Ectopic pregnancy after IVF in a patient with unilateral agenesis of the fallopian tube and ovary and with endometriosis: search of the literature for these associations

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Introduction

The real incidence of adnexal malformations is very difficult to determine because many women with these anomalies are not diagnosed since they are asymptomatic [1]. The association of mullerian and gonadal agenesis is also very rare; for example congenital absence of the ovary with absence of the fallopian tube [2] has been suggested to have an incidence of 1:11,240 women [3, 4]. Even rarer is the association of these anomalies with endometriosis. Here, we report a case of a woman with 18 months of infertility and with the incidental findings of unilateral agenesis of the ovary and fallopian tube as well as endometriosis, who after IVF/ICSI treatment developed an ectopic pregnancy. We also reviewed the literature seeking for these anatomic anomalies and their plausible causes.

Case report

A 31 year-old healthy woman with history of chronic pelvic pain and 18 months of primary infertility presented for evaluation. The patient had no past surgical history and her BMI was 21.6. She was treated unsuccessfully for 6 months with clomiphene citrate (50 mg/for 5 days) and intrauterine inseminations (IUI) in another center. Routine assessment of her ovarian reserve was in the upper range of normal (cycle day

3 FSH: 8.8 mIU/mL; E2:75; LH: 9.0 mIU/mL and Anti Mullerian Hormone (AMH) (0.66 ng/100 mL), lower than normal for her age); PRL was normal (22 ng/mL) and TSH was normal (2.2 mIU/L). Her karyotype was normal (46 XX). The Pap smear was normal and the Chlamydia/Gonorrhea-DNA screenings were negative. Her physical exam was completely normal, while a transvaginal ultrasound revealed a normal uterus and left ovary, but the right ovary could not be visualized.

Sonohysterography (SHG) showed a normal uterine cavity, while a *pelvic MRI* confirmed the absence of the right ovary and excluded the presence of adenomyosis as responsible for the chronic pelvic pain. However, it identified four hemorrhagic lesions in the left ovary suggestive of endometriomas. A *retroperitoneal ultrasound* showed normal kidneys with no focal masses or stones and no evidence of pelvic ectasia. A diagnostic *laparoscopy* for her pelvic pain confirmed total absence of the right ovary and revealed only about 2 cm proximal stump of the right fallopian tube (Fig. 1). The left ovary and the left fallopian tube were normal (Fig. 2). Filmy adhesions between the left ovary and the left pelvic sidewall were lysed and a large peritoneal window was located in the cul-de-sac, surrounded by foci of endometriotic lesions which were excised. Left ovarian endometriomas were excised or cauterized. Pathology report confirmed that the peritoneal and left ovary implants were consistent with endometriosis. *Chromoperturbation* showed fill and spill of the left fallopian tube while on the right there was proximal fill of the short cornual portion, but no spill.

The couple underwent to two cycles of ICSI because of male factor (sperm concentrations: 5 mil/ml; motility 30 %; normal morphology: 45 %). The ovarian stimulation for the first ICSI cycle consisted of recombinant FSH (rFSH) (with a total rFSH dose of 1912.5 IU) and GnRH antagonist with recombinant LH (rLH) (total dose of 300 IU); the maximum

Capsule Cases of Mullerian and gonadal malformations together are very rare and their etiology is not always clear as evidenced in literature.

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Normal left ovary and fallopian tube. Large peritoneal window and endometriosis.

Fig. 1 Normal left ovary and fallopian tube. Large peritoneal window and endometriosis

E2 level was 2180; two oocytes were recovered but only one fertilized; one embryo was transferred on day 3 but no pregnancy resulted.

For the second ICSI cycle the same protocol, except for higher doses of rFSH, was used (total rFSH 3000 IU and total rLH 300 IU); the maximum level E2 was 2980; 12 oocytes were retrieved, eight fertilized and two embryos were transferred on day 5. This cycle resulted in a left ectopic pregnancy (maximum level of hCG 4,700 IU) which was medically treated with metotrexate.

Discussion

The unique findings described in this case (absence of an ovary with ipsilateral fallopian tube, endometriosis and ectopic pregnancy after ART) prompted a comprehensive literature review (see Table 1). All cases reported in literature

Uterus with unilateral right tubal and ovarian agenesis

Fig. 2 Uterus with unilateral right tubal and ovarian agenesis

were discovered accidentally or during procedures to investigate primary infertility [2] and in some the partial or complete absence of ovary or tube is associated with uterine anomaly and urinary tract anomaly [5–8]. The reason given is that the development of the genital tract is partially shared with the development of the urinary and genital tract. But of the 28 cases reported in literature describing unilateral agenesis of ovary and fallopian tube, only four were associated with *urinary tract anomalies*. Five were associated with the absence of ovary and/or tube and *uterine anomalies*. Another 18 reports were associated with a normal uterus and in five cases there was no mention of uterine anomalies. The concomitant presence of endometriosis is reported in only three cases (3/28 cases, 9 %).

These anomalies are, however, rare and can originate from three possible causes: a) an asymptomatic torsion of the adnexa (ovary and tube), followed by ischemia and reabsorption [2, 4, 9–12]; b) congenital absence due to a developmental defect of the müllerian and gonadal structures either entirely on one side or localized to the region of the genital ridge and the caudal part [2, 3, 6, 13]; or, c) an underlying vascular anomaly causing ischemia [9].

