Delayed delivery of the second twin: Case report and literature review of diamniotic dichorionic twin pregnancy with very early preterm premature rupture of membranes

A. Canu, A. Giannini ⁎, P. Ghirri, E. Malacarne, F. Pancetti, T. Simoncini, P. Mannella

Department of Clinical and Experimental Medicine, Division of Gynecology and Obstetrics, Università di Pisa, Italy

ABSTRACT

In multiple pregnancies with threatened premature delivery or preterm premature rupture of membranes (pPROM) of a single sac, prolonging pregnancy after the delivery of the first baby may improve the chances of survival of the second baby. We report the delayed delivery of a second baby in a twin pregnancy with pPROM and very premature delivery of the first baby. This condition is exceptional and there are no validated medical protocols for its management; the scientific evidence is still controversial. In our case, after the birth of the first baby, pregnancy was continued for 29 days, with monitoring of maternal and fetal parameters, which enabled the delivery of the second baby with improved neonatal outcomes. This case supports the prolongation of pregnancy of the second twin.

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1. Introduction

Multiple pregnancies account for 1% of all gestations and this percentage is rising due to the increased use of assisted reproductive techniques.

Several conditions are more frequent in multiple than in single pregnancies: intrauterine growth restriction, discordant twin growth, fetal low birth weight, premature rupture of membranes, preterm birth (usually earlier than in a single pregnancy), intrauterine death, and the use of cesarean section or other forms of operative delivery [1,2]. Indeed, there is a higher prevalence of adverse neonatal outcomes in terms of mortality and morbidity [3,4].

Usually in multiple pregnancies, babies are born together but in some cases it is appropriate to delay the birth of the second baby, especially when delivery would be extremely premature. This intervention is very rare [2]. The delay between deliveries reported in the literature ranges from 1 to 152 days. Unfortunately, there is no standard approach to management in this clinical condition. Nonetheless, delayed delivery of the second fetus should be considered in the following situations [5]:

- delivery of the first fetus before the 30th week
- diamniotic dichorionic pregnancy
- intact membranes of the second fetus
- absence of intra-amniotic infection
- absence of fetal or maternal pathology requiring urgent termination of pregnancy.

In very premature delivery, immediate removal of the baby from the uterine environment could be compromised by chorioamnionitis; moreover, any benefits contrast with the risks of increased morbidity and mortality associated with prematurity [6].

There are few studies of delayed delivery in multiple pregnancies. Recently, a Cochrane review [7] and a systematic review [8] analyzed respectively 548 cases (588 babies: 548 singletons and 40 twins) and 128 cases of delayed delivery in very early pregnancy. These works did not find any relevant differences in rates of stillbirth, neonatal mortality, post-natal mortality (>28 days to discharge), cord pH < 7.00, Apgar score < 7 at 5 min, convulsions, interventricular hemorrhage or germinal matrix hemorrhage, necrotizing enterocolitis and periventricular leukomalacia or ventriculomegaly. The survival rate was, though, higher for the second fetus than for the first born; furthermore, the group of children born at immediate delivery had a higher incidence of cerebral palsy at two years than the children born after a delay.

Delayed delivery is a flexible procedure and its application depends on the clinical situation [9]. Clinical practice suggests the benefits of different treatment options. If there are no signs of chorioamnionitis, intensive monitoring of maternal status can help to prevent maternal sepsis, coagulation disorders, secondary maternal multi-organ failure and the death of the second baby. If the mother’s health is compromised, operative delivery or cesarean section should be considered.
2. Case History

A 29-year-old Caucasian woman with diastrophic dichorionic twin pregnancy at 24 + 1 weeks of gestation was admitted to the obstetric unit for preterm premature rupture of membranes (pPROM). This pregnancy was obtained with fertilized in-vitro embryo transfer. The patient had previously had a spontaneous abortion in the first trimester. During the first trimester of the current pregnancy, she had hyperemesis gravidarum, which was treated with chlorpromazine; on patient request, amniocentesis and CGH array were performed at week 18 to exclude micro-deletions and chromosomal abnormalities. At week 20, ultrasound check revealed discordant growth between the twins (35% discordance); also, the first fetus was small for gestational age (<3rd percentile) and his growth was slower than on previous checks. Both twins had ARSA (aberrant right suclavian artery); moreover, the first fetus had right ventricle hypertrophy, while the second had a double left renal artery.

