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SUCCESSFUL SINGLE EMBRYO TRANSFER AFTER STRATEGIC MOCK TRANSFER PLANNING IN SEVERE ADENOMYOSIS WITH RECURRENT PREGNANCY LOSS: A CASE REPORT

Pathology

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ABSTRACT

Background: Adenomyosis is increasingly recognized as an independent factor contributing to infertility and recurrent pregnancy loss (RPL). The disease alters uterine peristalsis, endometrial receptivity, and junctional zone integrity, making both implantation and embryo transfer technically challenging. **Case Presentation:** A woman with symptomatic adenomyosis presented with secondary infertility and three prior missed abortions. She had heavy menstrual bleeding and diminished ovarian reserve (AMH 1.2 ng/mL). Semen analysis showed teratozoospermia. Controlled ovarian stimulation was performed using a GnRH antagonist protocol. Oocyte pickup (OPU) was combined with hysteroscopy, which revealed a roomy uterine cavity without distortion. Three day-5 blastocysts were obtained (4AA, 3AA, 4AC). Preimplantation genetic testing for aneuploidy (PGT-A) revealed one euploid embryo. She underwent 3 months of GnRH agonist downregulation, triptorelin acetate followed by letrozole for 3 months. Hormone replacement therapy (estradiol hemihydrate 2 mg TDS) was used for endometrial preparation. The single euploid embryo transfer (SET) presented challenges due to the intricate negotiation of the cervical canal, attributed to adenomyotic uterine alterations. Nevertheless, the procedure was successfully executed with the aid of ultrasound guidance and prior mock embryo transfers. Subsequently, the patient conceived and is currently in her twentieth week of gestation. **Conclusion:** Adenomyosis contributes to infertility and RPL via inflammatory, immunologic, and mechanical mechanisms. Pre-treatment with GnRH agonist before IVF improves implantation and live birth outcomes. Careful attention to embryo transfer technique is critical in these patients. This case highlights the importance of individualized pretreatment, genetic embryo selection, and meticulous transfer strategy in achieving successful pregnancy.

KEYWORDS

Adenomyosis, Recurrent pregnancy loss, GnRH agonist, Difficult embryo transfer, PGT-A, Infertility.

INTRODUCTION

Adenomyosis is characterized by ectopic endometrial glands and stroma within the myometrium accompanied by reactive smooth muscle hyperplasia. While adenomyosis is commonly attributed to multiparity, it is gaining recognition as a crucial uterine contributor to infertility and recurrent pregnancy loss (1,2).

Recent meta-analyses demonstrate that adenomyosis is associated with reduced clinical pregnancy rates and live birth rates and increased miscarriage rates in women undergoing assisted reproductive technology (ART) (3–5). The mechanisms underlying these adverse outcomes are multifactorial and include disruption of the junctional zone (JZ), abnormal uterine peristalsis, chronic inflammatory activation, local hyperestrogenism, oxidative stress, and progesterone resistance (6–9).

In addition to impaired endometrial receptivity, adenomyosis may contribute to technically difficult embryo transfer due to uterine enlargement, altered uterocervical angulation, and hypercontractility. Difficult ET has been independently associated with significantly reduced clinical pregnancy and live birth rates (10,11).

We report a case of adenomyosis-associated infertility with recurrent pregnancy loss successfully treated with uterine suppression, preimplantation genetic testing for aneuploidy (PGT-A), and optimized embryo transfer technique.

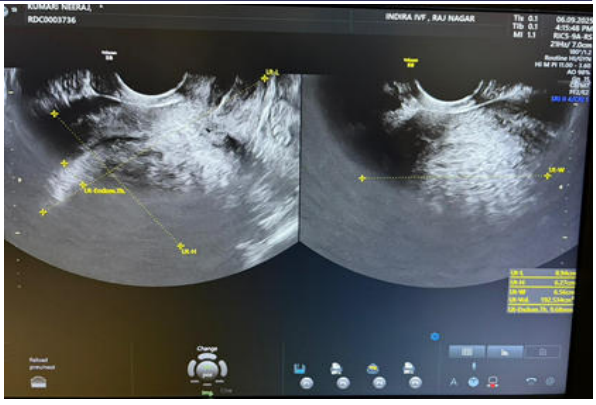
Case Presentation

A 38 years old woman presented at our center at Indira IVF, RDC Ghaziabad with infertility for 9 years and heavy irregular menstrual bleeding since 4 years. She had three prior missed abortions all of which were less than 9 weeks. No prior chromosomal analysis was performed.

