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Pregnancy outcome after pharmacological treatment of adenomyosis of the external myometrium: a case report

Xinyue Wang[a], Xiaoguang Shao[b], Xiaohan Lan[a], Jie Zhang[b]

[a]Department of Obstetrics & Gynecology, Dalian Medical University, Dalian, China, [b]Reproduction & Genetics Center, Affiliated Zhongshan Hospital of Dalian University, Dalian, China, Correspondence: Jie Zhang, Affiliated Zhongshan Hospital of Dalian University, Dalian, Zhongshan District, Liaoning, People's Republic of China, postal code: 116000. E-mail: zhangjiexjtu@163.com

ABSTRACT

Adenomyosis is the implantation of active endometrial tissue outside the uterine cavity, which is one of the common diseases that cause infertility in women. Adenomyosis can be classified into internal and external adenomyosis depending on the location of the lesions. External adenomyosis means that the lesion is in the outer layers of the myometrium, which is separated from the intact junction zone. Here we reported two cases of patients with external adenomyosis that caused infertility. After undergoing medical treatment for adenomyosis, both patients successfully became pregnant following frozen embryo transfer. Our results suggest that medical treatment of external adenomyosis may improve the chances of pregnancy after frozen embryo transfer.

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Introduction

Adenomyosis is the implantation of active endometrial tissue outside the uterine cavity, which is one of the common diseases that cause infertility in women. Adenomyosis can be classified into internal and external adenomyosis depending on the location of the lesions. External adenomyosis refers to the lesion in the outer layers of the myometrium, which is separated from the intact junction zone (JZ), and there are several layers of normal muscle fibers between the adenomyosis and the JZ. Internal adenomyosis means that the lesion develops in direct connection to the thickened JZ, which does not involve the outer layers of the myometrium [1, 2].

Although postoperative pathology is the gold standard for diagnosing adenomyosis, several studies have proposed that transvaginal ultrasound (TVUS) and magnetic resonance imaging (MRI) can be used as preoperative diagnostic tools [3]. Compared with TVUS, 3-dimensional (3D)-TVUS can display the uterine cavity and the areas of lesion involvement more clearly. An MRI can further confirm the uterine myometrium's status and classify the adenomyosis lesions. Besides the above two examinations, cancer antigen-125 (CA-125) is also an essential marker for assessing the condition and changes of this disease. Internal and external adenomyosis are usually considered as two different entities and their treatment strategies are distinct. Patients with adenomyosis may experience infertility, who should receive comprehensive evaluation using 3D-TVUS, MRI, and CA125, and undergo appropriate pregnancy planning.

Pharmacological treatment

Pharmacological treatment of adenomyosis is performed through the administration of gonadotropin-releasing hormone-antagonist (GnRH-a) (Leuprolide acetate microsphere®) at a dose of 3.75 mg per intramuscular injection. Hormone Replacement Therapy (HRT) is administered orally with estradiol valerate at a dose of 2 mg twice daily. Transformation of the endometrium is performed using a daily single injection of Crinone gel® and twice daily of oral 100 mg progesterone capsules, Crinone gel®.

Here we report two cases of adenomyosis with good pregnancy outcomes. This study was approved by the Human Assisted Reproductive Technology Ethics Committee of Dalian Women and Children's

Medical Group, and the patients gave their written consent for us to publish their clinical information.

Case 1

The first patient was a 26-year-old female named J.H., who had never conceived. J.H. had an ultrasound that was suggestive of adenomyosis and bilateral fluid-containing mucous cysts at her first visit for Assisted Reproductive Technology (ART) in 2017. J.H. had received several in vitro fertilization-embryo transfer (IVF-ET) procedures in the past five years, but none of them had been successful. Therefore, it was recommended that adenomyosis be treated before undergoing ART.

