

Successful Obstetrical Management of Over 100-day Interval between the First and Second Twin Delivery in an Infertility-Treated Patient: Counseling and Management Approach to Extreme Asynchronous Twin

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ABSTRACT

Background: This report describes a patient counseling approach, conservative and surgical management (cervical cerclage) of a dichorionic-diamniotic twin pregnancy, where delivery of the second twin followed the delivery of the first by 104 days.

Case presentation: A 35-year-old Indian lady, with 10 years of primary infertility, conceived twins, following ovulation induction with gonadotropin therapy. At 19 weeks and 4 days gestation, she aborted a female fetus of 410 gm. Tocolytic therapy was initiated; the placenta remained *in situ* and the umbilical cord of twin A was ligated high and McDonald's cerclage was placed and prophylactic antibiotics initiated. But since the patient's uterus continued to be irritable and the cerclage appeared to be under tension, at 20 weeks 6 days the stitch was taken out and all conservative treatment stopped for 24 hours, but reinitiated after this period, since the uterus remained quiescent. After 3 weeks of uterine inactivity, at 23 weeks 6 days gestation, McDonald's suture was reapplied following which conservative management was offered after counseling for possible risks associated with maternal sepsis, coagulopathy, need for extended hospitalization and potential for hysterectomy. Reassuring fetal status was observed for twin B without evidence of contractions or chorioamnionitis. A viable male infant (1,800 gm) was delivered vaginally at 34 weeks and 4 days gestation.

Conclusion: This report outlines a counseling approach useful for patients with premature delivery of one twin, and presents application of conservative obstetrical management principles for the aftercoming twin, even when delivery interval is extreme.

Keywords: Multiple pregnancy, Delayed delivery interval, Selective delivery, Twins.

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INTRODUCTION

The implementation of assisted reproduction during the last 10 years has increased the incidence of multiple pregnancies. The unavoidable birth of one premature neonate has led our efforts to the aim of delayed interval delivery for the other twin. According to the literature there is absence of unanimity about the best management for these pregnancies. Generally, the accepted policy is to augment labor after the birth of the first fetus in higher order pregnancies, if the uterine activity is inadequate. However, in these cases, if uterine inactivity or the phase of uterine relaxation can be prolonged after the birth of the first fetus, we may be able to achieve a safer gestational age for the remaining fetus or fetuses. The aim of this report is to add our experience to the currently limited literature regarding the best treatment of this serious obstetrical problem. It is important to find any parameters that can predict the length of the latency period, the risk for both mother and fetus, and the outcome of these pregnancies.¹

CASE REPORT

A 35-year-old Indian lady presented with 10 years of primary infertility for treatment. She conceived following pituitary downregulation with gonadotropin releasing hormone analogu (GnRHa) and gonadotropin therapy. The patient had no significant medical or surgical history. Transvaginal ultrasound at 7 weeks gestation revealed a dichorionic-diamniotic twin pregnancy. At 19 weeks and 4 days gestation, the patient experienced abdominal cramping and blood-tinged vaginal discharge and went into preterm labor. The pains progressed and the patient aborted a female fetus of 410 gm. Following abortion of the first twin, uterine activity subsided for a while. Hence, tocolytic therapy was started with beta sympathomimetic–isoxsuprine intravenous drip using 40 mg in 500 ml of Ringers lactate solution over 12 hours and the patient was shifted to the operation theater (OT) for an emergency cerclage. On per speculum examination in the OT, the membranes were seen to be at the level of internal os, in a 6 to 7 cm dilated cervical canal with the cord which was hanging out from one side. The vagina was washed

