

## Case Report

# Successful Pregnancy after Frozen Embryo Transfer after Recurrent Endometrial Collection in a Patient with Mosaic Turner Syndrome

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ABSTRACT

A 36-year-old female with Mosaic Turner Syndrome presented for oocyte donation program. She developed endometrial collection each time she was started on estradiol valerate for endometrial preparation. All causes of the endometrial collection were ruled out and empirical antibiotics given. Finally, the patient developed a satisfactory endometrium of 5.7 mm with no endometrial collection after being given low dose estradiol-estrogel (Transdermal application) and five doses of subcutaneous injections on granulocyte-colony-stimulating factor. The patient conceived after embryo transfer and is in follow-up.

**KEYWORDS:** *Frozen embryo transfer; granulocyte-colony stimulating factor; Mosaic Turner; repeated endometrial collection, transdermal estradiol*

## INTRODUCTION

Endometrial collection is a dilemma in the field of reproductive medicine, especially in patients who are exposed to estrogen after prolonged hypoestrogenism such as those with Turner's Syndrome. It contributes to cycle cancellations and increased financial burdens. We describe our experience with a patient with Mosaic Turner's Syndrome planned for oocyte donation programme who developed recurrent endometrial collection with oral estrogen and how it was mitigated with use of transdermal estrogen and G-CSF. We were able to achieve a good endometrium and a successful outcome following this approach.

## CASE REPORT

A 36-year-old female was referred to our institute for oocyte donation program (ODP). She was a diagnosed case of Mosaic Turner Syndrome (80%46XX, 20% 45 XO). She got her periods only after taking a course of combined oral contraceptives. She was a known case of diabetes and was on metformin and insulin. Her height was 131 cm, and body mass index 28.5 kg/m<sup>2</sup>. Husband's reports were normal. On ultrasound, the uterus was small, bilateral ovaries were not visualized

and endometrium minimally vascular with no evidence of hydrosalpinx. She was given four cycles of sequential regimen estrogen (estradiol valerate 10–12 mg) daily and progesterone (medroxyprogesterone 10 mg) to improve the vascularity before ODP. She was started on hormone replacement therapy (HRT), that is, 8 mg of estradiol valerate for the trial cycle, but she developed an endometrial collection along with hypoechoic fluid collection with maximum anteroposterior diameter of about 6 mm [Figure 1]. Hence, she was given progesterone withdrawal. Meanwhile, the oocytes were fertilized with husband's sperm by intracytoplasmic sperm insemination and were frozen at eight cell stage by vitrification, to be transferred after the resolution of the endometrial collection. The endometrial collection, however, occurred three times and each cycle had to be cancelled [Figure 2]. A hysteroscopy was decided, which revealed a normal study [Figure 3]. Endometrial sampling was done, which showed no evidence of inflammation or plasma cells and endometrial tuberculosis (TB) was also ruled out with TB-polymerase chain reaction. Histopathology report showed oedematous stroma with scanty endometrium. She was empirically given a course

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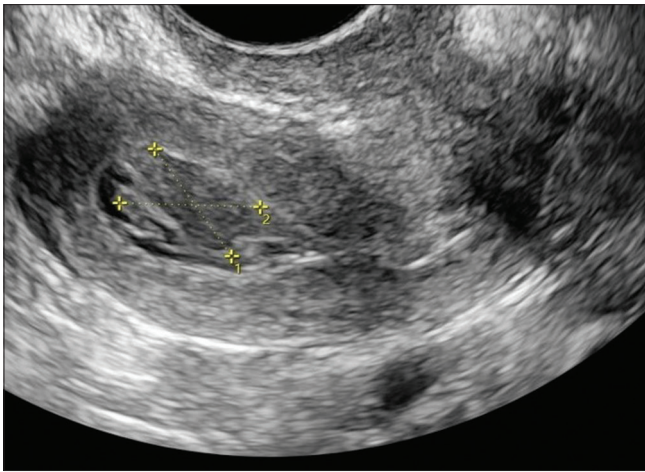
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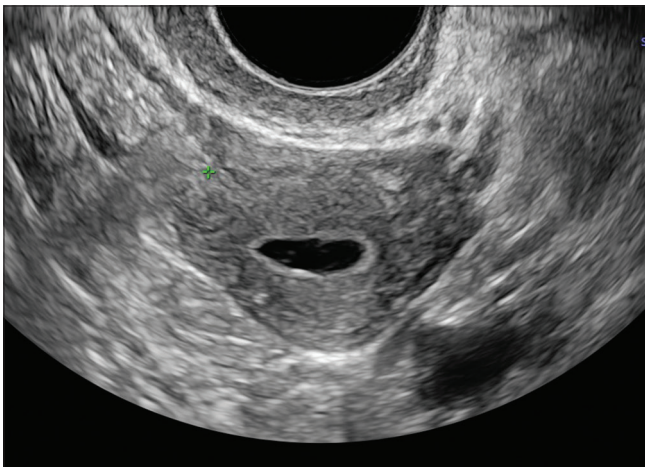
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of doxycycline and clindamycin for 14 days. She was again started on HRT twice, but she again developed an echogenic endometrial collection. Therefore, cervical dilatation and suctioning of the endometrial cavity were