To evaluate her conditions, a 3D-TVUS (Fig. 1a) was performed. The results showed a uterine size of 40 x 42 x 37 mm, with normal morphology of the uterine cavity (Fig. 1c). However, echogenic heterogeneity was found in the posterior wall of the uterus, which was approximately 24 mm thick, with a small anechoic interior of about 6 mm in diameter. She was considered to have an adenomyosis lesion that diffusely involved the external myometrium with a score of 2. At about the same time, she had a normal blood level of CA125 (10.92 U/mL). Later, an additional MRI (Fig. 2) was performed, which showed that the size of the uterus was 50 x 50 x 56 mm, with a normal uterine cavity, an anterior wall of 13 mm thick, and a posterior wall of 35 mm thick. MRI revealed abnormal mass-like signals in the outer muscle layers of the posterior and left anterior walls of the uterus, with sizes of 44 x 30 x 35 mm and 17 x 21 x 13 mm, respectively.

To treat her adenomyosis, she was given two injections of GnRH-a. Following the treatment, her CA125 level was slightly increased to 13.72 U/mL, which was still normal. A 3D-TVUS (Fig. 1b) was performed, which showed that the size of the uterus was reduced to 46 x 47 x 43 mm with a normal uterine cavity pattern and diffuse echogenic heterogeneity of the external myometrium of the posterior wall of the uterus that was about 27-mm thick, with a score of 2. The left mass was 36 x 35 x 25 mm in size, with irregular morphology and anechoic with light bands. Considering the remission of adenomyosis, HRT was started. The conversion from proliferative to the secretory stage of the endometrium was performed. Her serum estradiol values were checked to be 107.5 ng/mL and 95.48 ng/mL at a two-day interval, and her progesterone value was 11.75 μg/mL, indicating that her endometrium had been transformed to the secretory stage. At this time, two of her embryos (8C2G and 7C3GA) were transferred to her uterine cavity. A few days later, intrauterine pregnancy was confirmed by checking serum human Chorionic Gonadotropin (hCG) and TVUS. The NT (Nuchal Translucency) (Fig. 3) showed a single live pregnancy (13 weeks and 1 day of gestation) and a heterogeneous echogenicity of the anterior uterine wall in the range of 50 x 33 mm. TVUS was repeated a few days later and found that the placenta was at the posterior wall, indicating a successful pregnancy.

Case 2

A second case was Ms. S.Z., who was 42 years old with no history of pregnancy and childbirth. S.Z. has been undergoing assisted reproduction in our hospital since 2021 for infertility and advanced age. Her CA125 was abnormal, with a value of 245.7 U/mL. 3D-TVUS (Fig. 4a) showed a uterine size of 66 x 73 x 58 mm, with normal uterine cavity morphology (Fig. 4b). There was an intermural fibroid in the anterior wall of the uterus, measuring 29 x 27 x 25 mm. Echo heterogenicity of the uterus involves the external myometrium, about 17-mm thick. The echo heterogenicity of the posterior wall diffusely involved the internal and external myometrium, about 36 mm thick, with a score of 6, which was considered as adenomyosis foci. In addition, there was a mass measuring 40 x 38 x 33 mm in the left adnexa, which was considered a chocolate cyst. MRI (Fig. 5) was performed on the same day, showing a uterine size of 66 x 73 x 58 mm, with a normal uterine cavity. MRI confirmed adenomyosis of the anterior, posterior, bottom, and right wall of the uterus, and the thickness of the myometrium of the anterior wall was about 21 mm and that of the posterior wall was about 36 mm. It was recommended that her adenomyosis be treated before receiving IVF for pregnancy.

S.Z. was treated with three injections of GnRH-a. After the first injection, an ultrasound showed that the uterine size had shrunk to 56 x 61 x 54 mm, with a normal uterine cavity. Uneven echogenicity was diffusely involved in the external myometrium, with a posterior wall thickness of about 31 mm, an anterior wall thickness of about 12 mm, and a base wall thickness of about 19 mm, with a score of 3. The left adnexal mass was 38 x 31 x 25 mm in size, with a hairy wall and dense hairy glass-like dotted hypoechogenicity inside. CA125 value was reduced to 38.97

