Introduction

Heterotopic pregnancy (HP) is the simultaneous development of intra and extratubal gestations. Despite being a very rare event in natural conception, estimated as 1.25:10,000 (1), its risk gets higher for patients who have undergone ovulation-induction therapies with an incidence of 33:10,000 (2) and becomes quite common after in vitro fecundation (IVF), with an approximate ratio of 1:100 (3). Identification of HP is a diagnostic challenge because the identification of an intrauterine pregnancy may mislead the detection of an ectopic gestational sac (4). As a result, there should be a high index of suspicious after treatment with assisted reproductive technology (ART) and ovulation-inducing medications. When managing this peculiar condition early diagnosis is crucial, as one should care about both mother and intrauterine pregnancy. While the best surgical treatment is still debated, laparoscopy seems feasible and safe for both mother and viable pregnancies.

Herein, we report an extremely rare case of the laparoscopic management of a quadruplet HP after ovulation induction with clomiphene citrate, characterized by three intrauterine pregnancies and an abdominal heterotopic one.

Methods: clinical case

A 40-year-old nulliparous woman was admitted to the emergency room of “Villa Sofia - Cervello” Hospital at 9.2 weeks of gestation, suffering from a 3-day lower abdominal pain in the right iliac region. She was in good general condition, with no fever and her vitals parame-
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Ters were stable (blood pressure 120/70 mmHg; hemoglobin 12.1 g/dl). Because of a 3-year infertility, she underwent an ovarian stimulation with 50 mg clomiphene citrate on days 5 to 9 for ovulation induction under the care of her gynecologist. At admission, she complained of pain in the superficial and deep palpation of the right iliac region; she did not present vaginal bleeding. The trans-vaginal ultrasound examination revealed an intrauterine pregnancy containing a live embryo and two more empty gestational sacs (Figure 1). No signs of placental abruption were found, but there was a little amount of free fluid in the pelvis and a fourth gestational sac with a live embryo, beside the right ovary. After informed consent of the mother on the basis of findings, specifically focusing on the presence of an abdominal pregnancy, we performed a diagnostic laparoscopy in urgency setting. There was minimal hemoperitoneum associated with “organized” blood clots around the right adnexa, which was partially visible because of the adhesions of the right salpinx and the ovary with the left colon and sigma. Uterus, enlarged as 10 weeks of gestation, and left adnexa appeared regular. After evacuation of blood clots, we found the intra-abdominal pregnancy, implanted both on the right fallopian tube and the epiploic fat of the colon (Figure 2). While the right fallopian tube was grossly ruptured with fibrinous material and clot extruding from the sites of rupture, the right ovary was regular. We removed the abdominal pregnancy with minimal manipulation of the uterus and, because of the extent of tubal damage, we also performed a right salpingectomy (5). The anatomopathological examination was conclusive for trophoblastic tissue both on tube and epiploic fat. After laparoscopic surgery, to the patient was daily administered 200 mg of progesterone and tocolytic drugs, as luteal phase support until the end of first trimester. On postoperative day 1, ultrasonographic examination showed an ongoing intrauterine pregnancy with the two empty gestational sacs. Post-operative course was without complications and the patient was discharged on postoperative day 3. The mother continued her routine antenatal care and the pregnancy went on uneventfully. She has given birth a healthy baby, weighting 3.230 g, with no congenital malformation by vaginal delivery at 38 weeks of gestation.

Discussion

Although the extended use of ART procedures nowadays has increased the ectopic and subsequently the HP rates (6, 7), the heterotopic quadruplets remain a rare finding in clinical practice. This clinical entity could represent a potentially life-threatening condition both for the woman and the intrauterine pregnancy. While many cases are diagnosed after the rupture of the fallopian tube, with acute abdomen symptoms (8), around 50% of HP is asymptomatic. When HP follows IVF the diagnosis can be exceptionally difficult. In fact, the beta-chorionic gonadotropin may often continue to rise normally, the ovaries to be enlarged, and the ectopic gestational sac can easily be missed on ultrasound scan. Furthermore, the intermittent unilateral pain could be attributed to a hemorrhagic corpus luteum or to an ovarian hyperstimulation (9). To our knowledge, five cases have been
Laparoscopic management of quadruplet heterotopic pregnancy after ovarian stimulation cycle

reported in Literature. This report is the sixth heterotopic quadruplet and the fourth case with successful outcome. Medications that induce ovulation, such as clomiphene citrate, and in vitro fertilization and embryo transfer techniques are associated with an overall increased rate of HP (10-12). In this sense, pregnant patients undergoing I or II level of ART procedures should always be evaluated for ectopic pregnancy, despite the presence of an intrauterine gestation. On routine ultrasonography, the obstetrician should search the adnexa for a possible concurrent HP, especially in case of an acute abdomen. When this diagnosis is established on time, the rate of pregnancies that reach term after treatment is significant (13). The goal of management of HP is to terminate the extrauterine pregnancy while taking precautions to minimize the possible threat to the intrauterine gestation. During surgery the uterus should be minimally manipulated to prevent contractions during or after the operation. Nevertheless, special attention should be paid to prevent the disruption of the ovarian blood supply, particularly in the ovary with the corpus luteum. In the case of disturbance of the corpus luteum up to 12 weeks of gestation, the progesterone support is indicated (8, 14).

Although long-term effects of laparoscopic surgery during pregnancy on the fetus have not been widely investigated, laparoscopy has been increasingly used in surgical procedures in pregnant women and, according to the literature, no increase in adverse outcomes has been reported (8, 15-18). Nonetheless all efforts have been made to minimize the exposure of the fetus to anesthetic agents: general anesthesia was started after the preparation of all laparoscopic surgical instruments and operation-related procedures, and the carbon dioxide pressure was maintained at 10 mmHg or less, after trocars insertion (19). Furthermore all these cases might be performed by one surgical team experienced in gynecological and laparoscopic surgery in emergency setting (20-28).

Conclusion

In our experience, laparoscopic management of abdominal HP with an intrauterine viable fetus seems to be a feasible and safe procedure for both mother and fetus. Gynecologist should keep in mind that an adnexal mass in a pregnant patient with a history of ovulation induction or ART procedures may be suspect for a HP.

References


