Assisted Reproductive Techniques and submucous myoma

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ABSTRACT

Submucous myomas have negative effects on fertility. To maintain fertility, conservative treatment should be suggested to women who wish to become pregnant, especially young patients. The patient was a 33-year-old woman, who had had secondary infertility for 3 years. Upon vaginal ultrasound, we noticed a submucous myoma measuring 26 mm x 31 mm with a compressive effect on the anterior surface of the endometrium. Ovarian reserve was low. The gold standard of myoma treatment is surgical intervention. But, for the following reasons: the adverse effects of surgery on the endometrium (intrauterine adhesion), the patient’s refusal to undergo a myomectomy and her request for pregnancy, our strategy for treating was to reduce volume of submucous myoma and start the assisted reproductive techniques (ART) cycle, simultaneously. We administered three courses of Gonadotropin-releasing hormone analogues (GnRHa) and then induced controlled ovarian hyperstimulation. Ovum pick up was done. Finally, we transferred two embryos (4 and 6 cells). In subsequent patient visits, βhCG was positive after 14 days. At the last patient visit, the heart of the embryo was formed. From this finding, it may be concluded that combined GnRHa and ART is the treatment of choice for infertile women with uterine submucous myoma, considering the reduced ovarian reserve and response.

Keywords: infertility, myomas, assisted reproductive techniques (ART)

INTRODUCTION

Uterine fibroids (or myomas) are benign tumors, associated with the smooth muscle wall of the uterus (Geethamala et al., 2016). Studies estimate that it occurs in 20-50% of women during their reproductive years (Zhang et al., 2010). Myomas can cause many disorders, including: pelvic pain, abnormal uterine bleeding, and fertility disorders (Sparic et al., 2016). Uterine fibroids are treated differently concerning their location and size. The various methods of treatment include medical treatment, open myomectomy, laparoscopic, and magnetic resonance-guided focused-ultrasound surgery (Van Heertum & Barmat, 2014). There is general agreement about the opposing effects of myomas on fertility. To maintain fertility, conservative treatment should be suggested to women who wish to become pregnant, especially for young patients (Tinelli et al., 2018). Our goal with this case report is to discuss submucous myoma together with assisted reproductive techniques (ART) in a patient’s pregnancy.

CASE REPORT

The patient was a 33-year-old woman. She had been married for 10 years. She had no history of abortion and had a pregnancy that resulted in a 10-year-old girl. In her first pregnancy shed had had premature membrane rupture and had normal vaginal delivery. However, she had secondary infertility for 3 years. Therefore, she came to our fertility treatment clinic with a request for a new pregnancy on 7-29 of 2019.

The patient had regular menstruation cycles. Her past surgical history revealed that she had had a laparotomy due to ovarian cysts. In the initial examinations, there were no positive signs. In her vaginal ultrasound, we noticed a submucous myoma, measuring 26mm x 31mm with a compressive effect on the anterior surface endometrium. Her ovarian reserve (Anti-Mullerian Hormone and antral follicle counts) was low. The results of all systematic and ultrasound tests at the follow-up are summarized in Table 1.

To maintain fertility in these cases, conservative treatment should be suggested to women who wish to become pregnant, especially young patients (Tinelli et al., 2018).

In this patient, due to the mass effect on the endometrium, initial treatment for pregnancy can be surgical. But, for the following reasons: the adverse effects of surgery on the endometrium (intrauterine adhesion), the patient’s refusal to undergo a myomectomy and her request for pregnancy, our strategy for treating this case was as follows.

