic with the other two. Up to now the two remaining triplets have developed uneventfully.

**Case 2**

In a 33-year-old woman, gravida 1 para 0, a DC DA triplet pregnancy was diagnosed at 8 gestational weeks, after in vitro fertilization and replacement of only two “embryos”. Two chorionic sacs were visualized by transvaginal ultrasound with only one yolk sac in each of them. Cord entanglement between the two MA triplets was observed from 10 weeks onwards by color Doppler.

**Table 1**

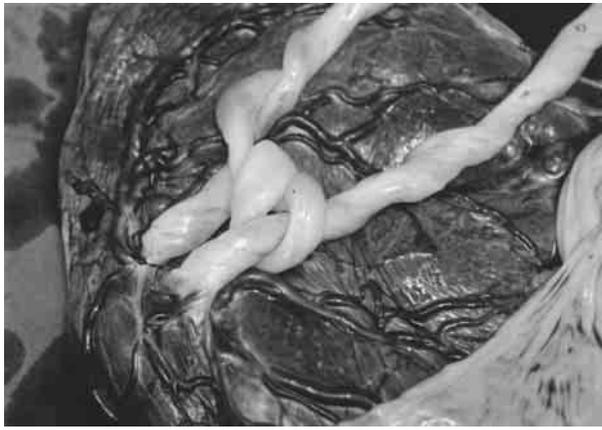
Chorionicity of Triplet Pregnancies (n = 29) Related to the Origin of Pregnancy

	MCMA	MCDA	MCTA	DCDA	DCTA	TCTA	TOTAL
Spontaneous				1	6*	1	8
Ovula-induction						4	4
IVF				1	3*	10	14
ICSI						3†	3
<b>TOTAL</b>				<b>2</b>	<b>9</b>	<b>18</b>	<b>29</b>

† one case with twin-to-twin transfusion syndrome (TTTS)

\* in all cases only two fertilized eggs had been retransferred

† after transfer of three “embryos”



**Figure 2.**

Cord entanglement confirmed after delivery at the chorionic placental surface with the close insertion of the two umbilical cords at less than 1 cm (Case 1).

Doppler velocimetry from the common segment revealed two different heart rates, measured by the peak velocity distances from the umbilical arteries similar as in case 1 (Figure 1b). Prenatal behavior and Doppler sonography were performed at weekly intervals. The waveform patterns in the umbilical and cerebral arteries, as well as in the ductus venosus of all triplets remained normal and there was no sign of constriction of the umbilical cords. The mother was admitted at 32 gestational weeks due to symptoms of preeclampsia. Lung maturity was only confirmed at 35 gestational weeks by amniocentesis from two compartments and a Cesarean section was performed. The birth weights were 1950 g (boy), 2160 g and 1980 g (MZ girls), Apgar and pH values were normal. Four-fold cord entanglement was confirmed between the two umbilical cords of the MA triplets. The distance of the two umbilical cord insertions at the chorionic plate was 6 cm. All triplets have developed uneventfully.

## Discussion

Preterm labor has been reported as high as 92.3% in triplets, more than double of the rate than in twins (Baldwin, 1994). Mortality and morbidity mainly depend on the rate of prematurity (Glinianaia et al., 2000) but also on the chorionicity of the placenta (Bleker et al., 1979). In MC twins, the mean gestational age and birth weight at delivery is less than in DC twins (Bleker et al., 1979).

The detection of chorionicity is not only essential in twins but also in triplet pregnancies. In multiple pregnancies, placentation is influenced not only by the number of zygotes but also by the number of blastocysts and, before or after implantation, the division of the inner cell mass. With regard to triplets, a fused placenta is more common, regardless of zygosity, simply because of uterine crowding (Derom et al., 1995). According to Derom the aphorisms for triplets are as follows:

- trizygotic triplets are trichorionic;
- dizygotic triplets are either di- or trichorionic;
- monozygotic triplets are either tri-, di- or monochorionic;

- dichorionic triplets are either mono- or dizygotic and
- monochorionic triplets are monozygotic.

A unique feature of placentation in multiple pregnancy is the high prevalence of marginal and velamentous insertion of one or more umbilical cords (Derom et al., 1995). However, this was not observed in our two cases.

