

The Full-Term Delivery of a Normal Female Infant by a Woman with a Levonorgestrel Intrauterine System in Situ and Identified as Having Uterine Adenomyosis: A Case Report

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Abstract This study reports an IVF patient who had adenomyosis underwent 2 in vitro fertilization (IVF) cycles and 3 frozen embryo transfer (FET) cycles but all failed. Then a Levonorgestrel-releasing intrauterine system (LNG-IUS) was inserted into her uterine. When her next menstrual period did not occur, the patient performed a urinary pregnancy test and it was positive. The pregnancy progressed normally and the delivery was uncomplicated. An elective Caesarean delivery was performed at 39 weeks gestation. The IUD was found in the placenta and the postpartum recovery was uneventful. This is the first report of a woman, who having been identified with uterine adenomyosis, delivered a normal female infant with an LNG-IUS in situ. This case report indicated that LNG-IUS may play some roles in changing the uterine environment of adenomyosis.

Keywords: *Levonorgestrel-releasing intrauterine system, in vitro fertilization, adenomyosis*

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1. Introduction

Uterine adenomyosis is a common gynecological disorder, characterized by the presence of heterotopic endometrial glands and stroma in the myometrium, with adjacent smooth muscle hyperplasia [1]. Therapy in the form of a levonorgestrel intrauterine system (LNG-IUS) may be beneficial in women with adenomyosis who wish to conceive after treatment. We report on a patient with an LNG-IUS in situ and uterine adenomyosis who became pregnant and delivered a normal female infant in 2016. Institutional Review Board approval for publication of this case report was requested and granted, and written permission from the patient was obtained. Written informed consent was obtained from each of the patients enrolled.

2. Case Report

In 2012, a 38-year-old woman, gravida 3, para 0, with secondary infertility for six years, and dysmenorrhea and intermenstrual bleeding, was referred to our unit for in vitro fertilization (IVF) and embryo transfer. The patient's past history included two artificial abortions and a spontaneous one. A hysterosalpingography revealed

partially obstructed Fallopian tubes.

In our unit, she underwent artificial insemination by her husband for two cycles but the urinary pregnancy test was negative. After that, she underwent 2 in vitro fertilization (IVF) cycles using and 3 frozen embryo transfer (FET) cycles between April 2012 and April 2015 but all failed. The ovarian stimulation protocol was progesterone primed ovarian stimulation which was previously described [2-6]. During this period of time, she also underwent times of Hysteroscopy and experienced 3 cancellation of embryo transfer as the as endometrial thickness was not thick enough.

2.1. Levonorgestrel-releasing intrauterine system insertion

A repeat ultrasound scan suggested the presence of adenomyosis. Confirmation of adenomyosis was then made using magnetic resonance imaging (MRI), according to traditional radiological criteria [7]. As reported, therapy with the LNG-IUS can be beneficial in women with adenomyosis who wish to conceive after treatment [8-12]. A Mirena® IUD was placed on 27th. August 2015. At the time of the appointment, the patient was on day 24 of a 30-day cycle and the urinary pregnancy test was negative. She reported having had unprotected intercourse on day 12. She had been warned about a potential pregnancy despite the insertion of the IUD during the luteal phase but

elected to proceed regardless. The IUD was inserted and a transvaginal ultrasound was performed. The location of the LNG-IUS was correct and a gestational sac was not observed in the uterine cavity. When her next menstrual period did not occur, the patient performed a urinary pregnancy test and it was positive. She requested a perinatal opinion. An ultrasound confirmed a single live

embryo consistent with eight weeks and three days gestation, with the LNG-IUS in place in the uterus and positioned inferolaterally to the gestational sac. The risks discussed with the patient included those that are general to a pregnancy with an IUD in situ and those that relate to embryonic exposure to the LNG.



Figure 1. Picture from the ultrasound showing the IUD in place. (45 days of gestation)



Figure 2. Picture from the ultrasound showing the IUD in place. (14 weeks of gestation)

3. Result

The pregnancy progressed normally and the delivery was uncomplicated. An elective Caesarean delivery was performed at 39 weeks gestation. A female infant weighing 3210g was born without congenital abnormalities. Masculinization or any other anomalies in the infant were not found. The IUD was found in the placenta and the postpartum recovery was uneventful. This case showed that in our experience a healthy infant has been delivered without any abnormality.

