Ovarian and Intrauterine Heterotopic Pregnancy Following Clomiphene Ovulation Induction: Report of a Healthy Live Birth

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Heterotopic pregnancy, or simultaneous intrauterine and ectopic gestation, has been reported since the early 18th century as a rare and curious obstetric event.[1-7] Although the generally accepted incidence of primary heterotopic pregnancy is 1 in 30,000 pregnancies,[7] there is some indication that techniques of ovulation induction in the past 15 years may have made the occurrence of heterotopic pregnancy more common.[1]

Heterotopic pregnancy is believed to result from the implantation of dizygotic twins at widely separated sites.[1,5,8] Several cases have been reported following the use of clomiphene citrate for ovulation induction.[1,4,6,9] Inasmuch as the incidence of twinning in clomiphene-induced pregnancy is raised to 12 percent, it has been suggested that the uncommon heterotopic variation may likewise be seen more frequently in pregnancies following clomiphene therapy.[1,4]

The majority of heterotopic pregnancies reported after clomiphene induction of ovulation have involved ectopic implantation in the fallopian tube.[1,4,6,9] The occurrence of the ovary as the ectopic site in clomiphene-induced combined pregnancies is distinctly less common than the tubal location,[7] just as ovarian implantation occurs less often in primary ectopic gestation[10] and in heterotopic pregnancy unrelated to ovulation induction.[2]

This report describes the presentation and management in a family practice of a patient with the rare combination of simultaneous ovarian and intrauterine pregnancies following clomiphene treatment for ovulatory failure. In this patient the ectopic gestation was responsible for the first symptoms, and following treatment, the intrauterine pregnancy was able to continue satisfactorily to term.

The case is of interest in two respects. First, this is the second report of simultaneous ovarian and intrauterine pregnancy following clomiphene administration. Second, this is the first report of the viable delivery of a healthy infant following heterotopic pregnancy where the ovary is the ectopic site.

CASE REPORT

A 29-year-old, gravida 1, para 1, married woman presented with a 2½-year history of inability to conceive with regular exposure and no contraceptive use. Her menstrual pattern was unpredictable (25- to 50-day cycles) but with fairly discrete, mildly crampy menses lasting two to five days. This irregular pattern had occurred off and on through her menstrual life. Other significant past history was a laparotomy 2½ years previously for ovarian cystectomy, at which time multicystic ovaries with thickened capsules were found and confirmed pathologically. At the time of her consultation for inability to conceive, her pelvic examination indicated a normal-sized uterus. The right ovary was felt to be enlarged, but not cystic.

A semen analysis was obtained, which was within normal limits. The clinical impression was secondary infertility because of oligo-ovulation with multicystic ovaries, and ovulation induction with clomiphene, 50 mg days 5 through 9, was prescribed.

The patient apparently conceived during her first clomiphene cycle, as she had no further menses following the period that preceded clomiphene administration. She had a positive anti-human chorionic gonadotropin agglutination inhibition urine pregnancy test six weeks following the last menstrual period and had noted some mild fatigue and breast tenderness.

Seven weeks following her last menstrual period,

Submitted February 14, 1986.

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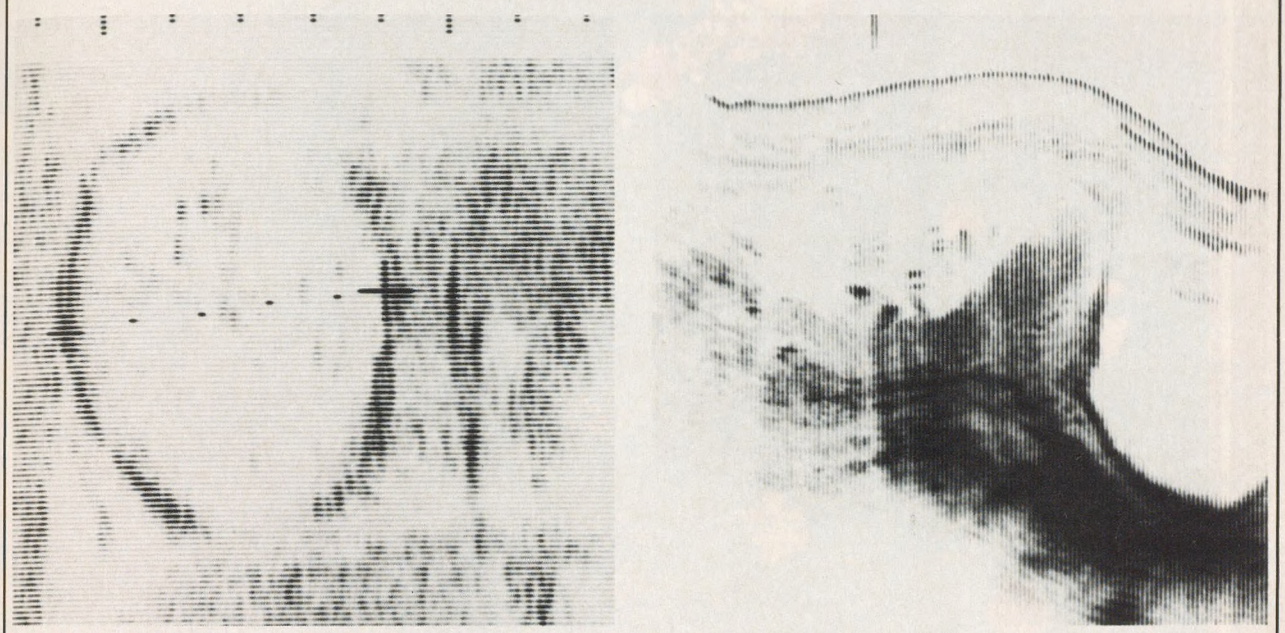