U/mL, which was still higher than the normal range. Considering that the disease was not yet well controlled, a third GnRH-a injection was administered. CA125 dropped to 18.98 U/mL, which was normal. 3D-TVUS (Fig. 4c) suggested that the uterine size was further reduced to 60 x 61 x 38 mm, with normal uterine cavity. The echo heterogenicity of the lesion in the uterus diffusely involved the outer muscular layers, with a base wall thickness of about 26 mm, a posterior wall thickness of about 27 mm, and a score of 3. As the condition was well controlled, HRT was started. Serum hormone levels were checked after conversion of the endometrium, showing an estradiol value of 162 pg/mL, and a progesterone value of 8.77 ng/mL, indicating that it was time to transplant the embryos. Two of her embryos (8C2G and 7C2G) were transplanted. A few days later, intrauterine pregnancy was confirmed by ultrasound as the NT (Fig. 6) showed live fetal pregnancy with placenta located in the anterior and bottom wall of the uterus.

Discussion

Both patients were treated with frozen embryo transfer after medical treatment for adenomyosis, resulting in successful pregnancies. We have learned some experiences to share. Firstly, the two successful cases may suggest that a combination of 3D-TVUS, MRI, and CA125 testing is helping in developing pregnancy strategies in adenomyosis patients with infertility. The three methods allow the reproductive physician to know the patient's conditions, especially the locations of the lesions and the uterine cavity's morphology. After a thorough evaluation, the physician can decide whether conservative medical treatment is sufficient for a favorable pregnancy outcome. Secondly, adenomyosis lesions within the external muscular layers may have little impact on embryonic implantation and growth, thus GnRH-a and HRT therapy are better choices for patients with adenomyosis. Both patients' pre-operative imaging indicates diffuse adenomyosis lesions in the external myometrium. The first patient's NT showed that the placenta was in the posterior wall of the uterus, and the fetus developed normally. This indicates that adenomyosis of the external myometrium may not affect the implantation of the embryo and placental blood supplies if adenomyosis is controlled by medical treatment. These considerations may provide a basis for individualized therapy, which is currently preferred by the medical community. Patients suffering from adenomyosis should be evaluated before making a treatment plan using a combination of transvaginal ultrasound, MRI, and CA125 testing. If the adenomyosis lesions are in the external myometrium, surgery may not be necessary for the patient to prepare for ART.

We admit that we only report two cases here, the findings of which shall be validated with larger sample sizes. It is hoped that our experience with the two cases may be helpful to the patients and clinical workers to develop better clinical treatment in the future.

Figures:

