Twin gestation induced by clomiphene citrate and bromocriptine in both horns of a bicornuate uterus

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Objective: To describe a case of twin gestation that occurred in both horns of a bicornuate uterus after the administration of clomiphene citrate and bromocriptine.

Design: Case report.

Setting: Department of Obstetrics and Gynecology, Seoul National University Bundang Hospital, Korea.

Patient(s): A 34-year-old woman presented with secondary infertility and hyperprolactinemia.

Intervention(s): Bromocriptine, 2.5 mg/day, was administered immediately, and clomiphene citrate, 150 mg/day, was started from menstruation day 5 for 5 days.

Main Outcome Measure(s): The establishment of pregnancy and obstetric outcome.

Result(s): A nonidentical twin pregnancy occurred but ended in preterm delivery at 24 weeks. One baby has survived for over 3 months.

Conclusion(s): Twin gestation can occur in both horns of a bicornuate uterus after clomiphene citrate administration. (Fertil Steril 2005;84:756.e9–10. ©2005 by American Society for Reproductive Medicine.)

Key Words: Twin, bicornuate uterus, clomiphene citrate

A bicornuate uterus is the result of a failure of the two Müllerian ducts to fuse, thus forming an anomalous uterus with two uterine horns and a single common cervical canal. Twin gestation in both horns of a bicornuate uterus is a rare event. Its incidence is unknown, although several cases have been reported anecdotally. In the available literature, the first case appeared to be successful (1), but the second ended in spontaneous abortion (2). In the 1980s, two cases with successful vaginal delivery were reported (3, 4). This phenomenon also may occur as a result of an induced superovulation cycle (4) or as a result of in vitro fertilization (IVF) and embryo transfer (ET) (5).

Here we report on a case of twin gestation in separate horns of a bicornuate uterus after ovulation induced by clomiphene citrate and bromocriptine. Unfortunately, the pregnancy ended in preterm delivery at 24 weeks.

CASE REPORT

A 34-year-old woman (gravida 1, para 1) visited our infertility clinic with secondary infertility. She had developed a pituitary microadenoma more than 5 years previously, and had hyperprolactinemia and amenorrhea. Her first term delivery had been 3 years before, after therapy with bromocriptine. At the time of her initial interview, she had no galactorrhea. Her serum PRL level had been determined to be 49.9 ng/mL at a private clinic. An initial transvaginal ultrasound revealed a bicornuate uterus, of which she was aware.

As her serum PRL level was 98.6 ng/mL, bromocriptine (2.5 mg daily) was immediately started. Because she wanted to achieve an early pregnancy, we added clomiphene citrate, 150 mg daily, for 5 days starting on her menstruation day 5. At menstruation day 20, two mature follicles were clearly seen (17 mm on her right ovary and 27 mm on her left), and her urine LH test was positive that morning. Two clear and abundant endometrial echoes were observed. We recommended sexual intercourse that evening without exogenous hCG administration, and no luteal supplementation was given.

Her urine hCG test was positive at 19 days after the LH surge. Two days later, two intrauterine gestational sacs were clearly seen, with one sac in each uterine horn (mean sac size: 0.54 cm in the right horn and 0.55 cm in the left). Thereafter, bromocriptine was discontinued. At gestational age 8 + 1 weeks, two embryos were observed with a regular fetal heartbeat (crown–rump length: 0.7 cm in each uterine horn) (Fig. 1). Her serum triple marker test performed at 15 + 2 weeks was normal, and screening ultrasonography at 23 + 1 weeks did not reveal any structural anomalies except for a slight size discrepancy between the two fetuses.

However, 5 days later, she was admitted complaining of labor pain without membrane rupture. At that time, we detected via ultrasonography that one of the fetuses had died.
Although intravenous ritodrine was immediately started, the labor pain did not subside. Because her body temperature had risen above 38°C, her leukocyte count was 14,630/H9262 L, and her serum level of C-reactive protein was 1.41 mg/dL, we started ceftriaxone intravenously and azithromycin orally. However, as the labor progressed, both fetuses were expelled the next day.

The stillbirth was delivered spontaneously in breech presentation (male, 760 grams); the remaining fetus was extracted as a footling breech (female, 540 grams). The Apgar score of the live fetus was 1 after 1 minute, 4 after 5 minutes, and 6 after 10 minutes. The preterm infant has been managed in our intensive care unit, and the mother was discharged uneventfully 2 days after delivery. The baby has since survived for over 3 months, at a postnatal 116 days, the baby's body weight was 2,500 grams.

**DISCUSSION**

This case presented as a twin pregnancy after clomiphene citrate and bromocriptine. The final two follicles were observed during her ovulation monitoring, so it seems reasonable that ova entered separate fallopian tubes and uterine cavities in a bicornuate uterus. Dizygosity in this twin was evident in view of the different sexes. A similar case was reported after superovulation using hMG (4), and another interesting report found that embryos resulting from IVF can migrate into the other uterine cavity within a bicornuate uterus (5).

Twin pregnancy occupying separate horns of a bicornuate uterus has been reported only sporadically in the literature, and its obstetric outcome seems modest. Of the six available articles, two cases ended in spontaneous abortion (2, 5), and the remaining four cases resulted in successful obstetric outcomes by either vaginal (3, 4) or cesarean delivery (1, 6). Our case, unfortunately, ended in preterm delivery at 24 weeks, although one baby has survived.

The incidence of miscarriage and overall fetal loss in women with a bicornuate uterus has been reported to be approximately 30% and 40%, respectively, although more recent reports do not confirm this finding (7, 8). As the uterine body containing two fetuses grows, it is likely that the cervical os becomes more incompetent. It has been reported that preterm delivery risks decrease as the size of the common lower uterine cavity increases (9). Although no report indicates that the likelihood of preterm delivery increases in a twin pregnancy occupying separate horns of a bicornuate uterus, we believe that this type of twin pregnancy may be at particular risk of preterm delivery because of the high incidence of cervical incompetence and twin gestation.

Because use of superovulation has increased and the detection of a bicornuate uterus has become feasible by ultrasonography, we expect that the reported incidence of twin pregnancy, either in the same or both horns of a bicornuate uterus, will increase. To improve outcome in cases of twin pregnancy in a bicornuate uterus, cerclage procedures may be warranted.

**REFERENCES**