

Treatment of cornual pregnancy in a patient with adenomyosis by high-intensity focused ultrasound (HIFU) ablation

A case report

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Abstract

Rationale: Cornual ectopic pregnancy in adenomyosis patients is a rare clinical condition, which may require careful approach for accurate diagnosis and treatment.

Patient concerns: A 38-year-old woman presented with amenorrhea for 8 weeks and serum HCG levels of 1455 mmol/L. The B ultrasound showed an endometrial thickness of 1.7 cm, and the presence of a cystic structure (16.6 mm) at the right uterine horn. Color Doppler flow imaging (CDFI) accurately detected and confirmed the position of the cystic structure with its clear boundaries.

Diagnoses: Cornual ectopic pregnancy in adenomyosis.

Interventions: The diagnosis was confirmed and treated by HIFU ablation. Total ablation was performed for 738 seconds without any bleeding.

Outcomes: Serum HCG levels decreased to <0.1 mmol/L after 60 days post operation, and follow-up for 11 months showed a regular menstrual cycle without dysmenorrhea. Gestational sac was not obvious at postoperative 90 days by MRI. The adenomyosis associated lesion with blood perfusion became smaller at postoperative 90 days.

Lessons: In this case, we successfully performed HIFU ablation and treated the cornual ectopic pregnancy in an adenomyosis patient for the first time, without any adverse complications.

Abbreviations: CDFI = color Doppler flow imaging, EMI = endometrial–myometrium interface, G2P1L1A1 = gestation twice and one birth, i.e. one live delivery and one abortion after an unplanned pregnancy, HIFU = high-intensity focused ultrasound, JZ = junction zone, LMP = last menstruation period.

Keywords: adenomyosis, cornual pregnancy, high-intensity focused ultrasound ablation

1. Introduction

Cornual pregnancy accounts for less than 3% of all ectopic pregnancies,^[1,2] and often poses a diagnostic and therapeutic challenge. Though the first successful noninvasive ultrasound aided diagnosis of unruptured cornual pregnancy was reported in 1983, the recently reported sensitivity of ultrasound diagnosis is only 26%.^[3] This may be due to the failure of conventional ultrasound in accurately diagnosing this rare condition. Other

factors may be the late clinical presentation at an average gestational age of 21 weeks, as well as the lack of definite diagnostic criteria.^[4] The currently adopted diagnostic criteria for cornual ectopic pregnancy were proposed by Jansen and Elliot.^[5]

The clinical presentation in a successfully diagnosed case of cornual pregnancy by laparotomy or ultrasonography may reveal the presence of an implanted blastocyst within the gestational sac in the uterine cornua, between the proximal part of the fallopian tube and uterine musculature, surrounded by a thin myometrial layer with increased vascularity.^[6] Unfortunately, 50% of cases are diagnosed following its rupture with massive hemorrhage and intra-abdominal bleeding that leads to uterine rupture, hemorrhagic shock, and death.^[7] The mortality rate reported is up to 2%.^[8,9] The common treatment of cornual pregnancy is cornual resection with uterus repair, negative pressure aspiration, conservative drug treatment, and ultrasound-guided puncture.

Adenomyosis of the uterus is a benign uterine disease commonly reported in multiparous women that are treated by hysterectomy. Frequently, it is also reported in nulligravid women and very rarely during pregnancy.^[10] Even though its prevalence rate is estimated at 5% to 70%, diagnosis of uterine adenomyosis by conventional ultrasonic methods is challenging,^[11] due to the lack of specific pathognomonic features.

The pathophysiology of uterine adenomyosis is characterized by invasion of endometrial glands and stromal cells in the uterine myometrium, most likely in areas of endometrial–myometrium interface (EMI) or the uterine junction zone (JZ).^[11] As

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adenomyosis leads to uterus enlargement, application of conventional abdominal ultrasound for the diagnosis and treatment of cornual ectopic pregnancy with other invasive and noninvasive techniques would be highly uncertain, which may delay treatment and prognosis. The clinical case described here was a complicated condition of cornual ectopic pregnancy in a patient suffering from adenomyosis. Coexistence of both conditions simultaneously may lead to misdiagnosis by ultrasound or MRI. Moreover, such cases are highly vulnerable to life threatening complications upon surgical intervention.