Ideally, chorionicity is determined by ultrasound early in pregnancy. When a MA multiple pregnancy is diagnosed, one has to be aware of cord entanglement. In cases of DC triplet pregnancies, the amniotic membranes need to be determined. In our cases, a DC DA triplet was diagnosed at 8 and respectively at 12 gestational weeks. By both transvaginal and transabdominal ultrasound no separate amniotic membrane was observed between two of the MC triplets. As in MC MA twin pregnancies (Bromley & Benacerraf, 1995) we found that the two MA triplets demonstrated with only one yolk sac.

Within the spontaneous triplet group, we noticed a high frequency of MC twin pairs (7/8). Whether this is just due to our small sample number or even reflects percentages within the whole population in the Netherlands is not yet possible to determine, because up to now there is no population-based detection of chorionicity and zygosity in this country.

Cord entanglement may be a cause of intrauterine death in more than 50 percent of MA twin pregnancies (Baldwin, 1994). Nevertheless, the cause-specific prenatal mortality can never be defined with absolute certainty. The estimated mortality of MA multiples due to cord entanglement in our unit is up to now 25% (2/8), including 2 cases with intrauterine death at 15 weeks. Whether enhanced ultrasound surveillance and timed delivery may have any influence on the further outcome is uncertain.

The postnatal death of one of our MA triplets with severe cardiac malformation was not directly correlated to entanglement. Whether the very close insertion of umbilical cords might have had an influence on the early development of cardiac malformation must remain open. Some explanations for the origin of monozygotic multiples discrepant for anomalies are mosaicism with variable expression, monovular dispermic twinning, postzygotic chromosomal non-dysjunction, X-chromosome inactivation or anastomoses leading to abnormal vascular events and residual organ damage (Machin & Keith, 1999). The frequency of anomalies does not appear to be greater in triplets than in twins, although some studies actually dismiss malformed infants from discussion (Baldwin, 1994).

Using color and pulsed Doppler, the diagnosis of cord entanglement in MA triplets is as feasible as in MA twins (Belfort et al., 1993; Rosemond & Hinds, 1998). Early diagnosis of multiple pregnancy, early determination of chorionicity and detection of cord entanglement can improve information of parents and future management. Until now, a consensus on prognostic criteria has not been established. There are still different opinions as to whether the risks of early delivery outweigh the risks of fetal death as a result of MA twinning (Aisenbrey et al., 1995; Carr et al., 1990; Ritossa & O'Loughlin, 1996). Because of the cord complications that can occur during a vaginal delivery,

we recommend to deliver all MA multiplets with cord entanglement by Cesarean section. In our cases, the patients were admitted for reasons other than cord entanglement. The Cesarean section was performed after lung maturity was proven.

Multicenter studies are required to determine the prognosis of triplets according to chorionicity, eventual complications such as transfusion syndrome or even cord entanglement and to optimize surveillance and the timing of intervention.