Fig. 1C The normal morphology of J.H.'s uterine cavity

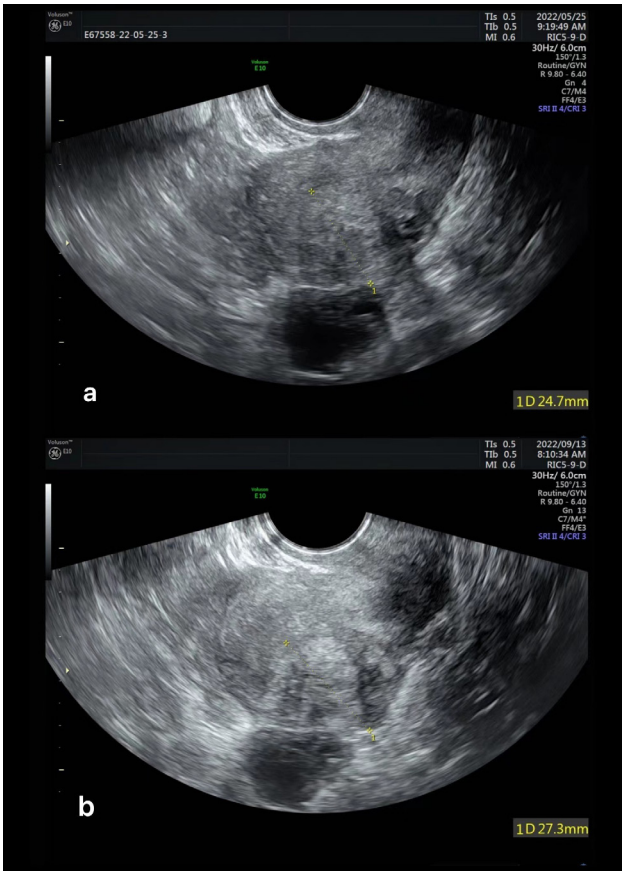


Fig. 1A & 1B The comparison of J.H.'s 3D-TVUS before (a) and after (b) treatment

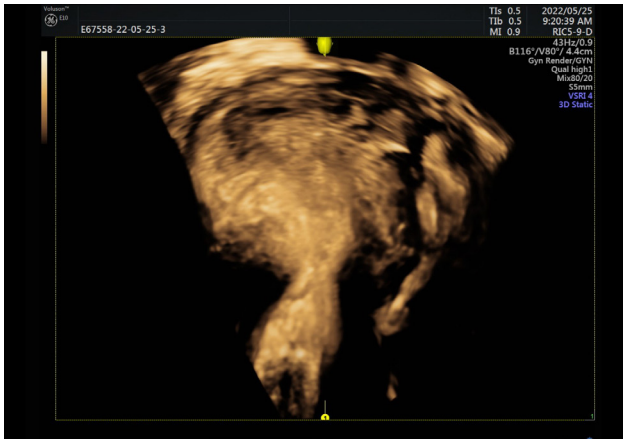


Fig. 2 The MRI of case 1

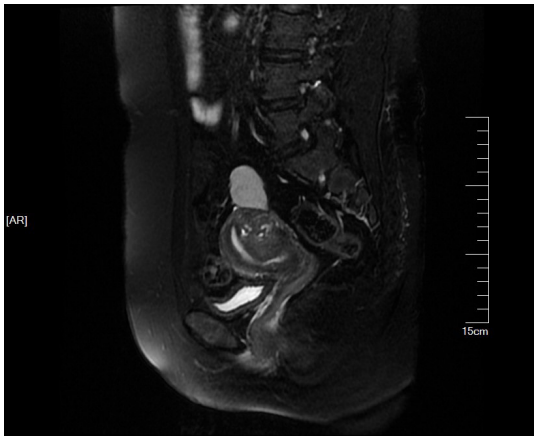


Fig. 3 The NT of Case 1

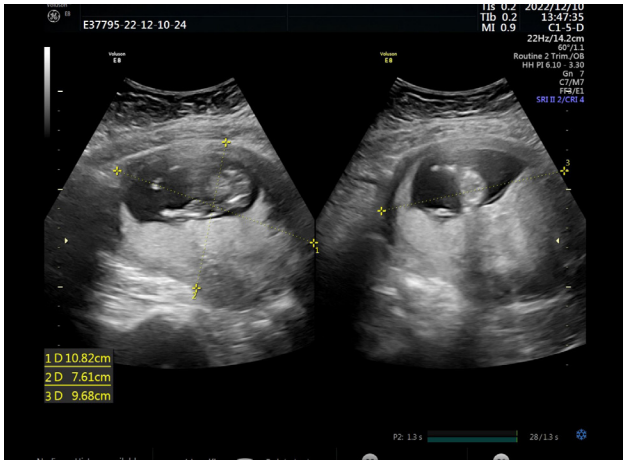
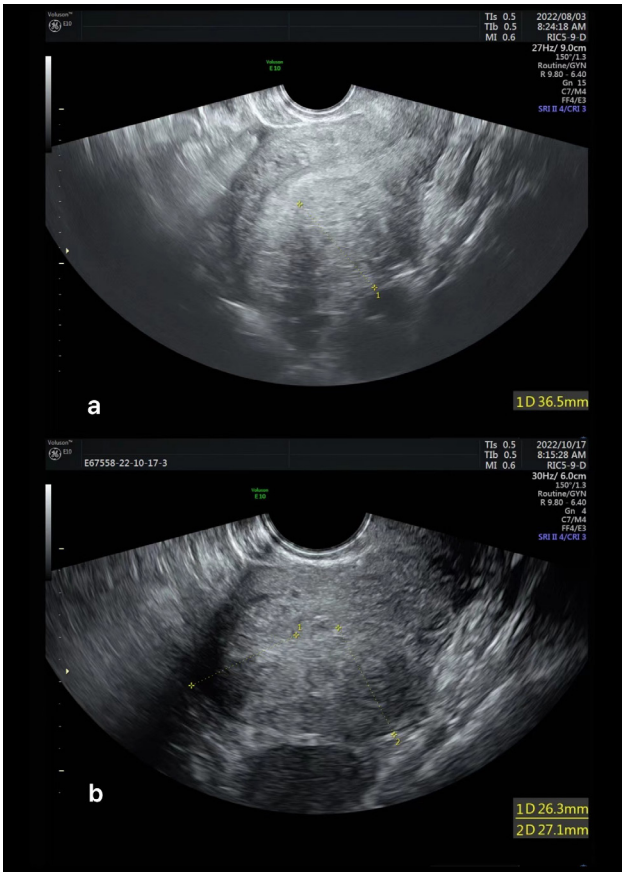


