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CASE REPORT

IVF and embryo development subsequent to ovarian torsion occurring during the resumption of meiosis

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Abstract This report describes an unusual case of ovarian torsion during an IVF cycle prior to vaginal oocyte retrieval and the subsequent embryo development. A 27-year-old, whose husband carries a balanced translocation, presented on stimulation day 11 (day after human chorionic gonadotrophin administration) with signs of right ovarian torsion. Transvaginal ultrasound identified decreased right ovarian venous flow but preservation of right ovarian arterial flow. She underwent emergency laparoscopic right ovarian detorsion followed by vaginal oocyte retrieval on postoperative day 1. Ten oocytes were retrieved from the right detorted ovary, 4/10 (40%) were fertilized and 3/4 (75%) became blastocysts. Fifteen oocytes were retrieved from the left ovary, 14/15 (93%) were fertilized and 9/14 (64%) became blastocysts. All 18 embryos biopsied for preimplantation genetic diagnosis carried unbalanced translocations and none were transferred. The markedly reduced fertilization rate of the oocytes from the previously torqued ovary is similar to the rate described in a prior report and likely related to decreased but maintained ovarian arterial flow. This report is unique because not only was the patient's ovarian torsion surgically corrected prior to oocyte retrieval but also the embryos originating from the previously torqued ovary had excellent development with 75% progressing to the blastocyst stage. 

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Case report

A 27-year-old nulliparous patient undergoing her second IVF cycle presented for an urgent outpatient visit on stimulation day 11 of a long-lupron, step-down protocol. She had been identified to have a peak oestradiol concentration of 4309 pg/ml and 14 mature follicles (measurements

ranging from 14 to 21.5 mm) on the previous day and had taken her Ovidrel injection (EMD Serono Randolph, MA, USA) the evening of stimulation day 10. On stimulation day 11, she presented to the clinic for outpatient evaluation complaining of the acute onset of right lower quadrant pain 10/10 intensity with radiation to her right lower back. She described mild right lower quadrant pain

starting approximately 2 h after her Ovidrel injection, which resolved then recurred approximately 2 h before presenting for evaluation. She noted nausea and emesis accompanying the onset of the severe pain. On evaluation, she was in moderate distress with significant discomfort and abdominal examination demonstrated profound tenderness to palpation in her right lower quadrant accompanied by guarding and rebound. Given the diagnosis of suspected right ovarian torsion, she was transferred by ambulance to the emergency department for further management.

On arrival in the emergency department, she described severe right lower quadrant pain, 10/10 intensity and unchanged since onset approximately 5 h prior, accompanied by nausea with emesis five times. On examination, she appeared very uncomfortable, lying on her side with minimal movement, but was haemodynamically stable with a heart rate of 75 beats per minute and blood pressure of 115/69 mmHg. Her abdomen was soft with significant tenderness to palpation in her right lower quadrant, accompanied by voluntary guarding and rebound. Her ovaries were nonpalpable abdominally secondary to body habitus (weight 166 pounds, body mass index 27 kg/m²). She was given intravenous narcotics and antiemetics, with resolution of her nausea but minimal improvement in pain. A transvaginal ultrasound revealed bilaterally enlarged ovaries consistent with ovarian stimulation, with right ovarian maximal diameter 8.3 cm and left ovarian maximal diameter 6.3 cm. The right ovary was noted to be heterogeneous in texture consistent with intermittent torsion and was also identified to be located in the left adnexa. Good arterial Doppler waveforms were identified in both ovaries, but there was diminished venous flow from the right ovary. Her serum laboratory evaluation showed normal white blood count (11,500/ μ l), normal haematocrit (35.7%) and quantitative beta human chorionic gonadotrophin concentration of 83 mIU/ml consistent with administration of Ovidrel injection the prior evening.

She was taken to the operating room for emergency laparoscopy for suspected right ovarian torsion approximately 8 h after the initial onset of pain. Intraoperatively, the ovaries were asymmetrically enlarged bilaterally with follicular cysts. The left ovary was present in the cul-de-sac. The right ovary was located outside the pelvic cavity superior to the uterus and appeared dusky in appearance. On closer inspection, the right ovary was noted to be twisted 360° anticlockwise around the infundibulopelvic ligament. The right ovary was easily detorted with a blunt probe and an atraumatic grasper, with rapid return to its normal pink color. Following right ovarian detorsion and given concerns for excessive mobility of the right ovary and potential re-torsion, the decision was made to gently deposit the right ovary in the posterior cul-de-sac. In this way, the right ovary was placed beneath the uterus and left ovary, which secured it in an anatomic but less mobile position. There was no bleeding encountered and the procedure was deemed to be complete. The patient recovered from her procedure, had resolution of her presenting symptoms and was discharged to home that evening with the plan to follow-up at the outpatient surgical centre the following morning for her previously scheduled vaginal oocyte retrieval.