Our treatment strategy for this patient was to reduce the volume of the submucous myoma and start the ART cycle. For this purpose, we administered three courses of Gonadotropin-releasing hormone analogues (GnRHa) (Dipherelin (triptorelin); Ipsen Pharma, Paris, France) (three times every 28 days at a dose of 3.75 mg). After 14 days of the last injection (in vaginal ultrasound, the myoma had shrunk (17 mm)), we induced controlled ovarian hyperstimulation with Gonal F (Merck Serono, Germany), Pergoveris (Merck Serono, UK) and Cetrotide (Cetrotide, Serono, Geneva, Switzerland). Then, we triggered ovulation with two subcutaneous Ovitrelle (250 µg, Merck Serono, Germany) vials. Then, 36 hours afterwards, we picked up the ovum. On the day of puncture, we obtained 5 oocytes (MII). We then performed intracytoplasmic sperm injection (ICSI) by fresh sperm on the same day. 48 hours after ICSI, we transferred two embryos (4 and 6 cells). In subsequent patient visits, βhCG was positive after 14 days. At the latter patient visit, the heart of the embryo was formed.

DISCUSSION

There are different treatment options available to treat myoma complications. Treatment strategies are typically devised by considering the following: severity of symptoms, size and location of the myoma, the age of patient and the her desire for fertility (Viswanathan et al., 2007). Surgical intervention is the basic myoma treatment standard. Even though hysterectomy is a primary treatment, myomectomy is usually performed in women who wish to have a future fertility (Parker, 2007). However, it is not without the morbidities, and mortalities of any surgical
Table 1. Summary of the laboratory tests report and ovarian ultrasonography.

| Test          | Right ovary | Left ovary |
|---------------|-------------|------------|
| *BMI (kg/m²) | 37          | 37         |
| b TSH (mIU/L) | 1.25        | 1.25       |
| c PRL (ng/ml) | 8.2         | 8.2        |
| d FSH (IU/ml) | 3.8         | 3.8        |
| e LH (IU/ml)  | 1.8         | 1.8        |
| f AMH (mg/ml) | 0.4         | 0.4        |
| * AFC (number)| 2           | 4          |

* body mass index, b Thyroid Stimulating Hormone, c Prolactin, d Follicle-Stimulating Hormone, e Luteinizing hormone, f Anti-Mullerian Hormone, g Antral Follicle Counts.

methods (Donnez et al., 2003). As, uterine scars are associated with risks following: vicious placental implantation and uterine rupture (Rovio, 2008).

In this case, we encountered a submucous myoma (31x26 mm) accompanied by the compressive effect on the uterine endometrium. Given the effects and complications of myometomy (e.g. asherman's syndrome), and considering the reduced ovarian reserve and response, our strategy for treating infertility in this case were as follows:

1. Minimizing the size and volume of the submucosal myoma (by long acting GnRH agonist).
2. Performing the ART cycle followed by embryo transfer.

We used GnRHa to reduce the submucosal myoma volume and this is supported by "GnRHs can effectively reduce uterine myoma volume, reduce heavy menstrual bleeding, and restore hemoglobin levels by inducing an iatrogenic reversible menopause" (Deligdisch et al., 1997; Friedman et al., 1991; Khan et al., 2010; Palomba et al., 2002). According to studies, this process can be explained at the molecular level: GnRH results in increased apoptosis, decreased angiogenesis and inflammatory responses in myoma lesions (Khan et al., 2010). So, the GnRH effect on its receptors, which have been identified in myomas and prevent their growth (Chen et al., 2005; Wiznitzer et al., 1988). This is supported by "those effects result in a 35% to 65% reduction in the myoma size along with the development of amenorrhea" (Witherspoon & Butler, 1934).

In this case, when the size of the submucous myoma was reduced (17 mm), we introduced the patient to the ART cycle. Currently, the patient is pregnant and, the volume of the submucous myomas has decreased to a minimum. Therefore, in submucous myomas, treatment strategies can be based on the volume and size of the myoma, demand and age of the patient to achieve the best possible outcomes.

CONCLUSION

From these findings, we may conclude that combined GnRHa and ART is the treatment of choice for infertile women accompanied by uterine submucous myoma, considering the reduced ovarian reserve and their response.

CONFLICT OF INTERESTS

The authors reported no potential conflict of interest.

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