Fig. 4A & 4B The comparison of S.Z.'s 3D-TVUS before (a) and



after (b) treatment.

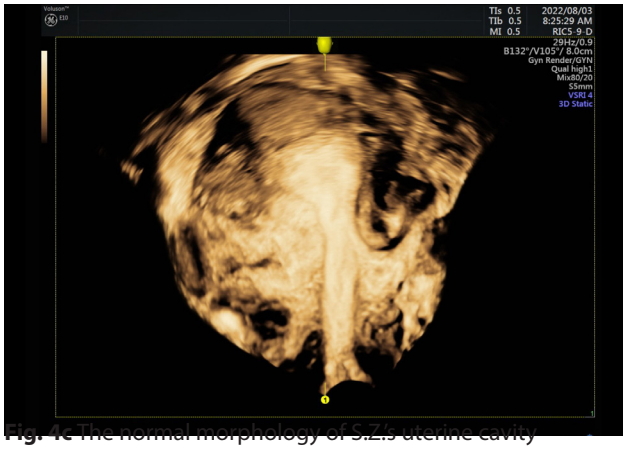
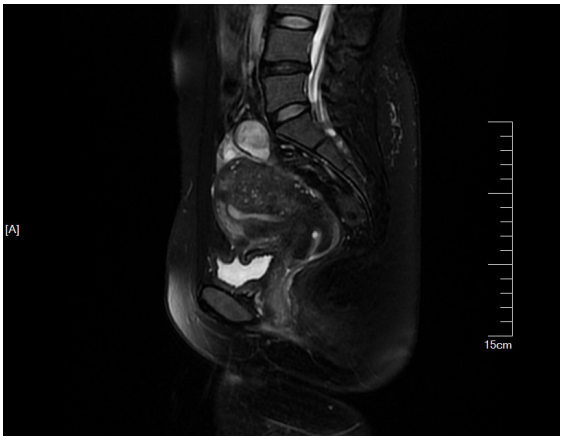


Fig. 4c The normal morphology of S.Z.'s uterine cavity

Fig. 5 The MRI of case 2



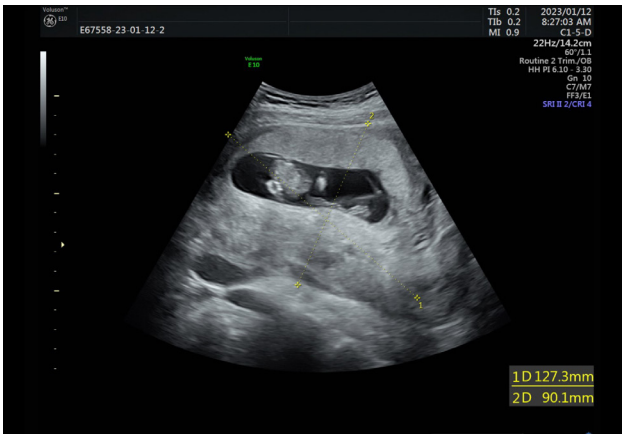


Fig. 6 The NT of case 2

lection, collation, and analysis of the cases, as well as writing the article. X.S. and J.Z. were involved in the collection and analysis of the cases, as well as instructions on writing articles. X.L. was involved in the collection and collation of the cases.

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Patient consent statement: Both patients listed have provided written consent.

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