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HETEROTOPIC PREGNANCY IN AN ASSISTED REPRODUCTION CONCEPTION: CASE REPORT AND LITERATURE REVIEW
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HETEROTOPIC PREGNANCY IN AN ASSISTED REPRODUCTION CONCEPTION; CASE REPORT AND LITERATURE REVIEW

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SUMMARY

Infertility management by assisted reproduction techniques has had rapid increase. While there is robust evidence supporting the efficacy and safety of assisted reproduction technique (ART), complications are encountered. Heterotopic pregnancy, defined as the presence of both an intrauterine and an ectopic gestation, is a rare eventuality of early pregnancy. A 42 years old patient (Para 0+1) with a diagnosis of secondary infertility is presented; she had In Vitro fertilization (IVF) with egg donation. Two weeks after the IVF, a positive serum Beta Human Chorionic Gonadotropin confirmed the pregnancy and she continued with intake of progestins for luteal phase support. At 7 weeks gestation she presented at a local hospital with acute pelvic pain. A diagnosis of heterotopic pregnancy was made after transvaginal showed right slow leaking ectopic pregnancy andintrauterine missed abortion. Laparoscopic surgery, right salpingectomy and manual vacuum aspiration were performed with good subsequent recovery. The case presented, discusses the aetiology, clinical presentation, diagnosis and management of heterotopic pregnancy.

INTRODUCTION

A heterotopic pregnancy is a life threatening, uncommon complication of early pregnancy where both extra-uterine (ectopic pregnancy) and intrauterine pregnancy can occur concurrently (1). It can also be defined as an amalgamated ectopic pregnancy, multiple-sited pregnancy, or coincident pregnancy (1).Heterotopic pregnancy is a rare complication of assisted reproduction technique. The overall rate of EP is 1–2 % in the general population, and 2–5 % among patients who have utilized assisted reproductive technology (ART) (1,2).Hence, the incidences of heterotopic pregnancies have increased due to extensive utilization of ART. Major diagnostic pitfalls are associated with heterotopic pregnancy

and the objective of this article is to expound on the therapeutic options.

CASE REPORT

Forty-two years old patient, (Para 0+1-Abortion) who had presented with secondary infertility is discussed. The hysterosalpingogram and pelvic ultrasound were normal. The etiologic factor for the infertility was low ovarian reserve with antimullerian hormone level as 0.1ng/ml (Normal level 1.0-5.0ng/ml). The spouse's semenalysis was normal. She was advised to undergo IVF with egg donation.

The donor underwent standard long luteal phase protocol of ovulation induction. She had oocyte retrieval and fertilization by ICSI with the husband's sperm. Incubation was done with fertilization being confirmed at 16-18 with two pronuleate and one polarbody. A total of 12 embryos were further incubated with global life media. She had transfer of two blastocysts on the fifth day after oocyte retrieval and luteal phase was maintained by progestin.

Pregnancy was confirmed fourteen days after the embryo transfer and she was maintained on progestin for luteal phase support. At seven weeks gestation she presented with acute pelvic pain at a local hospital. The clinical findings were; Stable general condition, no pallor, afebrile. The pulse was 92/minute and blood pressure of 110/70 mmhg. The significant finding was acute pelvic tenderness without a pelvic mass. Investigations were performed as indicated below:

Serum beta HCG: 5225mIU/ml

Haemogram: Hb 11.3g/dl, WBS 8.4, Neutrophils 77.8, Platelets 183 x 103

Urinalysis: Normal

Pelvic ultrasound confirmed heterotopic pregnancy: right slow leaking ectopic pregnancy and missed abortion. She was admitted at a local hospital where laparoscopic right salpingectomy and manual vacuum aspiration were performed. Post operatively she did well. She is scheduled for embryo transfer after three months.

DISCUSSION

Heterotopic pregnancy (HP) refers to the coexistence of an intrauterine pregnancy with an ectopic pregnancy in any of the locations. The incidence of heterotopic pregnancy (HP) has been estimated to be from 1:4000 to 1:30,000 women in the general population (2,12). The risk of heterotopic pregnancy following in vitro fertilization (IVF) has been estimated as high as 1:100 women (2,12,13). Ectopic pregnancy has a prevalence of 1-2% of all pregnancies and is a potentially catastrophic condition (1). An ectopic pregnancy (EP) refers to the implantation of an embryo outside of the uterus. The most common EP location is in the fallopian tube, predominantly the ampullary region of the fallopian tube. Heterotopic pregnancy can include an ectopic pregnancy in any of the locations; a triplet HP that comprised of tubal and cervical EPs has been documented (5). The majority of tubal heterotopic pregnancy (72.5 %)was in the ampullary or interstitial portion of the fallopian tube(3). The patient discussed had an ectopic pregnancy in the right ampullary region and an intrauterine missed abortion.

