Concurrent ovarian and ipsilateral tubal ectopic pregnancies after a double embryo transfer: a case report

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Introduction

Ectopic pregnancies are one of the few conditions which constitute a gynecologic emergency, as it may result in a life threatening complication. The incidence in the general population is approximately 2 % [1]; however a significant increase has been reported after the use of In-Vitro Fertilization (IVF), ranging from 2.1 to 8.6 % [2, 3].

An ectopic pregnancy may implant in different places throughout the female pelvis; however, tubal pregnancies are by far the most common implantation site. Ovarian localization of an ectopic gestation accounts for no more than 3 % of all ectopic pregnancies [4]. The clinical signs and symptoms of an ovarian ectopic are the same as those seen with a tubal pregnancy, and the diagnosis is usually made by pathology, due to the fact that an ovarian ectopic pregnancy is often misdiagnosed during surgery as a hemorrhagic corpus luteum. Though of little clinical use today, there are specific diagnostic criteria for an ovarian ectopic described by Spiegelberg in 1878: (1) an intact ipsilateral tube, clearly separate from the ovary; (2) a gestational sac occupying the position of the ovary; (3) a gestational sac connected to the uterus by the ovarian ligament; and (4) ovarian tissue in the wall of the gestational sac [5]. The risk of ovarian pregnancy after assisted reproductive techniques is approximately 0.3 % and is likely to increase with widespread use of these procedures [6–8]. However, given the extremely low incidence of an

ovarian ectopic pregnancy, even after ovulation induction and assisted reproduction, it still remains a very rare diagnosis.

Ectopic pregnancies may also be seen in the presence of another coexisting simultaneous pregnancy. The diagnosis of co-existing pregnancies may be delayed, as the patient may present without symptoms and normally rising HCG levels, and usually with an intrauterine pregnancy. There are different proposed theories to explain the increased incidence of these pregnancies after assisted reproductive technologies (ART). Those include the high proportion of patients with tubal disease, high levels of estradiol (E2) and progesterone (P), and high numbers of transferred embryos or ovulated oocytes in this population [9–11].

This case report describes the rare occurrence of a tubal pregnancy with a concurrent ipsilateral ovarian ectopic pregnancy.

Materials and methods

The patient is a 36 years old gravida 4 para 0, who presented in August 2008 for IVF with preimplantation genetic screening (PGS) due to her history of unexplained recurrent pregnancy loss.

Her first IVF cycle did not result in a pregnancy. The embryos from the second cycle were frozen and subsequently thawed and combined with embryos from her third cycle for PGS, resulting in delivery of a healthy female infant in October of 2009. A subsequent IVF treatment, without PGS, resulted in a pregnancy of unknown location with abnormally rising hCG levels, which was treated with Methotrexate administration and the hCG level was followed serially until it was negative.

Several months later, the patient returned for another IVF treatment, again without PGS. Ovarian stimulation was carried out utilizing a microdose leuprolide acetate flare protocol, which resulted in 8 oocytes retrieved, 6 of which were found to be metaphase II oocytes. Of these, 5 fertilized and 2

Capsule This case report describes the rare occurrence of a tubal pregnancy with a concurrent ipsilateral ovarian ectopic pregnancy after a double embryo transfer, diagnosed by genetic analysis.

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embryos were transferred (1 early blastocyst and 1 morula). Her initial beta hCG level nine days after embryo transfer was 38 mIU/ml, and her levels rose appropriately on repeat blood draws, with an hCG=1,737 mIU/ml at 5 weeks 3 days. That day, the patient was scheduled for a routine pregnancy ultrasound; however, 2 days later, at approximately 5 weeks and 5 days age of gestation, the patient called complaining of acute onset of severe lower abdominal pain. During her evaluation in the office, transvaginal ultrasound showed an empty uterine cavity, large amount of blood and clots in the pelvis, as well as a 0.54 cm gestational sac which was noted in the right adnexa with a small yolk sac. It was difficult to determine the location of this gestational sac, which appeared to be in the middle of a large blood clot in the pelvis. The right ovary appeared to be separate from this structure.

During laparoscopy, large hemoperitoneum was aspirated from the abdomen and pelvis followed by copious suction-irrigation. It became apparent that the bleeding had originated from a ruptured area in her right ovary, which was noted to be bleeding profusely (Fig 1). The contents of this presumed hemorrhagic cyst were removed and sent to pathology, and after coagulating the area with bipolar cautery, hemostasis was obtained. At this point, it was not conclusive if this cyst represented a ruptured hemorrhagic corpus luteum cyst versus an ovarian ectopic. After this portion of the surgery was completed, and given the ultrasound findings of a right adnexal mass, the patient's fallopian tubes were carefully inspected. The right fallopian tube had a subtle purple bulge in its isthmic portion, which appeared to be consistent with a right ectopic pregnancy (Fig 2). Although the tube was not the primary source of the patient's hemoperitoneum, the decision was made to proceed with a right salpingectomy.