Ultrasound demonstrated features suggestive of grade 4 adenomyosis, including heterogeneous myometrium, asymmetric thickening, and myometrial cystic areas. The endometrial cavity was not grossly distorted but uterine volume was more than 190ml (figure 1).

Ovarian reserve testing showed AMH of 1.2 ng/mL.
Husband aged 42 with semen analysis revealing mild teratozoospermia, who was then started on antioxidants.

Given history of recurrent pregnancy loss and uterine pathology, IVF with PGT-A was planned.



(figure 1- Initial scan of patient showing bulky adenomyotic uterus)

Treatment Protocol

1. Ovarian Stimulation

Considering diminished ovarian reserve, a GnRH antagonist protocol was used along with clomiphene citrate 100 mg to optimize follicular recruitment while minimizing premature LH surge. Oocyte retrieval was performed successfully and hysteroscopy was performed on the same day which revealed roomy cavity and bilateral ostia visualized.

2. Embryology and PGT-A

Three day-5 blastocysts were obtained: 4AA, 3AA, 4AC and PGT-A of these demonstrated only one euploid embryo.

3. Adenomyosis Suppression

The patient received:

- Triptorelin acetate 3.75 mg IM monthly × 3 months
- Letrozole 2.5 mg twice daily continuously for 3 months.

GnRH agonist therapy has been shown to improve ART outcomes in adenomyosis by reducing lesion volume, suppressing inflammatory mediators, decreasing local estrogen production, and normalizing uterine contractility (12–14). Aromatase inhibition further reduces intramyometrial estrogen synthesis, targeting the hyperestrogenic microenvironment characteristic of adenomyosis.

4. Endometrial Preparation

Frozen embryo transfer was planned followed by hormone

replacement therapy using estradiol hemihydrate (2 mg BD).

5. Mock ET was done 2 times prior to definitive embryo transfer. 1st mock ET was done with soft catheter which failed and then hard catheter was used in the 2nd time.

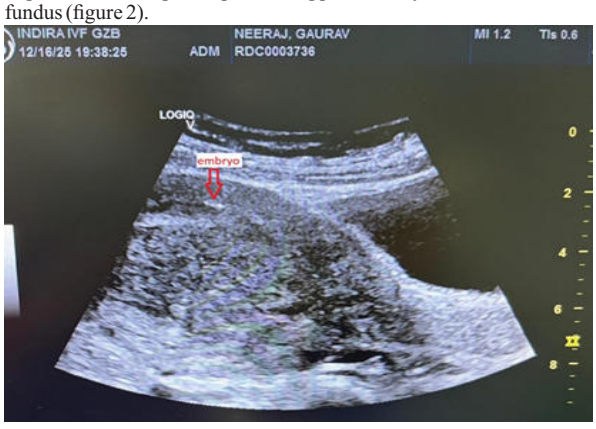
6. Embryo Transfer Technique

Atosiban 6.75 mg IV bolus, 30 minutes before ET was given.
Single euploid embryo transfer was performed under transabdominal ultrasound guidance. The transfer required careful navigation due to:

- Enlarged adenomyotic uterus
- Altered uterocervical angulation
- S shaped uterine cavity

A hard catheter (Allwyn) was used for the embryo transfer. The catheter with stylet was then introduced slightly beyond the internal os. The stylet was subsequently withdrawn, and the inner catheter loaded with a single embryo was advanced carefully until it aligned with the tip of the outer catheter. It was then gradually advanced further until it reached approximately 2–2.5 cm below the fundus.