When further questioned, our patient reported that about 10 years earlier she had an acute, but transient right-sided pelvic pain, which was not diagnosed as possible adnexal torsion when she sought medical attention (allegedly the patient was discharged home from the emergency room since her pain improved after receiving pain killers). In retrospect this acute pain could have been suggestive of torsion of her right adnexa [9]. The normal karyotype does not support a chromosomal condition related to the absence of the fallopian tube and ovary, such as pure or mixed gonadal dysgenesis (46 XY or 45X0/46XY).

Finally, it must be mentioned that despite intrauterine embryo transfer and the presence of only one tube, the patient developed an ectopic pregnancy. Although it is known that the incidence of ectopic pregnancy is higher in pregnancies after IVF (from 2.1 % to 8.6 %) [14, 15], the incidence in cases of unilateral absence of ovary and tube it is not known. A couple of interesting, but unproven, hypotheses could explain the ectopic pregnancy of this case, either as associated with the presence of endometriosis causing abnormal tubal ciliary function [16, 17], or the agenesis of one fallopian tube could be correlated with the inefficiency of the other as well [2, 4, 12, 18].

In summary, complex malformations of female genital tract, like unilateral absence of the ovary and the fallopian tube, with or without endometriosis, are not very common and a clear etiology for these anomalies is not known. Despite several classification systems have been proposed for Müllerian tract anomalies [32], those involving also the gonads remain “orphan of a classification” and are mostly justified as vascular accidents.

Table 1 Literature review on absence of fallopian tube and/or ovary and associated anomalies

Authors (reference)	Fallopian tube and/or ovary	Uterine Anomaly	Urinary tract anomaly	Others
Eustace DL. et al. [2]				
Case 1	Congenital absence right fallopian tube and ovary	Uterus normal	No	Primary infertility
Case 2	Congenital absence right fallopian tube and ovary	Uterus normal	NM	Discovered during sterilization
Sivanesaratnam V. [3]				
Case 1	Absence left ovary and fallopian tube.	Uterus normal	No	NM
Case 2	Absence right ovary and fallopian tube.	Uterus normal	No	Blocked right tube
Mylonas I. et al. [4]				
Case 1	Absent right tube and ovary	Uterus normal	NM	NM
Case 2	Absent right tube and ovary	Uterus normal	NM	<i>Endometriosis</i>
Case 3	Absence right adnexae, left ovarian agenesis	Uterus normal	NM	NM
Haydardedeoglu B. et al. [5]	Absent e left ovary and fallopian tube.	Unicornuate uterus with non-communicating horn	Ipsilateral renal agenesis	Spontaneous abortion, premature delivery
Muppala H. et al. [6]	Absent right ovary, tube and round ligament	Uterus normal	Right renal agenesis	Pyloric stenosis, <i>Endometriosis</i>
Zaitoon MM et al. [7]	Absent fallopian tube and ovary	OA – NM	Crossed renal ectopia	NM
Suh BY et al. [8]	Absent left distal tubal segment, absent left ovary	Uterine septum	NM	Primary Infertility
Uckuyu A. et al. [18]				
Case 1	Absent left distal tubal segment, streak left ovary	Uterus normal	No	Primary Infertility
Unilateral tubal patency				
Case 2	Absent right distal tubal segment, normal right ovary	Uterus normal	No	Primary Infertility Unilateral tubal patency
Case 3	Twisted left tube, absent right ovary	Uterus normal	No	Primary Infertiliy Unilateral tubal patency
Case 4	Left ovarian agenesis	Uterus normal	No	Incidental finding after torsion of the right adnexa.
Mulayim B. et al. [19]	Absence of left tube and ovary	Unicornuate Uterus	Pelvic Kidney	<i>Minimal Endometriosis</i>
Pabuccu E. et al. [20]	Absent left tube and ovary	Uterus normal	No	Primary Infertility
Demir B. et al. [21]	Absent left ovary and fallopian tube	Unicornuate uterus	No	Incidental finding during Cesarean delivery
Gotti G. et al. [22]	Absent right fallopian tube and ovary	Uterus normal	No	Incidental finding after extrauterine pregnancy
Rapisarda G. et al. [23]	Absent left ovary and fallopian tube	Uterus normal	NM	Pelvic pain, Suspected PID, Blocked right tube
Sirisena LA [24]	Absent left ovary and ipsilateral distal tube	Uterus normal	NM	Right ovarian cyst
Georgy FM et al. [25]	Absent left ovary and tube	Uterus normal	No	Abdominal hysterectomy for menorrhagia
Gold MA et al. [26]	Bilateral absence ovaries and distal fallopian tubes	Hypoplastic uterus	NM	Primary infertility, primary amenorrhea and normal karyotype
Dueck A. et al. [27]	Absent left ovary and rudimental left fallopian tube.	NM	NM	Right ovarian cyst
Petersen KR et al. [28]	Unilateral absence ovary and tube.	OA –NM	OA-NM	Anal atresia
Sinha MR et al. [29]	Absent fallopian tube and ovary	OA- NM	OA-NM	NM
Chan CL et al. [30]	Bilateral absence of fallopian tubes and ovaries	OA- NM	OA-NM	NM
Bulgan Kilicdag E et al. [31]	Absent right ovary and distal part of fallopian tube	Uterus Normal	No	NM
Modified from Pabuccu E et al. [20]	NM: not mentioned		OA: only abstract	

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