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Case Series

## Overcoming adenomyosis in *in vitro* fertilization: a case series

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### ABSTRACT

Adenomyosis is increasingly diagnosed in infertile women and is associated with adverse *in vitro* fertilization (IVF) outcomes. Individualizing ovarian stimulation and embryo transfer strategies may improve reproductive outcomes. This retrospective case series includes three women with imaging-confirmed adenomyosis who underwent IVF using a gonadotropin-releasing hormone (GnRH) antagonist protocol with a freeze-all strategy, followed by frozen embryo transfer (FET). Clinical characteristics, stimulation parameters, embryological outcomes, and pregnancy outcomes were evaluated. All patients completed ovarian stimulation with satisfactory oocyte yield and embryo development. Frozen embryo transfer was performed following GnRH agonist down-regulation and hormone replacement therapy. All three patients achieved ongoing clinical pregnancy. Favorable IVF outcomes can be achieved in women with adenomyosis using an antagonist protocol combined with a freeze-all strategy and frozen embryo transfer. Larger prospective studies are required to validate these findings.

**Keywords:** Adenomyosis, *In vitro* fertilization, GnRH antagonist, Freeze-all, Frozen embryo transfer, Case series

### INTRODUCTION

Adenomyosis is a benign gynecological disorder characterized by the presence of endometrial glands and stroma within the myometrium, often associated with dysmenorrhea, abnormal uterine bleeding, and infertility.<sup>1,2</sup> With advances in transvaginal ultrasonography and magnetic resonance imaging, adenomyosis is increasingly recognized among women undergoing evaluation for infertility.<sup>2,3</sup>

Several studies have demonstrated that adenomyosis negatively impacts *in vitro* fertilization (IVF) outcomes by impairing endometrial receptivity, altering uterine peristalsis, and creating a chronic inflammatory and hyperestrogenic uterine environment.<sup>1,4</sup>

Consequently, reduced implantation rates, lower clinical pregnancy and live birth rates, and increased miscarriage rates have been consistently reported.<sup>1,6</sup>

To overcome these adverse effects, individualized IVF strategies have been proposed. The use of GnRH antagonist protocols combined with a freeze-all strategy and subsequent frozen embryo transfer has gained attention, as it avoids supraphysiological estrogen exposure during stimulation and allows optimization of endometrial receptivity.<sup>5,6</sup> This case series describes IVF outcomes in three women with adenomyosis managed using a GnRH antagonist protocol, cycle segmentation, and frozen embryo transfer.

### CASE SERIES

#### Case 1

A 27-year-old woman with 4 years of secondary infertility with imaging suggestive of focal posterior wall adenomyosis (2.4×1.8 cm) abutting the endometrial cavity. No significant medical history and previously operated for right tubal ectopic pregnancy. She had undergone three previous *in vitro* fertilization (IVF)

attempts with an ectopic pregnancy after one IVF cycle. Controlled ovarian stimulation was performed using a GnRH antagonist protocol and dual trigger for final oocyte maturation. 9 oocytes were retrieved and ICSI yielded a fertilization rate of 75%. Following downregulation with leuprolide 3.75 mg in the preceding cycle and hormone replacement therapy was given with estrogen followed by progesterone for endometrial preparation and two day-5 blastocysts were transferred. She achieved a positive  $\beta$ -hCG and has an ongoing clinical pregnancy.

### Case 2

A 37-year-old woman with 15 years of primary infertility, severe dysmenorrhea. She had one prior failed IVF cycle. Patient underwent adenomyomectomy 6 months prior to present IVF cycle. Imaging post procedure demonstrated diffuse adenomyosis with posterior wall thickness of 9cm and anterior wall thickness of 4cm. Patient had normal ovarian reserve. Controlled ovarian stimulation was performed using a GnRH antagonist protocol and agonist trigger. 5 oocytes were retrieved and ICSI yielded a

fertilization rate of 80%. Frozen embryo transfer was performed after leuprolide downregulation and hormone replacement with transfer of two day-5 blastocysts. She achieved a positive  $\beta$ -hCG and has an ongoing clinical pregnancy.

### Case 3

A 38-year-old woman with 12 years of secondary infertility, with a history of ectopic pregnancy following spontaneous conception. She is a known case of hypothyroidism on treatment. Imaging showed a 2.2×1.0 cm posterior wall adenomyoma. Patient had a normal ovarian reserve. Controlled ovarian stimulation was performed using a GnRH antagonist protocol and dual trigger. 9 oocytes were retrieved and ICSI yielded a fertilization rate of 71.4%. Frozen embryo transfer was performed after leuprolide downregulation and hormone replacement with transfer of one day-6 blastocysts. She achieved a positive  $\beta$ -hCG and has an ongoing clinical pregnancy.

