A Case of Concomitant Pregnancy Following Supplement of Mestranol and Norethisterone to Control the Menstrual Cycle

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ABSTRACT

A 34-year-old nulliparous woman presented complaining of abdominal pain after taking middle-dose contraceptive pill to delay the onset of next menstrual cycle. The diagnosis of heterotopic pregnancy was confirmed, then, laparoscopic left salpingostomy for left tubal pregnancy was performed to maintain intrauterine pregnancy. However, dilatation and curettage was carried out following the diagnosis of intrauterine blighted ovum. Concomitant pregnancy could occur even when the contraceptive pill is administered to control menstrual cycle.

INTRODUCTION

Annual incidences of ectopic pregnancies (EP) have increased over the past 30 years. Currently, up to 2% of all pregnancies are ectopic in location. Although advances in diagnostic methods have allowed for earlier diagnosis, it still remains a life-threatening condition. Annual incidence of concomitant pregnancy (CP) also has been increasing with advent of ovulation inducing drug and assisted reproduction technology. It has been reported that incidence of CP with spontaneous conception is less than 1/30000 [1], however it increased to 1/900 in women treated with clomiphen and to from 1/500 to 1/100 in women of in vitro fertilization and embryo transfer (IVF-ET) [2]. We experienced a case of concomitant pregnancy occurred regardless of taking contraceptive pill to control menstrual cycle. As surgical treatment, laparoscopic left salpingostomy followed by dilatation and curettage (D&C) were carried out.

CASE REPORT

A 34-year-old nulliparous woman visited previous clinic wishing to delay the next period because of the private matter. After confirming the negative preg-

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nancy test, middle-dose pill (Norlutent-D™) which is including 0.05mg of mestranol and 5mg of norethisteron were administered for 12 days. After taking drug for 12 days, she visited previous clinic with complaint of amenorrhea. Urinary pregnancy test was positive, however, gestational sac (GS) was not identified by transvaginal scanning. She was referred to our outpatient clinic with suspect of ectopic pregnancy following controlling period by Norlutent-D.

She had no symptom such as vaginal bleeding and abdominal distention at initial visit. The cycle of her period was irregular, and there was no history of pelvic inflammatory disease and endometriosis.

Physical examination showed no abnormal findings except the slight tenderness of the uterus and scant uterine bleeding. Ultrasound (US) showed GS-like 5mm mass in the uterus and enlarged ovaries, in which the right ovary was 5.6 x 4.6 cm and left was 5.0 x 3.3 cm (Fig. 1). Moreover, scant fluid collection was confirmed in the pelvis. Culdocentesis was negative for blood, however, serum hCG level was 3,847 IU/ml. Although neither miscarriage nor ectopic pregnancy could be ruled out, patient returned home after taking the appointment of the next visit.

![Image](image1.png)

Fig. 1 US shows the enlarged ovary which appeared to be stimulated cycle.

However, 4 days later, patient came to outpatient clinic complaining severe abdominal pain complicated with vaginal bleeding, and serum hCG level elevated to 13,952 IU/ml. USG showed intrauterine GS (Fig. 2) and apparent hemoperitoneum, which was confirmed by positive pregnancy test. CP of intrauterine blighted ovum and ruptured tubal pregnancy were suspected, and then laparoscopic surgery was carried out. Laparoscopy showed about 200ml of blood loss in the pelvis, enlarged uterus, and the swollen left tube, which was about 2cm in a diameter with bleeding from fimbria (Fig. 3). GS-like tumor was identified in the left fallopian-tube, therefore left tubal salpingostomy was performed. Operation was finished with the drain left in the pelvis after securing hemostasis and intrauterine GS was confirmed by scanning. Postoperative course was uneventful and chorionic villi was confirmed with pathological examination. Although on 7th days post operation, GS showed no development, which confirmed the diagnosis of miscarriage, and then dilatation and curettage (D&C) was performed (Fig. 4). Pathologically, chorionic villi were identified in the specimen of the intrauterine contents, and the diagnosis of CP of intrauterine blighted ovum
and tubal pregnancy was made. There was no sign of hCG rise thereafter.

DISCUSSION

The incidence of CP in women with spontaneous fertilization is 1 in 30,000, whereas, with the aid of various assisted reproductive techniques, it increases to 1 in 100 [3, 4]. Moreover, the increased incidence of pelvic inflammatory disease (PID) has been contributing to the increasing incidence of CP during past years.

It is difficult to confirm the diagnosis of CP because vaginal bleeding with GS in the uterine cavity is suggestive of threatened abortion [5]. Especially, in this case, neither of ovulation induction nor vaginal bleeding was identified, therefore, CP was not confirmed at initial visit. The delayed diagnosis could cause more serious complications such as acute abdomen.

In 29% of CP cases reported by Tal et al. and 26% by Barrenetxea et al., the diagnosis of CP was confirmed beyond 9 weeks of gestation [3, 6]. The half of CP shows the symptoms such as acute abdomen due to the sudden rupture of the ectopic pregnancy, therefore, emergent surgical intervention is necessary [1,7]. In this case, patient took mestranol and norethisterone to delay next period for 12 days following negative pregnancy test, therefore, it was difficult to exclude CP from the diagnosis at first. However, the laparoscopy showed that ovaries were swollen and seemed to be a state of ovarian hyperstimulation syndrome, which revealed that multiple ovulation might have occurred.

The three main types of postcoital contraception in use are the combined oral emergency contraceptive (COEC), the progestogen-only emergency contraceptive (POEC) and a copper-releasing intrauterine device (IUD). The randomized trial by the WHO showed that the overall efficacy of the POEC was better than that of COEC (97%) [8]. Mestranol-norethisterone is well known as "Norlutent-D" for emergency contraception in Japan and prevents fertilization rather than implantation and development of embryo. Norlutent-D consists of 0.5mg of norethisterone and 0.05mg of mestranol. Ectopic pregnancy after failure of emergency contraception is quite rare, however, a case of EP following emergency contraception with ethinylestradiol-levonorgestrel and some cases of levonorgestrel contraception were reported [9-13]. Beral [14] and Liuko [15] reported high levels of progesterone are related to the occurrence of ectopic pregnancy and the risk of ectopic pregnancy among women using progestin oral pills or progestin implants for contraceptive is two to five-fold compared to other women of childbearing age. Paliti et al. reported that progesterone might cause ectopic pregnancy by blocking the ciliary activity in a dose-dependent fashion [10]. When the pills are taken too late to prevent fertilization, there are two possible outcomes: (a) Hormonal emergency contraception (HEC) will not be effective and the method fails. (b) HEC prevents pregnancy, if it acts after fertilization [16]. In this case, it is unclear why CP was caused during taking contraceptive pill, however irregular taking of contraceptive pill might cause unexpected multiple-ovulation on the contrary following a fall of serum estrogen and progesterone level.

In conclusion, we experienced a case of CP following administration of mestranol-norethisterone to control menstrual period. We should take into consideration that CP could be caused by taking contra-
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