thoroughly with saline. The placenta remained *in situ* and the umbilical cord of twin A was divided high and ligated near the cervix with 3-0 chromic gut suture. Monitoring of twin B confirmed stable heart tones and appropriate fetal movement. The membranes were gently pushed in with a wet saline swab and McDonald's cervical suture was applied with sutupack No. 1. Conservative treatment was continued with tocolytics i.e. intravenous isoxsuprine drip, indomethacin 25 mg three times daily and depot hydroxyprogesterone caproate injections 500 mg intramuscularly on weekly basis. Prophylactic third generation cephalosporins (cefotaxime 1 gm intravenous IV every 12 hr) were started. But since the patient's uterus continued to be irritable and the cerclage appeared to be under into tension, at 20 weeks 6 days (8 days later) the stitch was taken out. No attempts were made to induce or augment labor. The uterine activity ceased spontaneously. After 24 hours, prophylactic oral tocolytics were restarted. Follow-up was done by high vaginal swab culture, coagulation profile, white blood counts and C-reactive protein (CRP) estimation at weekly intervals. High vaginal swab culture on two occasions showed growth of *Candida* and *Gardnerella vaginalis* which were treated with clotrimazole and tinidazole vaginal pessaries, respectively. Ultrasound evaluation of fetal growth and amniotic volume index was done serially. After 3 weeks, i.e. at 23 weeks 6 days, sterile speculum examination found a closed cervix with the umbilical cord completely retracted *in utero* and the maternal vital signs stable hence McDonald's suture was reapplied. The patient was discharged 1 week later with advice to continue treatment with oral isoxsuprine and weekly injections of depot hydroxy progesterone caproate. Indomethacin was stopped as cervix had already reformed and also keeping in mind the effect it may have on premature closure of ductus arteriosus of the fetus.

There was no evidence of infection or coagulopathy at weekly clinical evaluations, which included serial ultrasounds until 34 weeks to assess fetal growth and cervical length. At 28 weeks gestation, 12 mg beta-methasone was administered intramuscularly with an additional dose 24 hours later, for fetal maturity. At 30 weeks and 3 days gestation, mild uterine irritability was detected which was reduced by isoxsuprine drip for 24 hours followed by oral isoxsuprine. Prophylactic third generation cephalosporins were started during 32nd week for rising counts which came back to normal gradually (14,000 cells/ml to 20,000 cells/ml to 15,000 cells/ml). Spontaneous labor began at 34 weeks and 4 days gestation. On per vaginal examination the cervix was 4 to 5 cm dilated with a vertex presentation, hence the cervical cerclage was cut off and labor allowed to proceed. An amniotomy was performed

and labor progressed normally. The patient delivered a viable male infant weighting 1,800 gm (1 and 5 minutes Apgar 8 and 10, respectively) over an intact perineum. Approximately 5 minutes later, two placentas were delivered spontaneously weighing 380 and 40 gm, respectively. The histopathological examination of the placenta from the second twin showed fields of recent infarction but no chorioamnionitis whereas, the histopathology of placenta from the first twin showed extensive infarction with maceration of the cord. The postpartum course was uncomplicated and mother and baby were discharged in stable condition 48 hours later. The child has normal neurodevelopmental progress and appropriate for age milestones till date.

DISCUSSION

Spontaneous delays between births improving neonatal outcome, in cases of multiple gestations have been seen to appear in newspapers and magazines from time to time as rare novelties. The successful outcome of this case prompted us to review literature and analyze the treatment policy, outcome, neonatal and maternal complications of similar cases reported, so as to be able to outline a reasonable management protocol for such cases.

The incidence of twins has increased substantially due to advancements in assisted reproductive technologies. Antenatal complications are common during multiple pregnancies and the number of the embryos influences both their frequency and the gestational age at which they appear. The main problem appears to be preterm labor and preterm rupture of the membranes, with one condition often leading to the other.¹

Suppression of premature contractions can be achieved with tocolytics like beta-mimetics, magnesium sulfate, oxytocin-receptors inhibitor or nonsteroid anti-inflammatory drugs mainly indomethacin. Tocolysis may be used prophylactically after the birth of the first twin, or only later during uterus contractions, but never in the presence of a well-established chorioamnionitis.² After premature rupture of the membranes, the suspicion of infection could be raised on the basis of a rise of the temperature, white blood cell count and CRP, which is considered as a good prognostic index for incipient chorioamnionitis.¹ In cases of high CRP, tocolysis may not be able to achieve pregnancy prolongation. Both fever and hemorrhage jeopardize our decision about the use of tocolysis.¹

Antibiotics like penicillin or cephalosporin must be started immediately after the birth of the first child. There is no unanimity about their administration. The scheme most frequently used is intravenous administration for the first 3 days and then oral for 7 or more days.¹ In our case it is

remarkable that the remaining placenta and umbilical cord of the expelled twin did not seem to initiate an intrauterine infection because of judicious use of antibiotics.