On postoperative day 1 following laparoscopic right ovarian detorsion, she underwent vaginal oocyte retrieval at the scheduled time 36 h after her Ovidrel injection, having had no recurrence of her prior severe pain or gastrointestinal symptoms. At the time of vaginal oocyte retrieval, the right ovary was identified to be approximately 8 cm in largest dimension and the left ovary was 6 cm in size. The right and left ovaries were of equal sonographic texture and both maintained large follicles. Clear fluid was aspirated from all follicles bilaterally.

A total of 25 oocytes were retrieved: 10 from the right previously torqued ovary and 15 from the left ovary. The oocytes retrieved from the right and left ovaries were maintained separately in the embryology laboratory. Microscopic evaluation on day 1 identified fertilization (2 pronuclei and 2 polar bodies) in 4/10 (40%) oocytes from the previously torqued right ovary and 14/15 (93%) oocytes from the left ovary. On day 3, the embryos from the right ovary had progressed to: (i) 9-cell, grade 3 (<20% fragmentation); (ii) 8-cell, grade 3; (iii) 6-cell, grade 3; and (iv) 6-cell, grade 3. Eighteen total embryos (four from the right ovary and 14 from the left ovary) were biopsied for preimplantation genetic diagnosis (PGD) secondary to the patient's husband's known balanced translocation, 46,XY,t(6;10)(q23;q22). On day 5, three of the four (75%) of the embryos from the right ovary had progressed to the blastocyst stage (two early blastocysts, one blastocyst) and one embryo was at the 8-cell stage. Nine of the fourteen (64%) embryos from the left ovary reached the blastocyst stage (eight early blastocysts, one blastocyst). Single-cell fluorescence in-situ hybridization analysis was completed with probes specific for chromosome 6 (6p25.1: 6PTEL48; 6q27:VIJyRM2158 and chromosome 10 (10p15.1: 10PTEL006 (GenBank Z96139); 10q26.3: 10QTEL24 (GenBank D10S2490, GDB 6244631)). Unfortunately, all 18 biopsied embryos were identified to have unbalanced chromosome complements and none were transferred.

Discussion

Ovarian torsion is a well-known complication of IVF treatment. Iatrogenic ovarian enlargement from gonadotrophin-stimulated follicular cysts increases the volume of the ovary making it susceptible to torsion. Despite the enlargement of the ovaries that occurs in all IVF cycles, the actual incidence of ovarian torsion is exceedingly low. Five large series evaluating complications related to ovarian stimulation have identified a risk of ovarian torsion ranging from 0.025–0.2% (Bodri et al., 2008; Gorkemli et al., 2002; Govaerts et al., 1998; Maxwell et al., 2008; Roest et al., 1996). Recognized risk factors for ovarian torsion include ovarian hyperstimulation syndrome (OHSS), past history of ovarian torsion, endometriosis, past abdominal surgery and ovarian cysts (White and Stella, 2005). It is unclear whether the increased incidence of ovarian torsion in patients with OHSS is due simply to the excess ovarian enlargement that can occur in OHSS or the combination of ovarian enlargement plus abdominal ascites which may facilitate ovarian mobility (Zhu et al., 2008). Although this complication of IVF is quite rare, ovarian torsion is a gynaecological emergency necessitating urgent surgical intervention to

avoid ovarian necrosis and ovariectomy. The importance of maintaining a high index of suspicion for ovarian torsion during IVF must therefore be emphasized.

Regardless of the underlying cause of ovarian torsion in IVF, however, the fact remains that the majority of patients (in fact, one could argue all patients) undergoing ovarian stimulation for IVF have at least one risk factor for ovarian torsion; yet this complication affects only a very small proportion of IVF patients. Furthermore, the vast majority of reports of ovarian torsion associated with IVF describe the torsion as occurring after oocyte retrieval. Govaerts et al. (1998) report two adnexal torsions in 1500 oocyte retrievals, one of whom underwent laparoscopic detorsion three hours following oocyte retrieval and the other who had spontaneous resolution of her symptoms but unclear timing of diagnosis. Gorkemli et al. (2002) describe nine instances of ovarian torsion out of 10,583 total cycles. Of these nine patients, six were pregnant at the time of ovarian torsion (thereby clearly post-oocyte retrieval), but the time course of torsion in the remaining three patients is not noted. Iwabe et al., Zhu et al., and Kang et al., describe cases of ovarian torsion diagnosed between 9 days and 5 weeks following embryo transfer (Iwabe et al., 1994; Kang et al., 2006; Zhu et al., 2008). The remaining large series identify scattered instances of ovarian torsion among IVF patients, but unfortunately the timing of these diagnoses is not at all delineated (Bodri et al., 2008; Maxwell et al., 2008; Roest et al., 1996).