**Figure 1:** Hyperechoic area 1.3 cm × 1.2 cm with hypoechoic collection of 6 mm seen on starting hormone replacement therapy for the first time



**Figure 2:** Hypoechoic collection occurred each time on starting hormone replacement therapy



**Figure 3:** Hysteroscopy showed normal study

done under ultrasound guidance. It drained only scanty old blood clots and the endometrial collection persisted on continuing estrogen. The patient was offered the option of surrogacy, but her close relative backed out.

It was a dilemma for the treating gynecologists. We decided to start her on low dose transdermal estradiol (oestrogel, 0.06% w/w), 1.25 g in the morning and in the evening for 10 days, followed by 2.5 g in the morning and 1.25 g in the evening for another 10 days. The patient did not develop an endometrial collection this time, but the growth of the endometrium was slow. She was given five subcutaneous granulocyte-colony stimulating factors (G-CSF) 300 mcg on alternate days for improving endometrial thickness while continuing estrogen. After 28 days of transdermal estrogen, she developed an endometrium of 5.7 mm with zone 3 vascularity according to Applebaum scoring.<sup>[1]</sup> Since it was the best endometrium thickness that could be obtained, a decision for embryo transfer was taken. The patient was started on vaginal micronized progesterone 300 mg thrice daily for 5 days. 2 embryos at eight cell stage (Grade 1) were thawed with Kitazatos thawing medium, and assisted laser hatching was done by diode laser in the compaction stage and transferred on the 5<sup>th</sup> day of progesterone. The beta-human chorionic gonadotropin report 14 days after the embryo transfer was positive. Scan showed a singleton live intrauterine gestation. The patient is in follow-up at our center.

## DISCUSSION

Fluid in the endometrial cavity is very often seen in patients with hydrosalpinx or those who are exposed to estrogen after prolonged hypoestrogenism e.g., premature ovarian failure, postmenopausal women, and Turners. This is due to the initiation of glandular activity in the endometrium. Aspiration of the fluid with staining for cytology reveals that it is noninflammatory in nature.<sup>[2]</sup> Aspiration of the fluid is generally unsuccessful as the fluid builds up again. The answer is to give HRT repeatedly. Fluid accumulation in the fresh cycle usually has a better outcome as its associated with favorable prognostic factors— small anteroposterior diameter of fluid and transient fluid accumulation. Frozen embryo transfer have a lower pregnancy rate as it is associated with persistent fluid collection.<sup>[3]</sup>

It is well known that uterine and endometrial development in women with Turners is not optimal despite HRT.<sup>[4]</sup> However, successful pregnancies with oocyte donation after HRT in patients with Turner syndrome has been

well documented. Patients with Turners have shown have better conception rates in fresh transfers as compared to frozen, with a higher and constant dose of estrogen, with hyerechoic endometrium >6.5 mm and in patients with Mosaic Turners than XO.<sup>[5]</sup>

The pregnancy rates with transdermal and oral estrogen have been found to be similar.<sup>[6]</sup> Transdermal estradiol valerate avoids systemic side effects as well as has little effect on lipid and coagulation profile. In a recent meta-analysis, G-CSF use by both intrauterine and systemic route has shown better clinical results in patients with recurrent implantation failure, but its role in thin endometrium still needs to be investigated.<sup>[7]</sup> Starting patients on low dose transdermal estrogen and increasing the dose gradually may be the solution to endometrial collections in patients undergoing oocyte donation. The additional influence of G-CSF in improving the endometrial receptivity and conception in endometrial thickness <6 mm is unique in this case.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

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