## References

- Aisenbrey, G. A., Catanzarite, V. A., Hurley, T. J., Spiegel, J. H., Schrimmer, D. B., & Mendoza, A. (1995). Monoamniotic and pseudoamniotic twins: Sonographic diagnosis, detection of cord entanglement, and obstetric management. *Obstetrics and Gynecology*, *86*, 218–222.
- Annan, B., & Hutson, R. C. (1990). Double survival despite cord entwinement in monoamniotic twins. Case report. *British Journal of Obstetrics and Gynaecology*, *97*, 950–951.
- Arabin, B., Laurini, R. N. & van Eyck, J. (1999). Early prenatal diagnoses of cordentanglement in monoamniotic multiple pregnancies. *Ultrasound in Obstetrics and Gynecology*, *13*, 181–186.
- Baldwin, V. J. (1994). *Pathology of multiple pregnancy*. New York: Springer.
- Belfort, M. A., Moise, K. J. Jr., Kirshon, B., & Saade, G. (1993). The use of color flow Doppler ultrasonography to diagnose umbilical cord entanglement in monoamniotic twin gestations. *American Journal of Obstetrics and Gynecology*, *168*, 601–604.
- Benirschke, K., & Kaufmann, P. (1990). *Pathology of the human placenta* (2nd ed.). New York: Springer.
- Bleker, O. P., Breur, W., & Huidekooper, B. L. (1979). A study of birth weight, placental weight and mortality of twins as compared to singletons. *British Journal of Obstetrics and Gynaecology*, *86*, 111–118.
- Blickstein, I., Verhoeven, H. C., & Keith, L. G. (1999). Zygotic splitting after assisted reproduction. *New England Journal of Medicine*, *340*, 738–739.
- Bromley, B., & Benacerraf, B. (1995). Using the number of yolk sacs to determine amnionicity in early first trimester mono-chorionic twins. *Journal of Ultrasound in Medicine*, *14*, 415–419.
- Carr, S. R., Aronson, M. P., & Coustan, D. R. (1990). Survival rates of monoamniotic twins do not decrease after 30 weeks gestation. *American Journal of Obstetrics and Gynecology*, *163*, 719–722.
- Colburn, D. W., & Pasquale, S. A. (1982). Monoamniotic twin pregnancy. *Journal of Reproductive Medicine*, *27*, 165–168.
- Derom, R., Derom, C., & Vlietinck, R. (1995). Placentation. In L. G. Keith, E. Papiernik, D. M. Keith, & B. Luke (Eds.), *Multiple pregnancy: Epidemiology, gestation & perinatal outcome* (pp. 113–128). Carnforth, UK: Parthenon Publishing.
- Glinianaia, S. V., Pharoah, P., & Sturgiss, S. N. (2000). Comparative trends in cause-specific fetal and neonatal mortality in twin and singleton births in the North of England, 1982–1994. *British Journal of Obstetrics and Gynaecology*, *107*, 452–460.
- Machin, G. A., & Keith, L. G. (1999). *An atlas of multiple pregnancy: Biology and pathology*. Carnforth, UK: Parthenon Publishing.
- Quigley, J. K. (1935). Monoamniotic twin pregnancy. A case record with review of the literature. *American Journal of Obstetrics and Gynecology*, *29*, 354–362.
- Ritossa, M., & O’Loughlin, J. (1996). Monoamniotic twin pregnancy and cord entanglement: A clinical dilemma. *Australian and New Zealand Journal of Obstetrics & Gynecology*, *36*, 309–312.
- Rodis, J. F., Vintzileos, A. M., Campbell, W. A., Dearon, J. L., Fumia, F., & Nochinson, D. J. (1987). Antenatal diagnosis and management of monoamniotic twins. *American Journal of Obstetrics and Gynecology*, *157*, 1255–1257.
- Rosemond, R. L., & Hinds, N. E. (1998). Persistent abnormal umbilical cord Doppler velocimetry in a monoamniotic twin with cord entanglement. *Journal of Ultrasound in Medicine*, *17*, 337–338.
- Salerno, L. J. (1959). Monoamniotic twinning: A survey of the American literature since 1935 with a report of four new cases. *Obstetrics and Gynecology*, *14*, 205–213.
- Sebire, N. J., Souka, A., Skentou, H., Geerts, L., & Nicolaides, K. N. (2000). First trimester diagnosis of monoamniotic twin pregnancies. *Ultrasound in Obstetrics and Gynecology*, *16*, 223–225.
- Shahabi, S., Donner, C., Wallond, J., Schlikker, I., Avni, E. F., & Rodesch, F. (1997). Monoamniotic twin cord entanglement. A case report with color flow Doppler ultrasonography for antenatal diagnosis. *Journal of Reproductive Medicine*, *42*, 740–742.
- Simonsen, M. (1966). Monoamniotic twins. *Acta Obstetrica et Gynecologica Scandinavica*, *45*, 43–52.
- Tessen, J. A., & Zlatnik, F. I. (1991). Monoamniotic twins: A retrospective controlled study. *Obstetrics and Gynecology*, *77*, 832–834.
- Timmons, J. D., & DeAlvarez, R. R. (1963). Monoamniotic twin pregnancy. *American Journal of Obstetrics and Gynecology*, *86*, 875–881.