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# Live birth after segmented intracytoplasmic sperm injection and pessary management for severe uterine prolapse

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## About the Author



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## ABSTRACT

Segmentation of the assisted reproductive technology (ART) treatment not only assists patients with conception through the *in vitro* process but also, as in our case, with the motivation to manage a severe uterine prolapse. The patient was previously unsuccessful in the management of her severe uterine prolapse with a vaginal pessary and in conception with traditional *in vitro* fertilization treatment. Using segmented treatment pessary accustomization formed part of her treatment schedule and, therefore, added to the motivation to take control of her prolapse management. In addition, her prolapse management received clinical support for the duration of treatment. This is the first report on the successful use of segmented ART treatment and pessary support in a case of severe uterine prolapse. The segmented treatment schedule allowed the patient to progress from consultation to pregnancy test within a 3-month period.

**Key Words:** Intracytoplasmic sperm injection, segmented treatment, uterine prolapse

## INTRODUCTION

Uterine prolapse is a rare, but significant uterine manifestation, which can preexist pregnancy or manifest during the course of pregnancy.<sup>[1,2]</sup> The risk factors for uterine prolapse include gravidity, parity, vaginal delivery, body mass index (BMI), familial genetics, race, and age.<sup>[3]</sup> An unmanaged uterine prolapse can significantly impact the quality of life of the woman. A uterine prolapse occurs when the pelvic floor muscles and ligaments are unable to support the uterus allowing it to descend into the vagina and in severe cases beyond the vaginal introitus.<sup>[1-3]</sup> Infertility can be a direct consequence of a prolapse, through reduced reproductive outcomes from normal intercourse and the loss of pregnancy because of prolapse associated complications.<sup>[3]</sup> Assisted reproductive technology (ART) may, therefore, be the most effective means to a pregnancy for prolapse-affected women.<sup>[4]</sup> The clinical management

strategies for prolapse-affected women of reproductive age have not changed significantly over the years. The mainly conservative strategies include manual reduction and pessary insertion or alternatively surgery, that is, vaginal sacrospinous colpopexy and abdominal sacral colpopexy.<sup>[1-5]</sup> In this case report, we examine the ART-related reproductive outcomes of a woman with a severe uterine prolapse, most probably caused by a previous vaginal delivery.

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## CASE REPORT

### Patient details

In 1999, the patient had a spontaneous pregnancy with a vaginal delivery of a male infant (3000 g) at 40 weeks of gestation. In 2004, her uterine prolapse manifested for the first time, as a lump protruding from her vagina, and she had a vaginal pessary inserted. The patient, however, found the pessary troublesome and unmanageable. In 2006, the patient underwent open abdominal surgery (abdominal sacral colpopexy) to correct the prolapse. However, in 2008 the prolapse reoccurred. The prolapse was not clinically managed between 2008 and 2012. In 2012, the couple presented at another *in vitro* fertilization (IVF) center for ART treatment with then prolapse related secondary infertility. An IVF and frozen embryo transfer (FET) cycle was completed, but none of the two treatments resulted in a pregnancy.

### Patient preparation

In July 2013, the couple presented at our center for fertility treatment. The female patient was a 34-year-old, G1P1, with 14 years of secondary infertility, decreased ovarian reserve (antral follicle count = 5), and weighing 82 kg (BMI = 35 kg/m<sup>2</sup>). The male partner was 35 years of age with oligoteratozoospermia. Her gynecological examination revealed the protruding cervix and uterine mucosa to be dry, the cervix to be fragile, hypertrophic, and edematous and the protruding organ to be “cold” to the touch. The prolapse was manually reduced at the examination and the patient was referred to an urogynecologist who inserted a Hodge Pessary (MedGyn Products Inc., USA). From then on the patient regularly received clinical support in the management of her prolapse, as part of segmented ART treatment.

### Freeze-all cycle

In August 2013, the couple's intracytoplasmic sperm injection (ICSI) with blastocyst freeze-all treatment commenced. Controlled ovarian stimulation was performed using a GnRH antagonist (0.25 mg; Orgalutran, Merck Sharp and Dohme Ltd., Turkey) co-treatment with rFSH (375 IU Gonal-F, Merck Serono, Istanbul, Turkey) and hMG (75IU, Menopur, Ferring Pharmaceuticals Ltd., India). In response, the patient developed 8 follicles of >14 mm after 10 days of stimulation. A dual trigger (0.2 mg, Gonapeptyl, Ferring Pharmaceuticals Ltd., India and 250 µg, Ovitrelle, Merck Serono, Turkey) was administered when >2 follicles reached 17 mm and a transvaginal ultrasound-guided oocyte retrieval performed 36 h posttrigger. 10 oocytes (six metaphase II, one metaphase I, one germinal vesicle, and two abnormal)

were recovered. Gamete manipulations and embryo cultures were performed using Sydney IVF (COOK Medical, Ireland) media and culture conditions were set at 6% CO<sub>2</sub>, 5% O<sub>2</sub> and 37°C (K-Systems, Kivex Biotec Ltd., Denmark). Seven metaphase II oocytes were inseminated by ICSI 40 h posttrigger. Seventeen hours postinsemination, seven zygotes with normal 2PNs were observed and 64 h postinsemination two good quality 8 cell embryos were obtained in culture and cryopreserved by vitrification. The five remaining embryos with <8 cells were graded fair to poor and were culture to day 5.<sup>[6]</sup> One hundred and fifteen hours postinsemination three blastocysts (3BB, grade 2 and grade 1) were obtained and cryopreserved by vitrification.<sup>[6]</sup> Vitrification and warming of embryos and blastocysts was performed with cryotop technology performing the procedure as described in the manufacturer's methodology packaging insert (Cryotop, Kitazato BioPharma Co., Ltd., Japan).