If cervical cerclage is decided, it is advisable to be undertaken in aseptic conditions, as early as possible, after the birth of the first fetus and of course when there is no evidence of infection. To avoid ascending infection, the cord of the first-born twin should be ligated under aseptic conditions, with an absorbable suture, as close to the cervix as possible. Cervical cerclage has been used with a reasonable success rate, even in widely dilated cervixes. It is recommended that women should stay in bed, for the rest of their pregnancy, although there are reports where patients were permitted to leave hospital under medical supervision,³ as it was in our case also. Corticosteroids for fetal maturity can be administered, in the absence of chorioamnionitis, beneficially at 28 weeks gestation.^{1,4}

Important risks associated with asynchronous twins include ascending infection and subsequent chorioamnionitis after delivery of the first twin, postpartum hemorrhage, retained placenta, abruption placenta and disseminated intravascular coagulation.^{5,6} For our patient, the development of intrauterine infection and possible septic abortion of twin B was carefully discussed,^{6,7} as was the potential for severe coagulopathy in the setting of undelivered placental tissue.⁵ Monitoring should be carried out and limited to a weekly full blood count, platelet count, fibrinogen and fibrin degradation products (FDPs). Even a large placental mass can be retained in the uterus and produce no demonstrable clinical symptoms.¹ Vaginal examinations should be avoided as far as possible. However, the length and dilatation of the cervix should be followed by ultrasound examination whenever indicated or by per-vaginal examination under aseptic condition.¹

Attempts for delayed interval delivery should definitely be made when the first neonate is born before the 24th week of gestation, aiming prolongation of second twin's delivery as long as feasible.⁸ Modern management procedures including tocolytics, corticosteroids and antibiotics with or without cervical cerclage would appear to be important in the overall success of treatment in a retained twin. Although both tocolytics and cerclage appear to prolong the mean delivery interval, no statistically significant difference was found with the addition of cerclage.³ The use of antibiotics is widely practiced, either after isolation of a specific pathogen in cervicovaginal secretions or prophylactically. Since, cases with positive outcomes (including the current report) are more likely to appear in the medical literature than those describing an unsatisfactory result, a publishing bias may favor the former.⁵ Even though delayed interval pregnancy appears to be safe for the mother and salvative

for the fetus; nevertheless both parents and doctors must realize that success can be neither predicted, nor easily achieved.¹

The longest reported intertwin delivery interval with cerclage is 153 days⁹ and without cerclage is 117 days.¹⁰ Our experience of twin pregnancy with a 104 days delivery interval confirms this potential for a satisfactory obstetrical course and appears to be one of the longest durations reported in the Indian scenario. Our management validates the principle that when the first twin is delivered very premature, extending the gestational age for an undelivered cotwin is advantageous for the second twin without significant morbidity in the mother in selected cases. Thus, in selected multiple gestations, attempts to prolong the pregnancy following spontaneous abortion or extremely premature birth of one fetus is efficacious and justified.⁸

REVIEW OF LITERATURE

In reviewing the literature the aim was to summarize the overall experience of the management and outcome of the retained fetus, in cases of twin pregnancies, after delivery of the first. In most cases the outcome of the second twin was favorable, in contrast to the bad outcome of the first twin. Survival of the first born was clearly linked to its gestational age and birth weight. The survival of the second born was dependent upon a number of factors, most importantly the delivery interval between the first and second twin and the presence of obstetric problems appearing during the latency period; the longer the interval, the greater was the chance for surviving. Likewise, the absence of significant obstetric problems in the latency period also improved survival. In cases where the membranes of the second twin remained intact with no evidence of ongoing labor or other obstetric risk factors, a conservative approach could be adopted.¹¹

First Reports

The first report to appear in literature where successful delay in delivery of the second fetus by 35 days occurred in a woman with single uterus, was by Abrams (1957). This delay was seen on expectant management only.¹²