At 24 + 1 weeks of gestation, the patient presented with pPROM of one of two sacs, but without fever or any other signs of chorioamnionitis. Biochemical exams revealed slight inflammation: white blood cells (WBC) 12,970; C-reactive protein (CRP) 0.58; procalctonin (PCT) negative. There were no uterine contractions. Both fetuses had cardiac activity and both had a cephalic presentation.

The patient immediately received corticosteroids (betamethasone 12 mg i.m. once a day, for two days) to promote fetal pulmonary ripening, while intravenous atosiban was given to prevent very early delivery (6.75 mg i.v. bolus over 1 min, followed by continuous infusion at 120 ml/min, then at 40 ml/min, with a total of 330.75 mg over 44 h). Subsequently, in consideration of the very early gestational age, atosiban administration was repeated for another 48 h to prolong pregnancy and delay labor. Magnesium sulfate infusion (4 g i.v. over 20 min, then 1 g/h i.v. for 24 h, for daily maintenance with 24 g until day 5, at 24 + 5 weeks) was started for twin neuroprotection. Finally, to reduce the risk of infection, cefazoline 1 g i.v. was given every 8 h, while bemiparin 3500 IU s.c. once a day was added to prevent thrombosis.

On day 4 (24 + 4 weeks) inflammatory marker values increased (WBC 14,920 cells/μL; CPR 1.34 mg/dL; PCT negative) and cefazoline was continued, although the patient still did not have fever or any other sign of infection. After one week, that is, on day 11 (25 + 4 weeks), WBC decreased to 10,100 cells/dL, while CPR and PCT were both negative.

At day 12 (25 + 5 weeks) the patient presented uterine contractions with substantial discharge of amniotic fluid. She received counseling on the imminent delivery of the first fetus and the risks of stopping labor; the patient decided together with her husband not to take any tocolytics if she did go into labor. Magnesium sulphate was restarted (at the same dose as previously) for neuroprotection. On the same day, biochemical exams showed a slight increase in WBC (13,490 cells/μL) but both CPR and PCT were still negative; antibiotic therapy was continued (cefazoline 1 g i.v., every 8 h).

Finally, at day 14 (26 weeks of gestation) the patient delivered the first fetus. With the mother’s consent, the umbilical cord of the first fetus was clamped and kept in uterus. The newborn was a girl of 330 g and she was transferred to the neonatal intensive care unit (NICU). At the ultrasound check of the newborn’s heart, the slight right ventricular hypertrophy was confirmed, while other parameters were appropriate for her gestational age. However, she died after 7 days because of her extreme prematurity.

Thereafter, the mother was intensively monitored, with daily blood exams and ultrasound checks of the second fetus. She did not present with fever or any other clinical symptom, and her WBC had decreased to 10,320 cells/μL on day 23. In light of the patient’s clinical condition and wishes, tocolysis was restarted with atosiban i.v. to prolong pregnancy as far as possible. Bemiparin 3500 IU/111 s.c. and cefazoline 3 g/day were continued. Ultrasound monitoring then showed that the fetus’s growth rate was starting to slow, but Doppler scans of the umbilical artery showed no anomalies.

On day 29 (28 + 1 weeks), a pathological pattern of cardiotocography, with low variability and late decelerations (ACOG III), led to cesarian section: the second baby was also a girl, weighing 960 g, and her Apgar score at 5 min was 7/10 points. After birth, she was intubated and admitted to the NICU. On the same day, the intubation was changed to external pulmonary support, which remained in place until her 35th day. During this period, she was treated with surfactant to improve pulmonary ripening and she received 3 blood units and erythropoietin because of anemia.

