

CASE REPORT

Delayed interval delivery in a quintuplet pregnancy

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We present a case report of delayed delivery of a quintuplet pregnancy. The pregnancy resulted from intrauterine insemination following hormonal treatment. This case may represent the first report of quintuplets delivered using the technique of delayed interval delivery. Three separate spontaneous labours and one Caesarean section for two fetuses took place between the 24th and 32nd weeks of pregnancy. The delay between the first and the last delivery was 61 days. Only a boy, born fourth, survived.

Key words: delayed interval delivery/multiple pregnancy

Introduction

New achievements in infertility treatment and new methods of assisted reproduction have led to an increasing number of multiple pregnancies, and a subsequent increase in the rate of premature labour. To reduce the frequency of multiple pregnancies, a reduction in early pregnancy of the number of embryos may be performed by an appropriate method. In a case of advanced multiple pregnancy, however, if premature labour begins, it may be possible to suppress the uterine contractility after the expulsion of the first fetus. This method may delay the birth of the remaining, immature fetuses, thus increasing their chances of survival.

Case report

Mrs N. (34 years old) consulted because of primary infertility. She and her husband had been diagnosed and treated for infertility 3 years previously. Diagnostic examinations and scans (hysteroscopy, hysterosalpingography, ultrasound) revealed the presence of an interstitial myoma (34 mm in diameter) located in the uterine fundus. An ultrasonographical monitoring of three consecutive menstrual cycles confirmed ovulation abnormalities. No signs of infection were seen in the endocervical or vaginal secretion. The husband's spermocytogram was normal.

The patient underwent an unsuccessful stimulation of the ovaries with clomiphene citrate (Clomifen[®]; Ratiopharm, Ulm,

Germany) under ultrasound control for 4 months. In the following, fifth menstrual cycle human menopausal gonadotrophin (Humegon[®]; Organon, Oss, Holland) was administered. On the 14th day of this cycle, ultrasound monitoring revealed the presence of multiple follicles in the left ovary. Three dominant follicles were 18, 24 and 26 mm in diameter respectively. An intramuscular injection of human chorionic gonadotrophin (Biogonadyl[®]; Biomed, Lublin, Poland), 10 000 IU, was administered to the patient on the same day. On the 15th and 17th day of the cycle two intrauterine inseminations by 'swim-up' technique were performed. The physical and ultrasound evaluations performed immediately after the second insemination showed an early, mild ovarian hyperstimulation (first degree in the Schenker classification) (Schenker, 1993). The patient was hospitalized until the ovarian hyperstimulation symptoms disappeared.

The pregnancy was confirmed at 6 weeks gestation by ultrasound, which revealed the presence of five separate gestational sacs. The course of the first trimester of this pregnancy was normal. At 20 weeks gestation the patient was admitted to hospital because of 15 mm dilatation of the internal cervical os, echographically confirmed. After bacteriological evaluation of vaginal and cervical canal smears, which were bacteria-free, cervical cerclage using the MacDonal method was applied. Symptoms of gestational sac lower pole infection appeared periodically so that systematic cultures of cervical canal smears were made from 20 weeks of pregnancy. During incidences of a rise in basal body temperature, venal blood cultures were performed.

From the cervical canal smear cultures *Enterococcus agalactiae*, *Streptococcus bovis*, *Enterobacter aerogenes*, *Enterococcus species* and *Candida albicans* were isolated. In contrast, all blood cultures were bacteria-free. According to the obtained antibiograms, the following drugs were administered: ceftazidime (Fortum[®]; Glaxo, Verona, Italy), piperacillin (Pipril[®]; Lederle, Puerto Rico), Vancomycin[®] (Lederle) and cefoperazone (Cefobid[®]; Pfizer, Brussels, Belgium) administered intravenously, penicillin (Tachomin-POLFA, Tarchomin, Poland), ampicillin (POLFA, Krakow, Poland) and Metronidazol[®] (JELFA, Jelenia Gora, Poland), administered as vaginal tablets. In spite of this general and intravaginal preventive regime, symptoms of amnionitis in the lower gestational sac pole were observed at 23 weeks gestation. At 24 weeks gestation amniotic fluid leakage was noted and the patient went into spontaneous labour. The cervical cerclage was removed. The patient gave rapid birth