Eiecher in 1970 was the first to try purposeful prolongation of gestation by 72 days after the first birth, with treatment, for which he used progesterone, diazepam and 'spasmolytics'. In this case the birth of the first twin occurred at 25 weeks and the birth weight difference was 1,680 gm between the two neonates. He was also the first to lay the primary rule in selecting cases of multiple gestations where prolongation could be tried (absence of bleeding and infection). Maternal complications, which occurred in his study, were manual removal of placenta and

abruption of placenta with disseminated intravascular coagulation (DIC).¹²

Tocolysis alone were used first by Woolfson et al in 1983 in a case of twin gestation. In his case he could prolong the delivery of second twin by 54 days after the birth of the first twin.¹²

Thomson applied the first cerclage in 1978 in a twin pregnancy at 27 weeks. Delay of 24 days was achieved.¹²

Recent Reports

We categorized all reported cases with favorable outcome into two broad groups according to the management policy taken up at that time for the case.

- Group A: Constituted of cases where tocolytics, antibiotics and progesterone therapy were used
- Group B: Patients were treated with tocolytics, antibiotics, progesterone therapy as well as cervical cerclage (Table 1).

Maternal complications like chorioamnionitis, postpartum hemorrhage, retained placenta and abruption were reported in very few cases and were managed appropriately.¹⁶

From the literature reviewed so far, it appears that prolongation of gestation in twin pregnancy more than 100 days is rare and reported in a handful of cases. The present case of 104 days prolongation of gestation in twin pregnancy after delivery of the first fetus appears to be one of the first and longest durations reported from India.

INFERENCES DRAWN FOR TREATMENT POLICIES

1. Prophylactic antibiotics are necessary after the first birth because once chorioamnionitis is established; prolongation of pregnancy cannot be attempted.

2. The use of tocolytics does not appear to be debatable in recent literature and gives consistent results in majority of cases.
3. Cervical cerclage appears to aid prolongation of pregnancy but is still debatable by clinicians. However, it appears to possibly lessen chances of developing intrauterine infection and abruption of placenta. It is best applied 2 to 3 days later when uterine activity has completely ceased and cervix has partly closed and is more manageable, as was in our case. In triplet pregnancy, cerclage appears to be more liberally indicated as the uterus continues to be overweight with remaining twin gestation and cervix is undoubtedly incompetent.

CONCLUSION

In an era where obstetricians are faced with an increasing incidence of multiple gestations due to advanced fertility management procedures, any procedure which will enable them to combat the inevitable increase in premature birth shall be a major step toward patient management. Even though this paper spans several decades of obstetrics practice and covers only few selection of reported cases, enough information is obtained to give this treatment modality, of delay in birth of the subsequent infant, a serious consideration in carefully assessed cases. Since, serious infection and coagulopathy has not been reported as a result of this management hence delay in delivering second sibling may improve neonatal survival. It is not known how many times attempt at delay has been met with failure therefore the incidence of success of the procedure is not known but already a clearer picture of efficacy of this approach can be seen, and tried, specially where neonatal units have yet to show good survival rates in cases of extreme prematurity.

Table 1: Recently reported cases with favorable outcomes

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<i>Group A</i>		
Van der Straeten et al 2001 ¹²	Tocolytics, antibiotics and progesterone therapy	14-117 days
Zhang J 2003 ¹³	Same as above	9 days
Labib M Ghulmiyyah et al 2004 ⁵	Same as above	110 days
Zhang J 2004 ¹⁴	Same as above	6 days (ranging from 2-107 days)
Oyelese Y 2005 ¹⁵	Same as above	1-4 weeks
Arabin B van Eyck J 2009 ¹⁶	Same as above	Mean delay was 19 days (1-107 days)
<i>Group B</i>		
Farkouh LJ 2000 ¹¹	Tocolytics, antibiotics, progesterone therapy and cervical cerclage	36 days (range of 3-123 days)
Hamersley SL et al 2002 ⁹	Same as above	93 days (range of 23-153 days)
Zhang J 2003 ¹³	Same as above	26 days
Livingston JC 2004 ¹⁷	Same as above	2 days (range: 1-70 days)
Tzafettas JM 2004 ⁸	Same as above	2 and 135 days
Cristinelli 2005 ¹⁸	Same as above	2-93 days (median: 7 days)
Klearhou N 2007 ¹	Same as above	48 days

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