4. Discussion

The LNG-IUS is a popular, cost-effective method of contraception. Pregnancy with the levonorgestrel released via the IUS is unusual. Recently, it has been used as a method with non-contraceptive benefits; including slight menstrual bleeding, a decrease in the number of dysmenorrhea incidents, and reduced pain associated with adenomyosis. The majority of women with an intrauterine pregnancy with an IUD in situ either elect termination of the pregnancy or experience spontaneous miscarriage [7]. If the pregnancy continues, there is an increased risk of chorioamnionitis, spontaneous abortion, and preterm delivery [13]. Pregnancies conceived with an IUD in place are associated with adverse pregnancy outcomes. The greatest risk pertains to those pregnancies in which the IUD was not removed. The manufacturer of the LNG IUS (Mirena[®]) and the World Health Organization recommend the removal of the IUD in desired intrauterine gestations [14]. Responses to a questionnaire received from 17 360 LNG IUS users were analyzed in a study on 64 pregnancies with the LNG IUS in situ. Thirty-three of the pregnancies were ectopic. The five-year cumulative pregnancy rate per 100 users was 0.5 and the five-year Pearl Index rate was 0.11 [15]. Elsewhere, it was reported that normal newborn infants (a girl and a boy) were delivered at full term despite the exposure of the mothers to the LNG-IUS, embedded in the omentum, during the pregnancy [16,17]. In another study, it was reported that two normal infant girls were born after first-trimester exposure to the LNG-IUS. One of the LNG-IUSs was expelled spontaneously [7] and the other was retrieved after eight weeks [18]. In other studies, a healthy female and a male infant were delivered at term with an IUS *in situ* [19,20]. Two full-term infants, the gender of which was not reported, were also born in this way in other research [15].

In the present case, the patient had previously undergone three unsuccessful FET cycles in our unit owing to repeated implantation failure. Thereafter, she was identified as having uterine adenomyosis by MRI diagnosis. According to the case report, the LNG-IUS was inserted 11 days after ovulation. This confirmed that conception must have occurred prior to the insertion of the IUS and was not considered a failure of the LNG-IUS system. Suggestions in the literature that adenomyosis interferes with embryo implantation are well known. Some investigators attribute thrombophilia and an immunological attack on the implanted embryo to be the

causes of implantation failure [21]. It was demonstrated in one study in which endometrial biopsies featured that adenomyosis was associated with a prominent aggregation of macrophages within the superficial endometrial glands which potentially interfered with embryo implantation [22]. The accumulation of macrophages in the superficial endometrial glands may give rise to an immune environment which is hostile to the implanted embryos. Moreover, some cytokines, such as tumor necrosis factor-alpha and interleukin-1, secreted from the macrophages, reactive oxygen, and nitrogen species, are all potentially toxic to embryos [23].

In our case, in view of the patient's spontaneous abortion and the failure of several embryos to successfully implant, we speculated that uterine adenomyosis could be the reason for these. This abovementioned studies prove our point. The patient was treated with hysteroscopy owing to her medical history of abortion by curettage and endometrial thickness of ≤ 5 mm. Several cycles of FET were cancelled for this reason. Our patient was diagnosed with adenomyosis with endometrial lesions.

Although the pathophysiology of adenomyosis has not been clarified, it was shown in a recent study that the altered expression of the steroid receptor co-regulators may play a role in its development. In addition, the LNG-IUS, which has been broadly applied to patients with adenomyosis in clinical practice, may impact on the disease by adjusting the signal transduction pathways which are activated by the steroid hormones [24]. In our case, the LNG-IUS was accidentally inserted 11 days after ovulation. The chances of a successful implantation were greatly enhanced by an improvement in the intrauterine environment, facilitated by the LNG-IUS. Meanwhile, the ability of the patient to maintain a normal pregnancy in the first trimester demonstrated the efficacy of the LNG-IUS in treating adenomyosis, while simultaneously preventing spontaneous abortion. The use of the LNG-IUS was also associated with an improvement in the number and quality of endometrial lesions.

Usually, risks of prematurity, miscarriage, and intrauterine infection are associated with an intrauterine pregnancy with an LNG-IUS in situ. The risk of potential masculinization of the female fetus is an additional theoretical concern with its use [25]. Nevertheless, this pregnancy was important to our patient, who wished to see it to full term. The pregnancy continued to progress normally and a healthy female infant was born.

Pregnancy is rare occurrence when an LNG-IUS is in situ. Nevertheless, women should be informed of this possibility before its insertion to avoid any potential risks. To the best of our knowledge, this is the first report of a woman, who having been identified with uterine adenomyosis, delivered a normal female infant with an LNG-IUS in situ.

5. Conclusion

We report on a patient with an LNG-IUS in situ and uterine adenomyosis who became pregnant and delivered a normal female infant in 2016. A female infant was born without congenital abnormalities. Masculinization or any other anomalies in the infant were not found. The IUD

was found in the placenta and the postpartum recovery was uneventful. To the best of our knowledge, this is the first report of a woman, who having been identified with uterine adenomyosis, delivered a normal female infant with an LNG-IUS in situ. This case report demonstrates that LNG-IUS plays an important role in the successful medical treatment of adenomyosis.

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