The complications involved include uterine rupture, profuse catastrophic hemorrhage with bleeding, and loss of childbearing capacity in case of hysterectomy.^[9] A large number of conservative noninvasive therapies are performed for preserving the uterus, but many of them are associated with decreased fertility and future complications. High-intensity focused ultrasound (HIFU) ablation, which was initially developed for the treatment of solid tumors, is now successfully implemented in the treatment of uterine fibroids and adenomyosis.^[12,13] Several studies have examined the safety profile of ultrasound-guided HIFU in treating patients with adenomyosis,^[14,15] besides sustaining long-term clinical improvements.^[16]

In this study, we present a case of cornual ectopic pregnancy, which was complicated by adenomyosis. Even though many cases of ectopic pregnancy in different sites have been treated by HIFU ablation, no cornual ectopic pregnancy cases with adenomyosis have been treated by this approach so far. Institutional Review Board (IRB)/Ethics Committee approval was obtained prior to this interventional study.

2. Case report

A 38-year-old married woman, with an obstetrical history of G2P1L1A1 (gestation twice and one birth, that is, one live delivery and one abortion after an unplanned pregnancy) was admitted to Weihai Maternity and Child Health Care Hospital on March 13, 2016. The patient had regular menstrual cycle after the menarche age of 14, with a slightly higher menstrual flow at normal times. The major complaints were amenorrhea for the last 48 days with back pain relieved on medication. The last menstruation period (LMP) started on January 24, 2016 with similar amounts and color as previous ones. Early pregnancy was confirmed by the patient herself with a urine test on March 4, 2016; serum HCG levels of 1455 mmol/L were reported after 2 days. Meanwhile, adenomyosis with an endometrial thickness of about 1.7 cm was revealed by B ultrasound examination.

Follow-up B ultrasound examination was conducted on March 14, 2016, and a cystic structure (16 × 6 mm) was observed at the right uterine horn with slightly hyper-echo intensity and low tension. The case was diagnosed as right cornual ectopic pregnancy with adenomyosis. Uterine aspiration was performed the next day under B ultrasound guidance. Before surgery, the patient was administered an intravenous injection of 75 mg pethidine and 25 mg chlorpromazine. There was no visible villus tissue in the aspirates, and decidual tissues were found by pathological examination. The B ultrasound examination was repeated 2 days after surgery, and revealed an enlarged uterus with unevenly distributed intramural parenchyma with enhanced intensities, especially at the posterior wall of the uterus. A cystic structure with a size of 16 × 12 mm was detected within the right side of myometrium and blood flow signal by color Doppler flow imaging (CDFI) at the boundary of the cystic structure. The lesion of the cornual pregnancy was located at the uterine horn, 10 mm to the

serosa and 18 mm to the uterine cavity. Serum HCG levels were retested and showed a slightly reduced value of 1325 mmol/L.

The diagnosis was confirmed. Routinely, laparotomy is performed to open the uterus, followed by lesion removal and suturing of the uterus. Since the current case was combined with adenomyosis, the uterus was large with a significantly thickened muscle layer, and traditional surgery might have caused high trauma that is unfavorable to muscle healing, and might also increase the risk of adenomyosis progression. Systemic drug therapy by methotrexate could also be administered; however, based on the patient's disease assessment, the success rate of this approach might be low, with the treatment cycle likely long. Therefore, after full explanation and communication with the patient, HIFU ablation was selected for the simultaneous treatment of cornual pregnancy and adenomyosis, and carried out on March 20, 2016. The drug preparation for the treatment included a combination of fentanyl (10 µg/mL) and midazolam (0.5 mg/mL). The patient was administered an intravenous injection of 6 mL fentanyl and 3.6 mL midazolam for 40 minutes intervals until treatment end. The HIFU treatment power was 400 W, for supply and ultrasound frequencies of 50 Hz and 1 MHz, respectively; HIFU was administered with a cycle of 1 second ablation/3 seconds rest (1:3 seconds), which was gradually increased to 1:2 seconds. The temperature in HIFU constantly fluctuates between 60 and 100°C. For a fixed focus, the temperature rises with ablation time, but would not exceed 100°C. The temperature also decreases with increasing focus distance, and the temperature on skin is around 40°C. The adenomyosis at the right posterior side of the uterus was treated first, followed with the right cornual pregnancy. Total ablation was performed for 738 seconds without any bleeding. The area around the cystic structure of cornual pregnancy showed nonperfusion volume ratio, which was estimated to be approximately 80% (Fig. 1A–D). The local and whole intensity at the original adenomyosis and cornual pregnancy was satisfactory; no obvious blood supply was revealed by postoperative MRI of the adenomyosis and cornual pregnancy location, and the effect of HIFU ablation was satisfactory (Fig. 2A and B).

The patient complained of slight abdominal falling pain after 8 hours of treatment without sacral pain, vaginal bleeding, lower limb radiation pain, or skin burns, and the falling pain was relieved after 8 hours. Serum HCG levels at postoperative day 1 were 2887 mmol/L, and decreased to 682 mmol/L, 397 mmol/L, 77 mmol/L, and <0.1 mmol/L at 10, 20, 47, and 60 days postoperatively, respectively. The patient had menstruation 30 days postoperatively, with relief from dysmenorrhea. Moreover, there was no obvious cystic structure detected by MRI at the right uterine horn on the 90th postoperative day (Fig. 2C and D). Follow-up was continued for 11 months, and showed regular menstrual cycle without dysmenorrhea. The patient had no requirement for pregnancy.