**Table 1: Baseline clinical characteristics.**

Parameter	Case 1	Case 2	Case 3
Age (years)	27	37	38
BMI (kg/m <sup>2</sup> )	23.6	24.8	22.5
Duration of infertility (years)	4 years	15 years	12 years
Type of infertility	Secondary	Primary	Secondary
Symptoms	Subfertility with previous ectopic pregnancy following IVF conception	Severe dysmenorrhea and subfertility with previous IVF failure	Subfertility with previous ectopic pregnancy
Medical/surgical comorbidities	Right salpingectomy for right tubal ectopic pregnancy	Previously operated for adenomyomectomy	Hypothyroidism on medication
Type of adenomyosis	Focal adenomyosis in posterior wall of uterus touching ET	Diffuse adenomyosis with bilateral ovaries adherent to uterus	2.2×1.0 cm posterior wall adenomyoma
AMH (ng/ml)	3.89	2.5	2.38
Previous IVF attempts	3	1	0

**Table 2: Ovarian stimulation details (antagonist protocol).**

Parameter	Case 1	Case 2	Case 3
Starting gonadotropin dose (IU)	Inj rFSH 225IU, Inj HMG 75IU	Inj rFSH 225IU, Inj HMG 75IU	Inj rFSH 225IU, Inj HMG 150IU
Day of antagonist initiation	Day 5	Day 6	Day 6
Total gonadotropin dose (IU)	9 doses each of Inj rFSH and Inj HMG	10 doses each of Inj rFSH and Inj HMG	Inj rFSH 225 IU (5 doses) and 300 IU (5 doses), Inj HMG 150 IU (5 doses) and 300 IU (5 doses)
Duration of stimulation (days)	9	10	10
Trigger used	Dual trigger	Agonist trigger	Dual trigger

**Table 3: Embryology outcomes.**

Parameter	Case 1	Case 2	Case 3
<b>Total oocytes retrieved</b>	9	5	9
<b>MII oocytes</b>	8	3	7
<b>Fertilization method</b>	ICSI	ICSI	ICSI
<b>Fertilization rate (%)</b>	75	80	71.4
<b>Embryos formed</b>	4 day 5 blastocysts	2 day 5 blastocysts	1 day 6 blastocyst
<b>Embryo grade</b>	3AA, 3AA, 4AA, 4AB	4AA, 3BB	4BB

**Table 4: Frozen embryo transfer details.**

Parameter	Case 1	Case 2	Case 3
<b>Downregulation before FET</b>	Inj Leupride 3.75mg on day 21 in previous cycle	Inj Leupride 3.75mg on day 21 in previous cycle	Inj Leupride 3.75mg on day 21 in previous cycle
<b>Endometrial preparation</b>	HRT cycle	HRT cycle	HRT cycle
<b>Endometrial thickness (mm)</b>	8.3 mm on day 13	9.0 mm on day 15	7.0 mm on day 13
<b>Number of embryos transferred</b>	2 day 5 blastocysts 3AA, 4AA	2 day 5 blastocysts 4AA, 3BB	1 day 6 blastocyst 4BB
<b>Luteal phase support</b>	Oral and vaginal progesterone	Oral and vaginal progesterone	Oral and vaginal progesterone
<b>Outcome</b>	Beta HCG positive with ongoing clinical pregnancy	Beta HCG positive with ongoing clinical pregnancy	Beta HCG positive with ongoing clinical pregnancy

## DISCUSSION

Adenomyosis has long been considered a challenging condition in assisted reproduction due to its negative impact on implantation and pregnancy outcomes.<sup>1,4,6</sup> Recent evidence suggests that cycle segmentation with frozen embryo transfer may improve outcomes by avoiding supraphysiological estrogen levels during controlled ovarian stimulation.<sup>5,6</sup>

In this case series, the consistent use of GnRH agonist down-regulation prior to frozen embryo transfer likely contributed to improved endometrial receptivity by suppressing adenomyotic lesions, reducing inflammatory mediators and thereby enhancing implantation potential.<sup>3,5</sup> Favorable outcomes were achieved despite adverse prognostic factors such as advanced maternal age, long duration of infertility, prior IVF failures, and severe adenomyosis.<sup>1,6</sup>

Although limited by small sample size and retrospective design, these findings support individualized IVF strategies incorporating freeze-all strategy, downregulation with GnRH agonist and frozen embryo transfer in women with adenomyosis.<sup>1,5,6</sup>

## CONCLUSION

Women with adenomyosis can achieve favorable IVF outcomes when managed with an antagonist protocol, freeze-all strategy, and frozen embryo transfer following GnRH agonist down-regulation. Individualized treatment

approaches may help overcome the negative impact of adenomyosis on implantation.

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