Only two accounts of ovarian torsion during an IVF cycle prior to oocyte retrieval can be identified in the literature. The first scenario involved a 37-year-old patient who was in her fourth IVF cycle and experienced acute onset of left lower quadrant abdominal pain accompanied by nausea early on the morning of her scheduled oocyte retrieval (Robson and Kerin, 2000). She presented for evaluation 1 h prior to her scheduled oocyte retrieval, but, unlike the patient in the current report, she did not initially have peritoneal signs and the differential diagnosis included left ovarian haemorrhage versus ovarian torsion. A transvaginal oocyte retrieval was performed at the scheduled time in an initial attempt to decrease the size of the ovaries and allow spontaneous resolution and seven oocytes were retrieved from the left torsed ovary. Notably, in contrast to the clear fluid aspirated from the detorted ovary in this case report, the follicular fluid aspirated from the left ovary was described as 'densely bloody.' Of the seven oocytes retrieved, six were inseminated and two fertilized yielding two 2-cell embryos on day 2. This fertilization rate was markedly lower than that from the right, non-torted ovary (33% versus 86%) and the authors concluded that given the low fertilization rate of the oocytes from the torsed left ovary, those embryos should not be transferred on day 2 for the planned gamete intra-Fallopian transfer. Since a day-2 procedure was planned and the two 2-cell embryos from the left ovary were not maintained in culture, the ability of those embryos to mature to the blastocyst stage is unknown (Robson and Kerin, 2000).

The second report of ovarian torsion antecedent to oocyte retrieval described a 33-year-old patient who underwent her first IVF cycle and developed the acute onset of left lower quadrant pain the day following human chorionic gonadotrophin injection (Stefunidis et al., 2002). She ini-

tially had only lower abdominal tenderness, but developed peritoneal signs by the morning of her scheduled oocyte retrieval. The oocyte retrieval was undertaken but no oocytes were retrieved from the left, presumed torsed, ovary. She, like the other patient who experienced torsion prior to oocyte retrieval, ultimately required laparoscopy and ovarian detorsion (Robson and Kerin, 2000; Stefunidis et al., 2002).

The case reported here is unique because not only was her ovarian torsion surgically corrected prior to oocyte retrieval, but also because of the excellent development of the embryos originating from the previously torsed ovary. Interestingly, the fertilization rate of the oocytes from the right, previously torsed ovary was lower than the contralateral side (40% versus 93%), as in the case reported by Robson and Kerin (2000). One hypothesis for the decreased fertilization rate of the oocytes from the detorted right ovary is that although arterial blood flow was maintained during the torsion, it was likely decreased compared with the non-torted state, thereby leading to some degree of ischaemic injury to the oocytes. Animal studies investigating ovarian transplantation suggest that ovarian ischaemia is associated with follicular injury and accelerated follicular recruitment (Baird et al., 2004; Israely et al., 2006). In humans, the impact of ovarian ischaemia on oocyte viability and fertilization is unclear, but reports on successful pregnancies following ovarian cryopreservation and heterotopic transplantation for fertility preservation following cancer therapy indicate that even the ischaemic injury sustained from oophorectomy is not universally fatal to the follicular pool (Donnez et al., 2004; Meirou et al., 2005; Rosendahl et al., 2006). The impact of ovarian ischaemia on embryo development is likewise uncertain, but as demonstrated by Oktay et al. (2004), a microscopically normal-appearing embryo can develop to the 4-cell stage following stimulation of heterotopic ovarian tissue transplanted after cryopreservation. The precise impact of transient ischaemia on human oocyte viability, fertilization and embryo maturation, however, is presently unknown.

The key difference between the case here presented and the previously described case is the continued normal development of the embryos arising from the detorted right ovary and the fact that 75% of fertilized embryos progressed to the blastocyst stage. Given the normal embryo morphology and development, embryo transfer with embryos from the detorted ovary would have been recommended in other clinical situations. This case is further complicated by the patient's husband's known balanced translocation between chromosomes 6 and 10. All 18 fertilized embryos (four from the right and 14 from the left) were found to have unbalanced translocations between loci 6p, 6q, 10p, and 10q. There was no discrepancy between the karyotypic abnormalities seen on fluorescence in-situ hybridization among embryos from the right compared with the left ovaries as 100% of embryos were identified to be abnormal. Unfortunately, due to unbalanced genetic material identified on PGD, all embryos were discarded and no embryo transfer undertaken.

In conclusion, although the impact of transient ovarian ischaemia on oocyte fertility potential remains unclear, in-cycle ovarian torsion can be managed operatively with ovarian detorsion if possible, followed by vaginal oocyte

retrieval as scheduled. In the case here reported, the fertilization rate was decreased on the side of prior ovarian torsion, but the embryos that did develop from the detorted ovary developed normally and the majority progressed to the blastocyst stage.

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