There has been rapid advancement of laboratory diagnostics, transvaginal ultrasound, chemotherapy and laparoscopy, in the evaluation, diagnosis and management of EP; hence, maternal mortality has significantly reduced (1). Even with the overall decrease in mortality over time, ruptured ectopic pregnancy still contribute up to 6% of all maternal deaths; a review of mortality in ART-associated ectopic pregnancy correspondingly observed a mortality rate of 31.9 deaths per 100,000 pregnancies (2,5).

Assisted reproductive technologies constitute a risk factor for EP, as 2–5 % of pregnancies from assisted reproductive technologies are ectopic (6). The three main factors contributing to this increased risk are the specific type of procedure, the reproductive health characteristics of the woman, and the estimated embryo implantation potential (6). A history of infertility, even in the absence of known tubal disease, is associated with ectopic pregnancy, with the ectopic pregnancy risk increasing with a longer duration of infertility (4). Tubal factor infertility specifically is associated with a two-fold risk of EP following IVF (7).

Several IVF cycle parameters may be associated with an increased risk of ectopic pregnancy. Patients undergoing cycles triggered with gonadotropin releasing hormone (GnRH) agonists instead of recombinant hCG may be at higher risk of ectopic pregnancy; these observations are hypothesized to be due to poor endometrial receptivity following GnRH agonist administration (8).

The number of embryos transferred may be correlated to the ectopic pregnancy risk; the rate of ectopic pregnancy following fresh cycles rose significantly from 1.7 % following single embryo transfer to 2.5 % following the transfer of 4 embryos (7). Depth of transfer may also have an effect; a randomized prospective study of deep versus mid-fundal transfer reported an ectopic pregnancy rate of 1.5 versus 0.4% (9). Day of embryo transfer has not been associated with risk of ectopic pregnancy (10). The transfer of fresh embryos is associated with a higher EP risk as compared to the transfer of thawed embryos (11). It has been hypothesized that the controlled ovarian stimulation and hyperestrogenic environment prior a fresh embryo transfer negatively effects endometrial receptivity (12). The IVF protocol used for the patient presented was long luteal agonist protocol and had 2 embryos transfer.

Ultrasound diagnosis of tubal ectopic pregnancy

Figure 1
Ectopic pregnancy by transvaginal ultrasound. The arrow indicates the ectopic gestation with a surrounding hyperechoic ring, called the 'bagel' or 'tubal' sign (13)