Figure 1. Ultrasound of the fetus obtained at 20 weeks' gestation. Biparietal diameter of 4.7 cm corresponds to 20.4 weeks ± 1.6 (left). Bladder, fetal head, and placenta can be seen in transverse view of abdomen (right)

the patient experienced sharp, sudden pelvic pain. When examined, she was found to have marked uterine and left adnexal tenderness with guarding and rebound tenderness suggesting pelvic peritoneal irritation. There was no vaginal bleeding. She was normotensive. At this time her white blood count was 11.5 $\times$ $10^3/\mu L$ with a mild left shift. Hemoglobin and hematocrit levels were normal. Pregnancy test was positive. Culdocentesis yielded nonclotting blood from the cul-de-sac, and the patient underwent laparotomy for ectopic pregnancy. Hematoperitoneum was found at surgery, and an actively bleeding tissue was present on the surface of the left ovary. The fallopian tubes were normal. The uterus was enlarged, compatible with a six-week gestation. Excision of the bleeding tissue was accomplished by a wedge resection of the left ovary. The pathologic report contained tissue evidence of an ectopic ovarian pregnancy with an associated corpus luteum.

The patient failed to have withdrawal bleeding postoperatively and failed to resume any kind of normal menstrual pattern subsequent to her surgery. When she was examined 13 weeks after her surgery, it was found that her uterus had grown to a size compatible with continuing intrauterine pregnancy. Ultrasound examination using fetal biparietal diameter measurements confirmed a single 20-week intrauterine gestation at 20 weeks from the last menstrual period (Figure 1). Uncomplicated prenatal care continued, and 41 weeks from her last menstrual period the patient spontaneously delivered a healthy 7-lb 13-oz female infant whose subsequent neonatal and infant course has been normal to 9 months of age.

DISCUSSION

The increasing use of ovulation-inducing drugs for infertility makes it likely that the prevalence of heterotopic pregnancy may increase. The diagnosis of combined pregnancy requires that the physician have a high level of suspicion and that appropriate use be made of generally available diagnostic aids to confirm the physical findings and the clinical impression. Especially suspect is the scenario of an ectopic pregnancy presenting after induction of ovulation in which vaginal bleeding is not present either before or after treatment.[2] Spontaneous abortion of an intrauterine pregnancy after ovulation induction should also prompt a search for an accompanying ectopic implantation. With the use of the beta human chorionic gonadotropin pregnancy test, the physician may determine the presence of continuing intrauterine or ectopic trophoblastic activity. In addition, Powell-Phillips[7] has emphasized the precision with which the contents of the uterus or the presence of an adnexal mass may be revealed by pelvic ultrasonography. Any abnormality found on ultrasound might then be investigated by examination through a laparoscope, and

Continued on page 79

HETEROTOPIC PREGNANCY

Continued from page 77

those results may help to define indications for full laparotomy and definitive treatment.

Koroly and Belsky[4] and others[3] have observed that through the use of modern diagnostic techniques and aggressive management of these unusual combined pregnancies, better than 50 percent of the intrauterine gestations should survive if they are undisturbed by maternal hypotension or surgical trauma during the diagnosis and treatment of the ectopic implantation.

References

1. Berger MJ, Taymor ML: Simultaneous intrauterine and tubal pregnancies following ovulation induction. Am J Obstet Gynecol 1972; 113:812-813
2. Eyton-Jones J: Concurrent ovarian and intrauterine pregnancy. Br Med J 1968; 4:298-299
3. Fleisher AA, Seamen I: Heterotopic pregnancy: The effect of shock on the first-trimester fetus. Obstet Gynecol 1961; 18:763-766
4. Koroly MV, Belsky DH: Heterotopic pregnancy as a result of induced ovulation. J Reprod Med 1982; 27:476-478
5. Smith DJ Neal, Siddique FH: A case of heterotopic pregnancy. Am J Obstet Gynecol 1970; 108:1289-1290
6. Paldi E, Gergely RZ, Abramovici H, et al: Clomiphene citrate-induced simultaneous intra- and extrauterine pregnancy: Case report. Fertil Steril 1975; 26:1140-1141
7. Powell-Phillips WD: Clomiphene citrate-induced concurrent ovarian and intrauterine pregnancy. Obstet Gynecol 1979; 53:37s-39s
8. Adash EY, Rock JA, Sapp KC, et al: Gestational outcome of clomiphene-related conceptions. Fertil Steril 1979; 31:620-626
9. Gemzell CA, Roos P: Pregnancies following treatment with human gonadotropins, with special reference to the problem of multiple births. Am J Obstet Gynecol 1966; 94:490-496
10. Kheng-Khoo T, Oon-Hock Y: Primary ovarian pregnancy. Am J Obstet Gynecol 1968; 100:240-249