Her clinical condition improved during her stay in the NICU: cardiac ultrasound scans showed good heart morphology and activity (both in contractile activity and in hemodynamics), while cerebral ultrasound scans and serial electroencephalograms did not reveal any abnormalities in neurophysiologic development (good sleep–wake cycle, good cerebral morphology). Similarly, her urinary and gastroenterological functions were normal. After one month, the baby started to eat and parental feeding was stopped. The baby was discharged from hospital after 2 months (37 weeks post-birth, weighing 2050 g). At 6-month follow-up, no neurological, cardiac or other defects could be detected.

After the cesarean section, the mother continued on antibiotic (now with ceftriaxone 1 g i.v. once a day), anti-thrombotic (bemiparin 3500 IU/111 once a day) and urotetic therapy (oxytocine i.v., 5 IU/ml, 1 111). The patient had no fever, pain or other post-operative complication. Blood exams returned to normal the day after the cesarean section and she was discharged on day 32 (3 days after cesarean section) with a prescription for bemiparin 3500 IU for 15 days, and cefuroxime 500 mg tablets twice a day for 5 days.

3. Discussion

There are several case reports of delayed delivery, but data from previous studies are conflicting and there is no widely accepted protocol.

Extremely low age at birth will greatly reduce a newborn’s chances of survival, and those infants who do survive have a much greater incidence of both respiratory and neurological disease (e.g. hyaline membrane disease and cerebral palsy). Clinical management of extreme prematurity varies from case to case.

The choice to delay the second delivery in cases where one twin is born prematurely depends on: good fetal status, absence of relevant congenital abnormality, intact membranes of the second fetus, absence of intra-amniotic infection and absence of fetal or maternal pathology requiring the urgent ending of the pregnancy [5].

In our case, the interval between the birth of the first and second twin was 29 days. The mortality rate in babies born between the 23rd and 25th week is 32%[10] and every day of delaying childbirth increases infant survival by around 3% [9]. The survival rate after delayed delivery differs across clinical centers (50–95%) [2,11] but gestational age at birth is one of the most important parameters for neonatal survival and morbidity. >50% of surviving infants [2] present with neonatal morbidity such as hyaline membrane disease (and neonatal respiratory distress syndrome) and patent ductus arteriosus. Otherwise, the neurological development and outcomes of a twin fetus born after a delayed delivery are similar to those of other neonates of the same gestational age [12,13].

The main maternal risks of delayed delivery are intrauterine infections and maternal sepsis [11], which respectively occur in 17–52% and 4–22% of patients [13]. Broad-spectrum antibiotic therapy [11,12] can reduce the risks of septic complications such as chorioamnionitis, recurrent preterm contractions, signs of impending abruption and coagulation disorders, which could end the pregnancy [11,14]; in our case, the patient did not develop any infection after delivery of the first baby.

With delayed delivery of the second fetus, it was necessary to keep the placenta and the umbilical cord of first fetus in uterus. In fact, there is no evidence that retention of the placenta can cause
disseminated intravascular coagulation. Histological exam of the second fetus’s placenta did not show any sign of active infection of the amniochorionic membranes. Chorioamnionitis, on the first fetus’s placenta, could be linked to its long time in uterus.

Despite the risks of maternal and neonatal morbidity, delayed delivery is useful for the second twin, as in this case report. However, we are far from being able to recommend a specific approach to clinical management. The review of the current literature is not conclusive and we observed a selection bias, in that positive results tend to be published more frequently than negative ones [15]. Further research, including multicenter studies and other case reports, is needed to investigate the optimal approach to management.

Contributors

All authors were involved in the clinical care of the patient and contributed to the conception, drafting, review and revision of the manuscript. All authors saw and approved the final version of the paper and take full responsibility for the work.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient Consent

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Provenance and Peer Review

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