BILATERAL SIMULTANEOUS ISTHMIC ECTOPIC PREGNANCY AFTER
CLOMIPHENE INDUCTION

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ABSTRACT
A rare case of a 32-year-old patient with simultaneous bilateral isthmic tubal pregnancy.

A 32-year-old woman with a 3-year history of primary infertility was admitted with light vaginal bleeding and mild abdominal pain. She was 41 days after her last menstruation and 23 day after intrauterine insemination with her husband’s sperm. Clomiphene citrate (CC) was used for the induction of ovulation. In cases of ectopic pregnancy with ovulation induced by CC, doctors must be aware of the possibility of bilaterality.

Key words: bilateral tubal pregnancy, ectopic pregnancy, clomiphene citrate

INTRODUCTION
Bilateral tubal pregnancy is very rare. The incidence of simultaneous bilateral ectopic pregnancy is 1 in 725 to 1580 ectopic pregnancies and 1 in 200,000 pregnancies.1 According to most authors, the incidence is associated with the use of different forms of assisted reproductive technology (ART).2 We report a 32-year-old patient with simultaneous bilateral isthmic tubal pregnancy after clomiphene induction and intrauterine insemination. A MEDLINE search was carried out, based on the following Medical Subject Headings (MeSH): “ectopic pregnancy”, “bilateral”, “isthmic”. No results were obtained.

CASE REPORT
A 32-year-old woman with a 3-year history of primary infertility was admitted to hospital with light vaginal bleeding and mild abdominal pain. She was 41 days after her last menstruation and 23 day after intrauterine insemination with her husband’s sperm. Clomiphene citrate (Clostilbegyt® Egis Pharmaceuticals LTD, Budapest, Hungary) was used for the induction of ovulation in doses of 100 mg/day for 5 days (days 3 to 7 of the menstrual cycle).

Gynecological examination found light uterine bleeding and painful bilateral adnexal masses. Ultrasound showed a normal empty uterus with endometrium 12 mm, adnexal bilateral hypogenic formations (59.0/61.0 mm and 62.0/67.0 mm). Ectopic tubal pregnancy was not imaged. There was no fluid in the pouch of Douglas. The serum human β-chorionic gonadotropin (β-HCG) was 18,022 mUI/mL.

Because of prior midline laparotomy in infancy, again laparotomy was performed. Unruptured ectopic pregnancies in the isthmic part of both tubes (3/2 cm and 3/3 cm) were found (Fig. 1). Both ovaries were presented as enlarged polycystic masses with the presence of corpus luteum on the right one. Bilateral salpingectomy was done. D&C was also performed. The patient had an uneventful recovery.

The pathology report revealed bilateral tubal pregnancies, with trophoblasts in the isthmic part of both fallopian tubes. Reaction of Arias-Stella...
and decidua without villi were found from the D&C specimen.

DISCUSSION
To our knowledge, this is the first case of simultaneous bilateral isthmic pregnancy that has been reported. We believe the present case can be accounted for by several factors. The first, and the most likely one, is the use of clomiphene citrate (CC) for induction of ovulation. Clomiphene is commonly used for ovulation induction in the treatment of infertility. Based on clinical observation and logical assumptions, some authors report of a higher risk of ectopic pregnancy in patients who use CC protocols for induction of ovulation.1 Recently Shao R et al.4 proved that chronic CC therapy induces isthmus-specific apoptosis of epithelial cells and activates cilia-ESR2 (estrogen receptor-β), which act in parallel to block gamete and embryo passage through the fallopian tube, eventually resulting in ectopic pregnancy. This apoptotic effect is dose-independent. The fact that CC induces changes in the isthmus of the fallopian tube, but not in the ampulla, gives us reason to affirm that this is the main cause for the bilateral isthmic tubal pregnancy in our case. In fact, this is the first clinical proof of the experimental study performed by Shao et al.4. Eze et al.5 have reported a similar case in which there was a ruptured left and unruptured right ampullar tubal pregnancies after clomiphene induction.

The other possible cause is postulated by Tabachnikov et al.6 that there are three possible factors associated with a bilateral ectopic pregnancy: 1) simultaneous multiple ovulation; 2) sequential impregnation, or 3) transperitoneal migration of trophoblastic cells from one extraterine pregnancy to the other tube with implantation there. It is obvious that the first factor is indispensable, the second one is probable, while the third one is irrelevant in our case.

Some authors claim that IVF is associated with the increased incidence of bilateral ectopic pregnancy. The obvious risk factor is connected with the process of embryonal transfer. Excessive medium and improper catheter insertion may lead to dispersion of embryos, called the “spray and drift” effect.7 The insemination is not the typical ART, according to Centers for Disease Control and Prevention8, so it can be excluded as a possible etiologic factor.

CONCLUSION
In cases with ectopic pregnancy, when CC is used for induction of ovulation, the doctor must be aware of the possibility of bilaterality. We emphasize that a close inspection of both tubes must always be done when performing surgery in such cases.

REFERENCES

ДВУСТОРОННЯЯ ИСТМИЧЕСКАЯ ТРУБАРНАЯ БЕРЕМЕННОСТЬ ПОСЛЕ ИНДУКЦИИ КЛОМИФЕН-ЦИТРАТОМ
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РЕЗЮМЕ
Авторы описывают редкий случай симультанной двусторонней истмической трубной беременности.