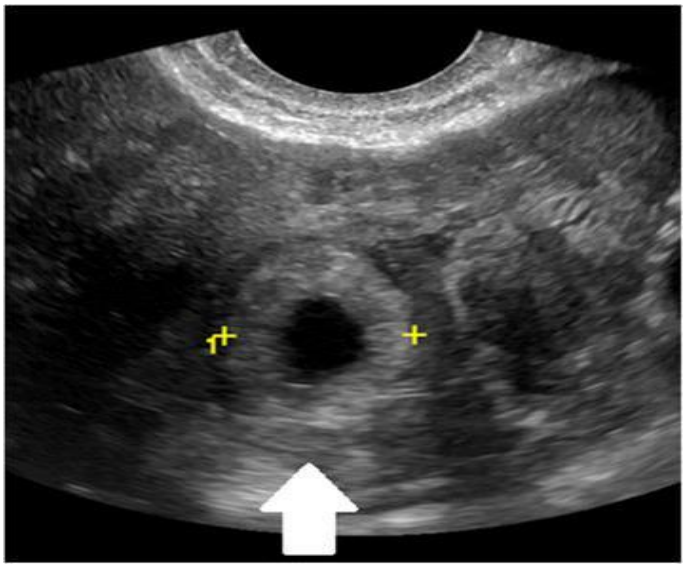
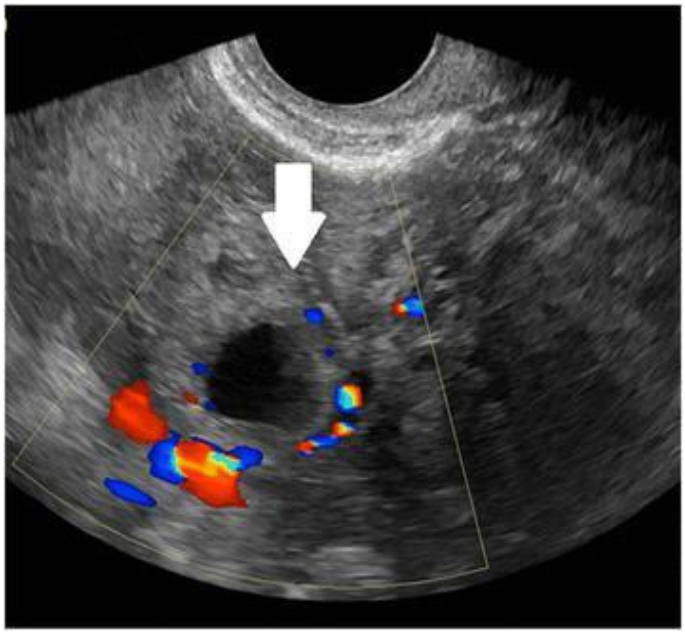


Figure 2
Tubal ectopic pregnancy by transvaginal ultrasound. The arrow indicates the ectopic gestation with circumferential Doppler flow, called the "Ring of Fire"(14)



Recognition of a gestational sac and foetal pole, with or without cardiac activity, or a hyperechoic ring called the 'bagel' or 'tubal' sign (Figure 1) and with circumferential Doppler flow (Figure 2) is highly suggestive of an ectopic pregnancy (13,14). If a suspicious mass moves separately from the ovary, called the 'blob' sign; the positive predictive value is above 90 % in a symptomatic woman with a positive serum b-hCG and no intrauterine pregnancy on transvaginal ultrasound (15). The diagnosis of heterotopic pregnancy in the case presented was made by a positive serum human chorionic gonadotropin and demonstration of right slow leaking ectopic pregnancy and non-viable intrauterine pregnancy by transvaginal ultrasound.

Management of heterotopic pregnancies

Treatment of a heterotopic pregnancy is tailored to the specific ectopic pregnancy location, and the patient's clinical presentation and stability. The most common interventions for the treatment of ectopic pregnancy are medical management with systemic methotrexate and surgical removal of the pregnancy. Medical management of ectopic pregnancy with methotrexate has been demonstrated to be more cost-effective than surgical management while maintaining similar treatment success and future fertility (16).

Medical management of tubal heterotopic pregnancy includes local injections of potassium chloride or a hyperosmolar glucose solution, though over half of tubal heterotopic pregnancy managed with local potassium chloride may require subsequent salpingectomy (3). Treatment with systemic or local methotrexate is contraindicated in the presence of a viable intrauterine pregnancy(17). Surgical management has been described more frequently, as patients with tubal heterotopic pregnancy present more often with rupture and hemodynamic compromise than those with tubal ectopic pregnancy. Salpingectomy is preferable to salpingostomy, as persistent trophoblastic tissue cannot be monitored in the setting of ongoing intrauterine pregnancy (18). Patients with heterotopic pregnancies suffer spontaneous abortions at higher rates than intrauterine-only pregnancies (up to 30 %) (4).

The patient presented had a slow leaking pregnancy with a missed abortion after IVF; and hence a laparoscopic salpingectomy with manual vacuum aspiration was our preferred option.

CONCLUSION

The case review describes the incidence, risk factors, diagnosis, and management heterotopic pregnancies. Treatment in stable patients is often medical, though patients with raptured ectopic pregnancy or with ectopic pregnancy outside the fallopian tube may require differing and/or more invasive treatment, including excision by laparoscopy. Of patients with tubal ectopic pregnancy the likelihood of future intrauterine pregnancy is high and independent of treatment modality. As the rates of both ectopic pregnancy and women receiving fertility treatments have increased, the observed rate of heterotopic pregnancy has increased as well. Consequently, early sonographic examinations should be performed after ART and more attention should be paid specifically on the evaluation of the adnexa.

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