

Delayed-Interval Delivery in Dichorionic Twin Pregnancies: A Single-Center Experience

Mauro Cozzolino, MD, Viola Seravalli, MD, Giulia Masini, MD, Lucia Pasquini, MD, Mariarosaria Di Tommaso, MD

Department of Biomedical, Experimental, and Clinical Sciences—Division of Obstetrics and Gynecology, University of Florence, Florence, Italy

Background: Preterm delivery is the most common complication of multiple gestations and is associated with high perinatal mortality. When preterm labor occurs, delivery of the first fetus is inevitable. However, successfully delaying the delivery of the second fetus can be lifesaving.

Case Report: We report 2 cases of delayed-interval delivery of dichorionic diamniotic twin pregnancies admitted to our emergency department at 17+5 and 22+1 weeks of gestation. After abortion of the first fetus, the second twin was left in utero, and uterine contractions ceased. The patients received antibiotics, and tocolytic therapy was administered when needed after 24 weeks. This management prolonged pregnancy for 64 and 16 days, respectively.

Conclusion: Although no accepted protocol for the treatment of this condition currently exists, an excellent outcome for the second fetus is possible if these pregnancies are managed in a tertiary perinatal center.

Keywords: Cerclage–cervical, delivery–obstetric, pregnancy–twin, tocolysis

Address correspondence to Mauro Cozzolino, MD, Department of Biomedical, Experimental, and Clinical Sciences—Division of Obstetrics and Gynecology, University of Florence, Largo Brambilla 3, 50134, Florence, Italy. Tel: (+39) 055-794-6219. Email: maurocoz@yahoo.it

INTRODUCTION

The number of multiple pregnancies has drastically increased in recent years, and the principal reason is the use of assisted reproductive technology.¹ Preterm delivery is the most common complication of multiple gestations and is associated with high perinatal mortality and morbidity. Frequently, when preterm labor occurs, delivery of the first fetus is inevitable. Traditionally, this situation is managed by delivery of both fetuses, either vaginally or by cesarean section. However, an increasing number of case reports describe delaying delivery of the second twin for days and even weeks (delayed-interval delivery or asynchronous delivery).² The successful delay of the delivery of the second or even third fetus can be lifesaving.

Gestational age is the most important predictor of neonatal survival for babies born before 25 weeks of gestation.² Currently, to extend the time in utero of the second twin, tocolytics, antibiotics, and cerclage are used.^{3,4}

This report describes 2 cases of twin pregnancies with preterm labor and delayed-interval delivery at the Department of Maternal and Child Health of Careggi University Hospital in Florence, Italy, between 2012 and 2013. We describe our management of the cases and the deliveries and the neonatal outcomes.

CASE REPORT

Two patients with dichorionic, diamniotic pregnancy were admitted to our emergency department at 17+5 and 22+1

weeks of gestation, respectively, because of regular contractions and cervical modification. Both pregnancies were achieved with in vitro fertilization, and one patient had received an oocyte donation. No clinical signs of chorioamnionitis were noted at the time of admission. Both patients exhibited cervical dilatation, but no tocolytic therapy was administered because of the low gestational age of the fetuses. Pregnancy and delivery outcomes are reported in Table 1.

During their hospitalizations, both patients delivered the first fetus within 2 weeks of admission, and the fetuses were stillborn. In both cases, the expulsion of the first twin was preceded by the rupture of the amniotic sac and by an increase in white blood cells and C-reactive protein. Immediately after the delivery of the first twin, uterine contractions ceased, the umbilical cord was ligated as high as possible in the cervix under aseptic conditions, and the placenta was left inside the uterus. The perineum and vagina were rinsed with chlorhexidine. The fetal heart rate of the second twin was normal, and membranes remained intact.

After delivery, both patients started systemic antibiotic therapy with clarithromycin 1 g per day with intravenous (IV) ampicillin 8 g for the first 2 days and oral amoxicillin 750 mg per day for the next 5 days, for a total of 7 days of combined therapy. Vaginal progesterone was administered to the patients after the delivery of the first fetus. One patient also

Table 1. Pregnancy and Delivery Outcomes in the Two Cases

	Patient 1	Patient 2
Mode of conception	ICSI	ICSI
GA at admission, weeks	17+5	22+1
GA at delivery, weeks, first twin	18+1	23+1
Birth weight, g, first twin	135	510
GA at delivery, weeks, second twin	27+2	25+3
Birth weight, g, second twin	1,070	542
Interval, days	64	16
Mode of delivery	Vaginal delivery	Cesarean section

GA, gestational age; ICSI, intracytoplasmic sperm injection.

received IV metronidazole because of abnormal vaginal discharge.