Table I. The course and the outcome of the delayed interval delivery in a quintuplet pregnancy

Labour				Fetus			
no.	character of the labour	weeks of gestation	days of delay	sex	birth weight (g)	Apgar score	survival 1st min
one	spontaneous	24	0	female	400	1	died after 10 h
two	spontaneous	26	21	male	700	1	died after 22 days
three	spontaneous	27	23	male	700	2	died after 35 days
four	Caesarean	32	61	male	1000	3	survived at least 1 year
	section for two fetuses	32	61	female	850	3	died after 6 days

to a girl weighing 400 g, who died 10 h later. Immediately after delivery, tocolysis using an intravenous Fenoterol infusion (1–3 µg/min) was applied. The umbilical cord was ligated with silk thread and cut as close as possible to the cervical internal os. Appropriate antibiotic therapy, according to an antibiogram obtained from the culture of vaginal and endocervical smears, was applied to the patient who remained in the Trendelenburg position. In spite of tocolysis, at the 26th week of pregnancy (21 days of delay), the leakage of amniotic fluid from the lowest gestational sac was noted. Uterine contractility recommenced and the patient again went into labour, giving birth to a boy weighing 700 g. The umbilical cord was ligated and cut as previously described. After this second delivery, tocolysis was continued (Fenoterol orally 8×5 mg and periodically 1–3 µg/min in an intravenous infusion was applied).

At 27 weeks of gestation, in spite of tocolytic treatment, the patient went into a third labour and a third infant, a boy weighing 1000 g, was delivered. The umbilical cord was ligated and cut as previously described. Tocolysis was effectively continued for a further 5 weeks by oral 8×5 mg and periodical intravenous infusions of 1–3 µg/min of Fenoterol. An ultrasound evaluation of the fetus, performed at 30 weeks of gestation, revealed symptoms of intrauterine growth retardation of the remaining two fetuses (fourth and fifth). For this reason, complementary treatment with acetylsalicylic acid (Aspirin; POLFA, Starogard, Poland) and xantinol nicotinate (Sadamin®; POLFA, Kracow, Poland) was applied. With the aim of accelerating fetal lung maturation, ambroxol hydrochloride (Mucosolvan®; Boehringer, Ingelheim, Germany), 50 ml daily in slow intravenous infusions for 5 days, was administered. On the last day of the 32nd week of gestation, in spite of the continued tocolysis and supplementary treatment, the patient went into labour with unsuppressible, regular uterine contractions. The clinical symptoms showed threat of an intrauterine fetal asphyxia (silent cardiotocography oscillation, fetal tachycardia, maternal basal body temperature rise up to 38°C). Hence, a Caesarean section was performed.

A boy weighing 1000 g and a girl weighing 850 g, respectively, were delivered. Examination revealed the presence of five separate placentae with five separate amniotic sacs. Four placentae (fetuses one, two, three and five) were joined and together weighed 600 g. The separate placenta of the fourth fetus weighed 200 g. Histopathological evaluation revealed an acute inflammatory process of the basal placental disc of the fourth fetus. In the joined placentae of the first,

second, third and fifth fetuses, multiple calcifications in the villous part, acute inflammatory process of the amnions and of the umbilical cords, and autolytic changes were observed.

All infants were delivered with extremely low birth weight and showed symptoms of prematurity and of hypoxia. Each infant was admitted to the intensive neonatal care unit of the neonatology clinic. Three newborns, born spontaneously, died in spite of intensive care. The first infant died 10 h after delivery. The next two infants died on the 21st and 35th day of life, respectively. The fifth baby also died on the sixth day of life. Only the first infant delivered by Caesarean section (boy, 1000 g) survived, despite being born in a critical state (severe hypoxia, intrauterine infection). On the 79th day of life he left hospital in good health, weighing 2100 g. He is currently healthy and presents normal psychomotor development 1 year later (Table I).

