CASE REPORT
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Transabdominal follicular aspiration in an *in vitro* fertilization cycle: experiences with an unusual but necessary intervention in a resource-limited setting

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Controlled ovarian hyperstimulation is one of the major steps of *in vitro* fertilization. The inaccessibility or non-visualization of developing follicles on transvaginal sonography (the preferred imaging method) may be misjudged as a poor response, resulting in cycle cancellation. It is necessary to scrupulously appraise proxy indicators for ovarian response, such as estradiol levels, endometrial thickness, and other individual clinical characteristics. This can prompt meticulous transabdominal ultrasound follicular monitoring and oocyte retrieval with the goal of averting cycle cancellation and improving treatment outcomes.

Keywords: Fertilization *in vitro*; Infertility; Oocyte retrieval; Ovulation induction; Ultrasonography

Introduction

In vitro fertilization-embryo transfer (IVF-ET) is an increasingly common treatment for infertility in sub-Saharan African. However, the region remains resource-constrained and this treatment option correspondingly places a tremendous financial burden on clients, meaning that a client's first attempt may well be the last. Thus, it is imperative for caregivers in this region to take measures to enhance the likelihood of success of each attempt. Having one's IVF treatment cancelled can be devastating for patients. Cycle cancellation can occur before or after oocyte retrieval (OCR). Cancellation before OCR may occur due to a poor response to the drugs used to stimulate the ovaries, a high risk of over-response to the fertility drugs and developing ovarian hyperstimulation syndrome, any situation or illness preventing egg collection at the time of oocyte maturation, or post-surgical adhesions and/or displacements impeding the accessibility of the ovaries. Other reasons include the incorrect timing of human chorionic gonadotropin (hCG) injections, triggering the release of the mature eggs before recovery, and the individual choice of patients to postpone the cycle for reasons that may be personal [1-3].

A poor response to ovarian stimulation is the most common reason for cycle cancellation [2,4]. In order to mitigate this, a range of response predictors have been employed, including age, body mass index (BMI), previous ovarian surgery, previous ovarian stimulation experiences, basal follicle-stimulating hormone levels, anti-Müllerian hormone assays, the antral follicular count, and serial folliculometry with ultrasound [2,4,5]. Our local experience showed that poor ovarian response to stimulation based on ultrasound folliculometry was a common reason for cycle cancellation. We observed that a perceived poor ovarian response was occasionally due to the inadvertent non-visualization of developing follicles caused by ovarian displacement or encasement from previous surgery. Thus, we instituted a protocol [6] in which, prior to cycle cancellation for poor ovarian response, scrupulous attention was paid to proxy indicators of the response such as estradiol levels, basal follicle-stimulating hormone or anti-Müllerian hormone levels, endometrial thickness, and other individual clinical characteristics before arriving at a final decision.

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We present our experiences over the past 24 months (July 2013 to June 2015) in a case series, describing patients in whom the meticulous review of proxy indicators for ovarian response provoked a painstaking ultrasound search for the developing ovarian follicles with positive results, allowing cycle cancellation to be averted.

1. Method of transabdominal follicular aspiration

The need for transabdominal aspiration was recognized during follicular monitoring when one or both ovaries were not clearly visualized transvaginally and were much more apparent transabdominally. At the time of OCR, the urinary bladder was emptied by patient voiding or in-and-out catheterization, and we then attempted to access the ovaries transvaginally using the usual technique, additionally applying abdominal pressure to push the ovaries into the pelvis. However, this technique failed in these cases. We then converted to transabdominal retrieval using analgesia and conscious sedation (with pentazocine and diazepam) as typically used" should be added for transvaginal aspiration. The patient was repositioned from the dorsal lithotomy position to the supine position. The operator resumed scanning the patient's abdomen using regular ultrasound gel and an abdominal probe (3.5 MHz probe, Mindray Digi Prince DP6600, Mindray, Shenzhen, China) to identify the area in the abdominal wall that would provide the most feasible and safest access to the ovary or ovaries. The gel was wiped off and, using sterile techniques, the predetermined abdominal wall area, including the skin and subcutaneous tissues, was injected with local anesthetic (1% lidocaine hydrochloride). The abdominal area was then cleaned with sterile water and under ultrasound guidance, using a 6.5 MHz vaginal probe with a needle guide, a standard retrieval needle was inserted through the abdominal wall to aspirate the follicles. A deliberate effort was made to aspirate the follicles via a single transabdominal needle insertion in order to minimize the quantity of skin punctures.