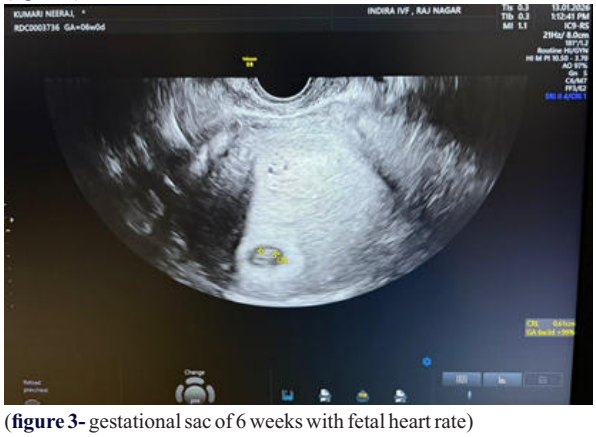
We were unable to position the catheter at 1–1.5 cm below the fundus because the uterine cavity was very long due to a bulky adenomyotic uterus. Therefore, a hard push was applied to place the embryo as close as possible to the optimal position, approximately 1–1.5 cm below the fundus (figure 2).



(**figure 2-** embryo transfer)

7. Progesterone Support Post Transfer

The patient received vaginal progesterone gel in combination with oral and injectable progesterone, aiming to achieve both optimal endometrial exposure and adequate systemic progesterone levels.
The patient achieved pregnancy and is currently 20 weeks gestation (figure 3).



(**figure 3-** gestational sac of 6 weeks with fetal heart rate)

DISCUSSION

Adenomyosis as a Disorder of Endometrial–Myometrial Crosstalk

Adenomyosis disrupts the functional integrity of the junctional zone, a hormonally responsive inner myometrial layer responsible for uterine peristalsis and embryo positioning (6). Thickening and architectural distortion of the JZ alter uterine contractility, resulting in hyperperistalsis and dysperistalsis. Abnormal uterine contractions have been associated with reduced implantation rates in ART cycles (15).

At the molecular level, adenomyosis is characterized by chronic inflammatory activation with elevated IL-6, TNF-α, prostaglandins, and macrophage infiltration (7,8). This inflammatory milieu interferes with implantation by impairing embryo apposition and trophoblast invasion.

Furthermore, adenomyosis is associated with progesterone resistance, reflected by reduced progesterone receptor expression and impaired decidualization capacity (9). Downregulation of implantation markers such as HOXA10 and integrin αvβ3 further compromises endometrial receptivity (16).

Adenomyosis And Recurrent Pregnancy Loss

Meta-analyses demonstrate increased miscarriage rates in adenomyosis patients undergoing IVF (3,4). Mechanistically, defective decidualization and impaired spiral artery remodeling may lead to inadequate placentation. Oxidative stress and inflammatory cytokines further contribute to early trophoblast dysfunction (8,9).

In this patient, two prior missed abortions likely reflected a combination of embryonic aneuploidy and uterine receptivity impairment. The identification of only one euploid embryo among three high-grade blastocysts underscores the contribution of embryonic chromosomal abnormalities to RPL.

Reduced progesterone receptor expression leads to impaired decidualization and defective stromal transformation. This is particularly relevant in patients with recurrent pregnancy loss, where inadequate decidual support may compromise early placentation. Additionally, adenomyotic tissue produces increased inflammatory cytokines such as IL-6, TNF-α, and prostaglandins. This chronic inflammatory microenvironment negatively affects implantation and trophoblast invasion.

Another critical infertility mechanism is altered expression of implantation markers such as HOXA10 and integrins. Downregulation of these markers reduces endometrial receptivity even in morphologically normal cavities. Thus, adenomyosis is increasingly recognized as a functional uterine factor rather than merely a structural abnormality.