Results

The pathology report of the right ovarian contents demonstrated chorionic villi, portions of corpus luteum, and fibrous

Fig. 1 Laparoscopic image of the right adnexa, including an actively hemorrhagic right ovary

Fig. 2 Laparoscopic image of the right adnexa, including the right fallopian tube. The bulging of the tube is clearly visualized, findings suggestive of a tubal ectopic pregnancy

connective tissue with hemosiderin-laden macrophages. In addition, the right fallopian tube pathology showed findings consistent with ectopic pregnancy. These results were consistent with an ovarian ectopic and a concurrent ipsilateral tubal pregnancy.

In order to determine if the two implantations originated from two different embryos, glass slides were obtained from the paraffin blocks corresponding to the ovarian and tubal pathology specimens. The slides were sent to a reference genetics laboratory, Natera™ San Carlos, CA, for karyotyping.

Paraffin tissue samples were submitted as 2 sets of paraffin slides (1 Hematoxylin and Eosin stained slide and 9 unstained paraffin slides per set) corresponding to tissue obtained from the ovarian (Figs. 3 and 4) and fallopian tube (Figs. 5 and 6) sites. Fetal tissue, as identified by groups of small and irregularly shaped purple stained tissue, was dissected from unstained paraffin slides. DNA was extracted and purified from paraffin tissue samples using the Repli-g FFPE (Formalin-Fixed, Paraffin-Embedded) kit (Qiagen, Venlo, Netherlands). In parallel, DNA from both biological parent blood samples was extracted using the QIAcube (Qiagen,

Fig. 3 Pathology slide of the ovarian tissue

Fig. 4 Enlarged image for enhanced detail of the pathology slide for the ovarian tissue

Venlo, Netherlands). Purified DNA from dissected tissues and parental samples were analyzed using HumanCytoSNP-12 microarrays (Illumina, San Diego, CA). The microarrays contain 317,000 probes covering all 24 chromosomes, with a median distance between probes of 6,500 bases. Data was analyzed by Natera's Parental Support™ algorithm [12], which incorporates parental genotypic information to predict all possible fetal genotypes and potential resulting SNP allele patterns. Inclusion of maternal genotypic information allows accurate identification of maternal cell contamination (MCC), which is especially important in a 46,XX fetus. The method generated a report with both chromosome content and parental source.

The Natera Parental Support report from the ovarian sample was: 46 XX (without MCC). The Natera Parental Support report for the sample from the fallopian tube tube showed: 46 XX (without MCC), and in addition, the DNA was different from the ovarian tissue sample, indicating two distinct fetal tissues.

Approximately 2 months later, the patient presented with a spontaneous conception and was discharged to her obstetrician at 8 weeks with a confirmed intrauterine pregnancy.

Fig. 5 Pathology slide of the fallopian tube specimen

Fig. 6 Enlarged image for enhanced detail of the pathology slide for the fallopian tube specimen

Discussion

To our knowledge this is the first case report to confirm the presence of an ovarian ectopic pregnancy with a concurrent ipsilateral tubal pregnancy. A review of the literature was carried out by searching Pubmed using the keywords: ovarian ectopic and primary ovarian pregnancy (in English). Several case reports and small case series were obtained, with a wide variety in the presentation of these ovarian pregnancies, ranging from a small adnexal mass treated with methotrexate [13, 14], the presence of an ovarian twin pregnancy [15], to a term ovarian pregnancy delivered via laparotomy [16]. The largest case series reported in the literature to date includes 49 cases over a period of thirteen years [17], emphasizing the fact that ovarian pregnancy alone is still a rare entity.

The diagnosis of ovarian pregnancy can be difficult and relies mostly on intraoperative findings. In this patient's case, the diagnosis of an ectopic pregnancy was made by the presence of an adnexal mass with free fluid in the pelvis on ultrasound and absence of intrauterine gestation. However, intra-operatively the bleeding was clearly coming from the right adnexa, specifically the ovary. If the procedure had been limited to cauterizing the bleeding site on the ovary, without removing ovarian contents, the clinical diagnosis of a ruptured corpus luteum cyst would have been made. If the right Fallopian tube had not been carefully inspected, the tubal ectopic may have been left in place, putting the patient at risk for future tubal rupture and hemorrhage.

Finally, the pathology report, followed by the genetic analysis of the paraffin slides, confirms that these were in fact two separate gestations, one implanted in the right ovary and one in the right Fallopian tube. To our knowledge, this is the first case report in which chromosomal analysis utilizing microarrays has been applied on pathology specimens to confirm the diagnosis of a simultaneous, yet distinct, ovarian and tubal heterotopic pregnancies.

This case is not only novel in its presentation and diagnosis, but also reaffirms the need to have a heightened awareness for unusual clinical presentations in the case of any patient who

presents with positive hCG levels above the sonographic threshold and no intrauterine pregnancy, such as occurred with this patient.

Conflict of interest There is no conflict of interest or financial support for this study.

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