Case reports

1. Case 1

A 36-year-old nullipara presented for treatment in 2014 with an 8-year history of secondary infertility and a previous myomectomy that was performed in 2006. Her BMI was 24.7 kg/m^2, and she was counseled and selected for IVF-ET treatment following the confirmation of bilateral tubal blockage. She underwent controlled ovarian hyperstimulation following our protocol, and was commenced on five ampoules of human menopausal gonadotropin (hMG) (75 IU per ampoule) daily. A baseline transvaginal scan (TVS) at the commencement of stimulation (on day 3 of her menses) showed antral follicles in both ovaries and no residual follicles or cysts. On stimulation day 5, a TVS revealed tiny follicles in the left ovary, but the right was not visualized. On stimulation day 8, a TVS revealed a poorly defined left ovary with very tiny follicles, whereas the right ovary was not visualized. Her stimulation day 5 estradiol level of 413 pg/mL and endometrial thickness of 7.8 mm were suggestive of apparent follicular development (i.e., a good response). This necessitated a further search using a transabdominal scan, which showed four follicles in the right ovary and two follicles in the left ovary, with the largest measuring 15.5 mm. On stimulation day 11, the six follicles were still visualized on a transabdominal scan, with the largest measuring 20.1 mm, and the endometrial thickness was 10.5 mm. She underwent an intramuscular injection of 10,000 IU of hCG on the same day and OCR was carried out 34 hours after the hCG injection. At the time of OCR, seven follicles were aspirated transabdominally and five oocytes were retrieved. Three good-quality embryos were transferred on day 3 post-OCR. A pregnancy test was positive 2 weeks after embryo transfer and clinical pregnancy was confirmed by ultrasound (a single live gestation) 4 weeks after transfer.

2. Case 2

The second case, also a 36-year-old, presented with a 5-year history of primary infertility. She had underwent a myomectomy 4 years prior to presentation for menorrhagia. Her BMI was 26.7 kg/m^2, and further investigations revealed bilateral tubal blockage and mild oligospermia. Following clinical evaluation and discussion, the couple gave informed consent for IVF-ET. She subsequently underwent controlled ovarian hyperstimulation following our protocol, commencing at five ampoules (375 IU) per day of hMG. On the fifth day of stimulation, a TVS revealed multiple tiny follicles in the right ovary, but the left ovary was not visualized. Her estradiol level was 456 pg/mL on the eighth day; the ovaries were not visualized on a TVS, but the endometrial thickness was 8.1 mm. Therefore, a transabdominal scan was performed, showing nine developing follicles in both ovaries, with the largest measuring 13.6 mm. A good response was demonstrated on transabdominal folliculometry, as 12 follicles were visualized on the day 11 of stimulation, with the largest measuring 20.5 mm. She underwent hCG administration and subsequent OCR 35 hours later. Ten follicles were aspirated transabdominally, yielding seven oocytes; of these, three were fertilized and three good-quality embryos were transferred on day 3. A pregnancy test was positive 2 weeks later, and ultrasound confirmed a viable twin pregnancy 6 weeks after ET.

3. Case 3

A 32-year-old with a BMI of 28.9 kg/m^2 presented to the clinic with a 2-year history of primary infertility. A hysterosalpingogram showed bilateral tubal occlusion with uterine fibroids, and the semen analysis was normal. She was counseled to undergo a myomectomy prior to

definitive IVF-ET treatment; she consented and underwent a successful myomectomy. Six months after the myomectomy, she commenced ovarian stimulation for IVF following our protocol. She was commenced on four ampoules, and on the fifth day of stimulation, her estradiol level was 514 pg/mL, but the follicles were barely visualized on a TVS, and the hMG was increased to five ampoules. On the eighth day of stimulation, her ovaries were not visualized, but the endometrial thickness was 8.5 mm; following a detailed search on a transabdominal scan, nine follicles were found, with the largest measuring 13.9 mm. Transabdominal folliculometry was continued, and on stimulation day 12, she had over 12 follicles, with the largest measuring 22 mm. At this point, hCG was administered, and she went on to undergo transabdominal retrieval 35 hours after hCG administration. Approximately 18 follicles were aspirated, with an oocyte yield of 10, of which six were fertilized, and three good-quality embryos were transferred on the third day after OCR. A pregnancy test was negative 2 weeks after ET.