Discussion

Our experience in the use of delayed interval deliveries suggests that this technique may provide a chance for the infertile woman to have a baby. Delayed interval delivery in a case of multiple pregnancy was first described by Carson (1880). Up to the present, 27 similar cases have been reported in the literature, 16 of which concerned gemellary pregnancies (Carson, 1880; Williams and Cummings, 1953; Dorgan and Clarke, 1956; Abrams, 1957; Drucker *et al.*, 1960; Eicher, 1970; Thomsen, 1978; Conradt and Weidinger, 1982; Woolfson *et al.*, 1983; Omsjo and Alsos, 1984; Brion *et al.*, 1986; Sakala and Branson, 1987; Wittman *et al.*, 1992), nine were triple pregnancies (Mashiach *et al.*, 1981; Banchi, 1984; Simpson *et al.*, 1984; Sakala and Branson, 1987; Cardwell *et al.*, 1988; Schaal *et al.*, 1989; Zurlinden *et al.*, 1990; Charkin *et al.*, 1994), and two were quadruplet pregnancies (Fignon *et al.*, 1993; Olatunbosun *et al.*, 1995). To date, however, no report of a delayed delivery in a quintuplet pregnancy has been published.

In the published literature, intervals between described deliveries of between 5 and 143 days have been reported and the gestational age of the fetus delivered first varied between 16 and 32 weeks. In our case the delay between first and last delivery was 61 days (24–32 weeks of gestation).

After analysis of the published data we attempted to determine the optimal and most effective method for applying the technique of delayed interval delivery. Appropriate monitoring of the delayed interval delivery is necessary, and several

criteria and conditions have to be fulfilled. If, after the first delivery, the remaining gestational sacs are intact, there is no evidence of placental ablation or fetal hypoxia and if the uterine contractions are suppressed, a decision to undertake delayed interval delivery may be made. With the aim of reducing the risk of infection, the umbilical cord must be ligated and cut as close as possible to the internal cervical os. Antibiotic therapy is necessary, if culture of cervical canal smears reveal the pathological presence of flora. It is advisable to limit manual examination, giving priority to cervical examination using the speculum and to echography. If dilatation of the internal cervical os persisted after expulsion of the first fetus, some authors have recommended the use of cervical cerclage (Dorgan and Clarke, 1956; Eicher, 1970; Mashlach *et al.*, 1981; Omsjo and Alsos, 1984; Cardwell *et al.*, 1988; Schaal *et al.*, 1989). We do not agree with this opinion as we believe that if there are any evident contra-indications, it is safer to administer tocolytic drugs immediately after the first fetal expulsion. This procedure favours the duration of pregnancy and permits the possible delivery of more mature fetuses. In the majority of published reports, the first placenta was not expelled after the first fetal delivery, but remained in the uterus and was expelled after the birth of the final fetus.

It is therefore necessary to monitor the patient's coagulation parameters. In reports of similar, delayed interval deliveries, apart from certain small, insignificant abnormalities, no symptoms of intravascular coagulation syndrome were observed. Severe abnormalities have been observed only in the case of an intrauterine fetal death or placental ablation (Omsjo and Alsos, 1984). Olatunbosun *et al.* (1995) recommended that, in similar cases, the patient should be informed of the possibility of complications of the coagulation system resulting from the use of delayed interval delivery. There are controversial opinions about the administration of preventive antibiotic therapy in this method. Witmann *et al.* (1992) suggested that experience had not confirmed its clinical usefulness. In our case, however, the use of wide-range antibacterial drugs was justified by the presence of symptoms of general and local infection.

We conclude that the delayed interval delivery technique may be applied in the case of multiple, multiamniotic pregnancy if the first premature labour occurs before 28 weeks of pregnancy, which gives little chance of survival of the fetuses after delivery. This procedure is justified in women treated for infertility, for whom it may provide the last chance to have a baby. The delayed interval delivery should be performed in a highly specialized centre, with appropriate equipment and a neonatal intensive care unit.

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