Rationale For GnRH Agonist Pretreatment

Several studies report improved implantation and live birth rates following prolonged GnRH agonist downregulation in adenomyosis patients undergoing IVF (12–14). Suppression reduces lesion vascularity, decreases local estrogen production, and attenuates inflammatory activity.

By inducing a hypoestrogenic state, GnRH agonists may also normalize uterine peristalsis and reduce hypercontractility, improving embryo retention at the time of transfer (13).

Given the elevated miscarriage risk in adenomyosis, uterine optimization prior to transfer is critical.In this case, combination therapy with letrozole likely enhanced suppression by inhibiting peripheral aromatization, further reducing estrogen-driven adenomyotic activity.

Surgical And Ablative Therapies In Fertility-seeking Women

Although adenomyomectomy may relieve symptoms, it carries risks including adhesion formation, impaired uterine compliance, and uterine rupture in subsequent pregnancy (17). Microwave ablation and other destructive therapies are highly controversial and compromise uterine structural integrity and therefore are not recommended in women desiring fertility (18) by many infertility specialists. Hence, medical suppression remains the preferred first-line approach before ART.

Integration Of Euploid Embryo Transfer

The transfer of a single euploid embryo eliminated embryonic aneuploidy as a confounder, isolating uterine receptivity as the key determinant. Emerging data suggest that adenomyosis may reduce implantation even in euploid embryo transfer cycles, reinforcing the importance of uterine suppression (5).

In this case, the combination of uterine optimization, euploid selection,

and meticulous ET technique likely contributed to successful ongoing pregnancy.

Why Adenomyosis Increases Risk Of Difficult ET

Adenomyosis predisposes to technically challenging ET due to:

- Uterine enlargement
- Altered uterocervical angulation
- Junctional zone thickening
- S-shaped cavity

These factors increase the likelihood of requiring cervical manipulation, which is associated with reduced pregnancy outcomes (11).

Thus, atraumatic, ultrasound-guided transfer with a soft catheter is particularly crucial in adenomyosis patients.

Embryo Transfer Technique As A Determinant Of Success

Embryo transfer is widely regarded as a critical determinant of IVF success, potentially accounting for up to 30% of cycle failures (10). Kava-Braverman et al. analyzed 7714 ETs and demonstrated that clinical pregnancy rates (CPR) decrease progressively with increasing procedural difficulty (11). Use of tenaculum or stylet significantly reduced pregnancy odds, with difficult transfers reducing CPR from 38% to 27% and live birth rates accordingly.

Difficult ET is objectively defined by the requirement for additional cervical instrumentation such as outer sheath, stylet, tenaculum, or hysterometer (11).

Mechanisms by which difficult ET reduces implantation include:

- Cervical manipulation-induced uterine contractions
- Endometrial microtrauma
- Fundal irritation
- Improper embryo deposition

Furthermore, proper ultrasound visualization during ET significantly improves clinical pregnancy and live birth rates. Poor visualization reduces CPR by nearly 12% (10) emphasizing the importance of bladder preparation and operator expertise.

Mock ET- Planning before placement.

In this patient, a mock embryo transfer was performed prior to the definitive frozen embryo transfer cycle, which proved invaluable in procedural planning. Mock ET has been shown to identify uterocervical angulation, cervical stenosis, cavity length, and potential resistance points that may predispose to difficult transfer (19,20). In adenomyosis, uterine enlargement and junctional zone distortion frequently alter the cervical–uterine axis, increases myometrial tone and utero-cervical length thereby increasing the risk of traumatic catheter manipulation. By performing a mock transfer, the precise uterine depth and optimal catheter curvature were determined in advance, minimizing intra-procedural instrumentation and avoiding the need for tenaculum or stylet use—maneuvers independently associated with reduced clinical pregnancy and live birth rates (11). Furthermore, mock transfer allows assessment of catheter trajectory under ultrasound visualization, ensuring atraumatic placement, 1.5–2 cm from the fundus without fundal touch, which may provoke uterine contractions.