### Frozen embryo transfer cycle

In September 2013, the couple's FET cycle commenced with oral contraceptive pill programming and after a 5 days withdrawal period determining the day 1 of cycle. At this point the patient had, had 3 months of pessary accustomization. In the FET cycle hormone replacement therapy (HRT) was used for endometrial preparation, embryo-endometrium synchronization, and subsequent luteal support. Fourteen days after the start of HRT the patient's endometrial thickness was measured (9.3 mm) by trans-vaginal ultrasound scan and the patient's transfer procedure scheduled for 7 days later.

### Blastocyst warming and transfer

On October 5, 2013, the couple's cryotop container containing the three blastocysts was removed from cryo-storage and warmed. The warmed blastocysts were placed in a culture dish with medium droplets covered with light mineral oil and placed in incubation for equilibration. The culture dish was removed from the incubator 2 h later to confirm survival and to rescore the blastocysts. All three blastocysts survived and were scored as, 5AA, 3BB, and grade 2. The 5AA blastocyst was selected for transfer and the 3BB and grade 2 blastocysts were re-vitrified. The blastocyst selected for transfer was aspirated using a Hamilton syringe (50 µL, Hamilton Syringe, Sigma-Aldrich, USA) into an embryo transfer catheter (Wallace, Smiths Medical International, UK). The loaded catheter was passed through the speculum exposed cervix into the uterus, and the blastocyst released >10 mm from the fundus. The patient was positioned in the lithotomy position with a moderately distended bladder for the transfer. The distended bladder straightened the cervicouterine

line and facilitated visualizing the uterine cavity when trans-abdominal ultrasound scan (TAUS). No anesthesia was used for the transfer procedure, and the vaginal pessary was not removed, even though its echogenicity did complicate cervicouterine visualization. Other than the visualization problems no further problems were encountered at transfer.

### Antenatal care

Pessary management was continued, with clinical support provided at every antenatal visit. On the 9<sup>th</sup> and 11<sup>th</sup> days after the transfer procedure serum  $\beta$ hCG concentrations were measured. The patient's 1<sup>st</sup> blood test showed a  $\beta$ hCG concentration of 120 IU/L and the 2<sup>nd</sup>, 288 IU/L. The first clinical antenatal examination was performed at 5w7d gestation. A TAUS confirmed the presence of a fetal sac and a cervical canal length of 38 mm. The second antenatal examination was performed at 7w1d gestation, at which the TAUS examination confirmed a normal fetal heart. Thereafter, the antenatal examinations were repeated at regular intervals, that is, 8w0d, 12w0d, 14w3d, 22w3d, 29w4d, and 31w0d. At the 22 weeks antenatal visit the vaginal pessary was removed, as the prolapse had spontaneously reduced, with the uterus positioned above the pelvis. On the June 10, 2014, the patient now 100 kg delivered a healthy male infant (3400 g) by cesarean section, at 38w1d of gestation.

### DISCUSSION

This successful treatment of a patient with a severe uterine prolapse using segmented ART is the first such case to be reported on in ART literature and importantly shows how segmented ART treatment incorporates prolapse support and management. Subfertile patients with a preexisting uterine prolapse who are to undergo ART to conceive must crucially have the prolapse reduced and supported (i.e., pessary) in the reduced position. This is to prevent complications that can lead to spontaneous pregnancy loss.<sup>[3]</sup> A protruding cervix, beyond the introitus, exposes the cervix to continuous trauma, increasing the risk of infection and edema, and to external environmental conditions, reducing cellular hydration and core temperature, and thereby possibly adversely affecting endometrial function. In both our report and the previous report<sup>[4]</sup> using traditional IVF, the surgery failed to support a severe uterine prolapse, while vaginal pessaries were in both cases successful, ensuring conception, and term delivery.

The increase in FET as the result of the increase in single embryo transfer and the increase in FET success rates seen over the last decade has made many ART centers more confident in the use of segmented treatment, and that includes its strategic use for individual cases.<sup>[7-9]</sup> The use of the segmented treatment in cases of uterine prolapse can take advantage of the psychology of motivation for prolapse management because pessary accustomization essentially takes place between blastocyst cryopreservation and blastocyst transfer. This goal orientation of treatment can boost the patient's motivation to take control of her prolapse management. In addition, the patient receives clinical support in the management of her prolapse for the 3 months of her treatment. This is in contrast to traditional IVF, where the patient was usually asked first to become accustomed to the pessary management of her prolapse (3 months pretreatment), and then to return to the clinic for treatment. The treatment schedule of segmented ART, therefore, provides for a more caring and efficient treatment process in cases of uterine prolapse.

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### Conflicts of interest

There are no conflicts of interest.

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