The patients were continuously monitored for blood pressure, heart rate, body temperature, and microbiological vaginal and urine cultures. Twice per week, blood tests were performed to evaluate infection parameters, including white blood cell and C-reactive protein levels. To reduce the risk of infection, digital vaginal examinations were not performed. After their deliveries, the patients' white blood cell and C-reactive protein levels progressively decreased.

Tocolytic therapy was administered to both patients only if contractile activity occurred after 24 weeks. Atosiban was our first-choice drug. Betamethasone was also administered to accelerate fetal lung maturation. Tocolytic therapy was continued for 48 hours to allow betamethasone to act fully.

Fetal monitoring consisted of ultrasound examinations at regular intervals to assess amniotic fluid volume, fetal growth, and umbilical artery Doppler. Cardiotocography for fetal heart rate monitoring was performed daily from 27 weeks of gestation. Under 27 weeks, we recorded the fetal heart for 1 minute using ultrasound. No abnormal findings were noted during the hospital admission.

One patient was discharged; the other patient remained in the hospital until the end of her pregnancy. A cesarean section was performed in one patient after the onset of spontaneous labor because of nonvertex fetal presentation at 25+3 weeks. In the other patient, gestation contractions started at 27+2 weeks, membranes of the second twin ruptured spontaneously, and the baby was delivered vaginally.

The interval between delivery of the first and the second fetus was 16 and 64 days. No maternal morbidity occurred before or after delivery. Neonatal outcomes are reported in Table 2.

The placentas were sent for histopathologic examination. Results showed marked neutrophilic infiltrations in the chorion and amnion of the first twin in both pregnancies. Chorioamnionitis was also present in the second twin delivered at 25+3 weeks, but no signs of infection were observed in the chorion and amnion of the twin delivered at 27+2 weeks. Neither vasculitis nor funisitis was present in either umbilical cord.

Table 2. Neonatal Outcomes

	Patient 1	Patient 2
Birth weight, g	1,070	542
Sex	Female	Female
Duration of admission, days	70	112
Weight at hospital discharge, g	2,110	2,450
Clinical condition at discharge	Good	Good

DISCUSSION

In the literature, some case reports of delayed-interval delivery exist, but the management and the reported survival rate (50%-95%) vary widely between centers.³⁻⁵

The primary maternal risks associated with attempting delayed-interval delivery are intrauterine infection and maternal sepsis.² Before attempting this procedure, the following conditions should be excluded: nonreassuring fetal status, congenital abnormalities, rupture of the membranes of the remaining fetus, severe hemorrhage, and maternal infections or diseases. Monochorionicity is not a contraindication.⁵

Our cases were not complicated by signs of infection. Our management consisted of antibiotic therapy after the first delivery and a repeated course of antibiotics when increased white blood cell and C-reactive protein levels were documented in blood tests. Antibiotic therapy is routinely administered in cases of asynchronous delivery.⁵ However, unlike other reports, we used 3 types of antibiotics, applying the same antimicrobial therapy protocol used in our department for premature rupture of membranes.

We did not perform cerclage on our patients. Some studies report that cerclage leads to a longer delivery interval;^{6,7} however, cerclage is considered to increase the risk for infection and rupture of the membrane in twin pregnancies^{5,8} and is therefore contraindicated in such pregnancies to prevent preterm birth.⁹ Because the risk of infection has not been sufficiently studied in cases of cerclage placed after the delivery of the first twin, we prefer not to employ it in such cases. Reinhard et al³ placed cerclage in all cases of delayed-interval delivery and observed a shorter duration of delay compared to Arabin and van Eyck⁵ who did not employ cerclage. Reinhard et al³ did not report the occurrence of infection in their patients.

Tocolysis and corticosteroids for fetal lung maturity were administered to both patients when the risk of preterm delivery of the second fetus seemed high, but they were never used before 24 weeks. In other studies of delayed-interval delivery, tocolytic use started after the delivery of the first fetus—even when delivery occurred before 24 weeks—and was continued until contractions ceased.^{3,10} The aim of tocolytic therapy is to prolong gestation to allow a corticosteroid effect on pulmonary maturity, but the use of tocolytics as maintenance therapy is not beneficial. Therefore, the administration of tocolytics is not indicated before 24 weeks when the gestational age has not reached viability and when type II pneumocytes have not completely formed to release surfactant.¹¹ For these reasons, we do not use tocolytic therapy before 24 weeks or for more than 48 hours. Progesterone was administered to our patients after the

delivery of the first fetus. Its use is described only in a minority of the other reports on asynchronous delivery.⁴

The intervals between delivery of the first and second fetus in our cases were 16 and 64 days. The longest interval was achieved in the patient who delivered the first fetus at the earliest gestational age in accordance with the findings by Farkouh et al who reported that the interval between delivery of the 2 fetuses appears to be highly dependent on the gestational age of the first fetus at delivery.⁶

During the period between the 2 deliveries, monitoring should focus on the early detection of chorioamnionitis, recurrent preterm contractions, signs of impending abruption, and coagulation disorders.⁵ When any of these signs is present, the birth of the second twin must be promoted without hesitation. Asynchronous delivery is a flexible procedure because no accepted protocol for the treatment of this condition currently exists. We recommend evaluating each situation on a case-by-case basis, depending on the possible risks and contraindications.