In complex uterine pathologies such as adenomyosis, pre-cycle rehearsal of transfer technique serves as an important strategy to reduce procedural variability and mitigate the well-documented adverse impact of difficult embryo transfer on implantation outcomes. Thus, mock ET functioned not merely as a technical adjunct but as a critical optimization step in achieving successful euploid implantation in this case.

On the day of embryo transfer, therefore, meticulous technique is mandatory. We used the afterloading technique. Ultrasound guidance allows precise catheter placement while avoiding contact. Use of a soft catheter minimizes trauma. Slow injection of the embryo and delayed catheter withdrawal along with twisting of inner catheter by approximately 90^0 reduces reflux risk. In this case, strict adherence to atraumatic technique was essential in achieving implantation.

Although soft embryo transfer (ET) catheters are generally preferred due to reduced endometrial trauma and lower induction of uterine contractions, clinical scenarios such as cervical stenosis, uterine angulation, or uterine distortion secondary to adenomyosis may necessitate the use of a firmer catheter (21,22). Adenomyosis alters uterine architecture through myometrial hypertrophy, increased stiffness, and disruption of the junctional zone, which may contribute to technical difficulty during catheter negotiation across the internal os (6,21).

In the present case, at the time of mock ET initial negotiation with a soft catheter was unsuccessful due to cervical resistance; therefore, a firm catheter was used under continuous transabdominal ultrasound guidance. Historically, harder catheters were associated with lower implantation and pregnancy rates due to possible endometrial trauma and stimulation of uterine contractions (21,23). However, contemporary evidence suggests that when used selectively and atraumatically—particularly under ultrasound guidance—clinical pregnancy rates are not significantly compromised (22,10).

Importantly, difficult embryo transfers requiring excessive manipulation, repeated attempts, or cervical instrumentation are independently associated with reduced implantation and pregnancy outcomes (11,24). In such cases, a single, controlled passage with an appropriately firm catheter may be preferable to multiple traumatic attempts with a soft catheter. In our patient, the absence of blood or mucus contamination and the atraumatic nature of the transfer likely mitigated the theoretical disadvantages associated with a firm catheter. This case reinforces the importance of individualized ET strategy tailored to uterine anatomy rather than rigid adherence to catheter type. This case also underscores that adenomyosis-associated infertility requires a comprehensive, multidisciplinary approach. Suppressing disease activity prior to IVF, selecting euploid embryos, and optimizing transfer technique collectively overcame multiple implantation barriers. The successful ongoing pregnancy demonstrates that even in the presence of diminished ovarian reserve, RPL, and adenomyosis, favorable outcomes are achievable with tailored reproductive strategies.

Counteracting Progesterone Resistance In Adenomyosis Through Intensive Luteal Support

In view of underlying adenomyosis and the associated risk of impaired implantation due to altered uterine contractility and inflammatory milieu, intensive luteal phase support was instituted following embryo transfer. Vaginal progesterone ensures high local endometrial concentrations through the "first uterine pass effect," which is particularly advantageous in adenomyosis where endometrial receptivity may be compromised. The addition of oral and injectable sprogesterone provided systemic support, potentially enhancing overall luteal adequacy and contributing to suppression of uterine activity. This dual-route progesterone supplementation was chosen to maximize luteal phase stability, counteract progesterone resistance reported in adenomyotic uteri, and optimize implantation potential in this high-risk clinical scenario.

CONCLUSION

Adenomyosis represents a complex uterine disorder that impairs implantation and increases miscarriage risk through inflammatory activation, progesterone resistance, abnormal uterine contractility, and defective decidualization. GnRH agonist pretreatment may restore uterine receptivity and improve ART outcomes. Surgical and ablative therapies are suboptimal in fertility-seeking women due to uterine structural compromise.

Difficult embryo transfer significantly reduces clinical pregnancy and live birth rates and must be minimized, particularly in adenomyosis patients predisposed to anatomical and functional challenges.

This case illustrates that comprehensive uterine suppression, euploid embryo selection, and optimized atraumatic embryo transfer can overcome multifactorial infertility barriers and result in ongoing pregnancy.

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