4. Case 4

A 39-year-old with a BMI of 23.4 kg/m^2 presented with a 5-year history of primary infertility. She had two previous myomectomies in 2003 and 2012, as well as undergoing two previous failed intrauterine insemination attempts. She presented with the desire to undergo IVF-ET. She was counseled and selected for IVF-ET treatment following our protocol, and was commenced on five ampoules of hMG (75 IU per ampoule) daily. A baseline TVS at the commencement of stimulation (on day 3 of her menses) showed antral follicles in both ovaries and no residual follicles or cysts. On stimulation day 5, TVS revealed tiny follicles in the right ovary, but the left ovary was not visualized. On stimulation day 8, we experienced difficulties visualizing both ovaries. Her stimulation day 5 estradiol level of 311 pg/mL and endometrial thickness of 7.2 mm were suggestive of possible follicular development, necessitating further search using a transabdominal scan, which showed two follicles on the right ovary and one on the left ovary, with the largest measuring 12.5 mm. The hMG was increased to six ampoules daily and her follicular response was monitored using the transabdominal approach. On stimulation day 11, seven follicles were found, with the largest measuring 20.6 mm. OCR was performed transabdominally 35 hours after hCG and five oocytes were successfully fertilized. A day 3 transfer of two good-quality embryos was carried out successfully, but a pregnancy test was negative 2 weeks later.

Discussion

OCR is one of the major steps in the process of IVF-ET. Techniques for OCR have evolved over the years; it was first performed laparoscopically, and then ultrasound-guided retrieval (transabdominal-transvesical and transvaginal) was introduced [7]. In contemporary IVF-ET treatment cycles, the transvaginal route of retrieval has become the default OCR technique, although some clinical situations may prohibit this approach [7,8]. This case series has demonstrated that in scenarios of transvaginal ovarian inaccessibility, OCR using transabdominal ultrasound-guided follicular aspiration can be done safely and efficiently with the consequent avoidance of cycle cancellation. A previous study noted that inaccessibility of the ovaries transvaginally is uncommon, but does occur, especially in situations involving anatomic distortions [9]. In agreement with this observation, we noted that all four cases in this series had a prior history of abdominal surgery, which likely caused anatomical displacement of the ovaries. Ovarian or pelvic surgery has also been associated through varying mechanisms with a decline in ovarian reserve and function, with consequent poor response during IVF-ET treatment cycles [3,10].

The pertinent finding of this study is the need for the rigorous appraisal of multiple proxy indices for ovarian response as a means of follicular monitoring in order to arrive at informed treatment decisions. In these cases, an apparent poor response was noted on transvaginal folliculometry, but the backdrop of previous abdominal surgery and values for estradiol and endometrial thickness indicating a favorable response prompted a more thorough search for developing follicles. Estrogen is produced by developing follicles and causes proliferation of the endometrium. Researchers have shown that after 4 days of gonadotropin stimulation, an estradiol level of >350 pg/mL is highly predictive of successful ovarian follicular response, a higher embryo grade, and successful pregnancy outcomes, whereas a value of <75 pg/mL is predictive of a poor response and cycle cancellation [11,12]. Additionally, proliferation of the endometrium to a thickness of at least 7 mm has been associated with good follicular response and favorable IVF-ET outcomes [13,14]. Thus, one can hypothesize that if favorable estrogen levels and endometrial thickness are noted, then there must be follicles somewhere in the body, meaning that the clinical imperative is to identify those follicles and prevent the devastating outcome of cycle cancellation.

Transabdominal retrieval is not without complications, ranging from damage to adjacent structures and contamination of the follicular aspirate to multiple punctures on the abdominal skin with increased potential for discomfort, infection, or scarring [15]. Additionally, previous studies have documented poor oocyte yield and treatment outcomes in comparison with transvaginal OCR [16]. In this study, despite the potential for complications from pelvic adhesions, we successfully aspirated follicles transabdominally under ultrasound guidance without damaging other abdominal structures and with an appreciable oocyte yield. Although we did not compare the oo-

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cyte yield with that obtained using a transvaginal approach in this series, the satisfactory oocyte yield may have been due to a background positive response to stimulation, as demonstrated by the estradiol levels and endometrial thickness, as well as other factors that may influence IVF outcomes. The necessity of a meticulous approach to the procedure of transabdominal retrieval cannot be over-emphasized. Additionally, the patients in this case series were not obese and their ovaries were displaced closer to the skin anteriorly by post-surgical adhesions. We may posit that transabdominal retrieval can be carried out safely and efficiently in indicated cases with good outcomes.

Infertility remains a challenge in sub-Saharan Africa, placing attendant social, psychological, and economic burdens on the individuals involved. Cycle cancellation further increases this burden, with devastating sequelae. The need for judicious patient selection, the appraisal of several clinical indices, and the individualization of care should be emphasized as a means of improving treatment outcomes and enhancing the satisfaction of clients.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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