In our experience, delayed-interval delivery can prolong pregnancy for a sufficient amount of time to achieve good prognosis for the second baby. Moreover, we did not have any case of maternal morbidity. One patient was discharged, indicating that a prolonged hospitalization is not necessary in all cases of delayed-interval delivery of the second twin. This aspect is not sufficiently discussed in previous reports: some physicians have discharged mothers after cerclage,^{12,13} while others preferred strict bed rest in the hospital until the delayed delivery.⁴ We encourage discharging patients after delivery of the first twin if gestational age has not yet reached fetal viability and if the mother's clinical conditions are stable. However, currently no management has proved to be superior to any other. Arabin and van Eyck proposed a 4-step protocol and used it on a large group of patients.⁵ They point out that designing randomized trials for delayed-interval delivery is difficult because the number of such cases in any given center is small. No randomized controlled trials are reported in the literature. Consequently, each situation should be individualized, depending on possible risks, patient wishes, and contraindications.

CONCLUSION

We believe that delayed-interval delivery can be effective in prolonging gestation until a gestational age at which the chance of survival for the second fetus is higher. Therefore, delayed-interval delivery should be encouraged in tertiary-level hospitals to reduce mortality.

ACKNOWLEDGMENTS

The authors have no financial or proprietary interest in the subject matter of this article.

REFERENCES

1. Luke B. The changing pattern of multiple births in the United States: maternal and infant characteristics, 1973 and 1990. *Obstet Gynecol.* 1994 Jul;84(1):101-106.
2. Zhang J, Johnson CD, Hoffman M. Cervical cerclage in delayed interval delivery in a multifetal pregnancy: a review of seven case series. *Eur J Obstet Gynecol Reprod Biol.* 2003 Jun 10;108(2):126-130.
3. Reinhard J, Reichenbach L, Ernst T, et al. Delayed interval delivery in twin and triplet pregnancies: 6 years of experience in one perinatal center. *J Perinat Med.* 2012 Sep;40(5):551-555.
4. Fayad S, Bongain A, Holthfeld P, et al. Delayed delivery of second twin: a multicentre study of 35 cases. *Eur J Obstet Gynecol Reprod Biol.* 2003 Jul 1;109(1):16-20.
5. Arabin B, van Eyck J. Delayed-interval delivery in twin and triplet pregnancies: 17 years of experience in 1 perinatal center. *Am J Obstet Gynecol.* 2009 Feb;200(2):154.e1-154.e8.
6. Farkouh LJ, Sabin ED, Heyborne KD, Lindsay LG, Porreco RP. Delayed-interval delivery: extended series from a single maternal-fetal medicine practice. *Am J Obstet Gynecol.* 2000 Dec;183(6):1499-1503.
7. Kalchbrenner MA, Weisenborn EJ, Chyu JK, Kaufman HK, Losure TA. Delayed delivery of multiple gestations: maternal and neonatal outcomes. *Am J Obstet Gynecol.* 1998 Nov;179(5):1145-1149.
8. Van der Straeten FM, De Ketelaere K, Temmerman M. Delayed interval delivery in multiple pregnancies. *Eur J Obstet Gynecol Reprod Biol.* 2001 Nov;99(1):85-89.
9. Berghella V, Odibo AO, To MS, Rust OA, Althuisius SM. Cerclage for short cervix on ultrasonography: meta-analysis of trials using individual patient-level data. *Obstet Gynecol.* 2005 Jul;106(1):181-189.
10. Wouters KA, Gianotten J, Bayram N, Doornbos JP. Term life birth after late abortion of the first twin. *Acta Obstet Gynecol Scand.* 2009;88(10):1148-1152.
11. Antenatal corticosteroids to reduce neonatal morbidity and mortality. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); October 2010. Green-top Guideline No.: 7. <http://www.rcog.org.uk/files/rcog-corp/GTG%207.pdf>. Accessed August 28, 2014.
12. Arias F. Delayed delivery of multifetal pregnancies with premature rupture of membranes in the second trimester. *Am J Obstet Gynecol.* 1994 May;170(5 Pt 1):1233-1237.
13. Lavery JP, Austin RJ, Schaefer DS, Aladjem S. Asynchronous multiple birth. A report of five cases. *J Reprod Med.* 1994 Jan;39(1):55-60.

This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care and Medical Knowledge.