3. Discussion

Cornual ectopic pregnancy is a rare condition,^[3] which is mainly manifested as amenorrhea, abdominal pain, and vaginal bleeding. The B ultrasound examination is usually preferred for the diagnosis of cornual pregnancy, and is further assisted by hysteroscopy and laparoscopy. Cornual pregnancy is an abnormal ectopic pregnancy condition, where the fertilized egg is implanted at the uterine horn or the uterine cavity close to the fallopian tube.^[17] The uterine horn is extremely vulnerable for rupture, because the myometrium in this region is relatively thin

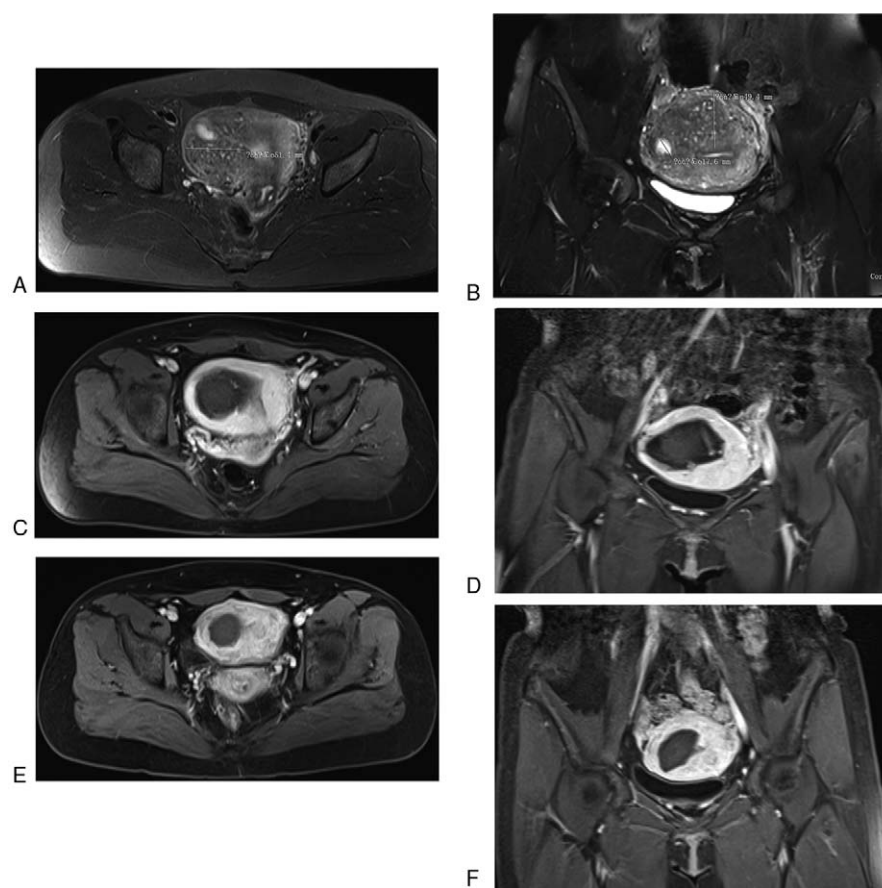


Figure 1. MR image obtained from the adenomyosis patient with cornual pregnancy. (A) Transverse and (B) coronal views of preoperative T2-weighted images showing diffused thickening of the low signal junction zone at the posterior wall of the uterus, with volumes of the adenomyotic and cornual pregnancy sac lesions. (C/E) Transverse and (D/F) coronal views of postoperative T1-weighted contrast enhanced images showing the nonperfused region at the posterior wall of the uterus at post-HIFU (C/D) and 3 months after HIFU (D/F). HIFU=high-intensity focused ultrasound, MR=magnetic resonance.

and weak. Moreover, hemorrhagic complications are much more frequent in this uterine area, where the uterine and ovarian arteries join each other.

Conventional therapeutic methods for cornual pregnancy include open or laparoscopic surgery to remove pregnancy lesions, which may result in pelvic adhesion and eventually destroy the integrity of the uterine horn by incision and suture during embryo removal and hemostasis. Conservative methods, such as drug treatment, have the shortcoming of long course and potential failure, switching toward surgery. Other methods rarely utilized in the clinical practice include local injection to remove the embryo under vaginal ultrasound guidance, uterine aspiration guided by vaginal ultrasound, and uterine artery embolization. HIFU ablation is a noninvasive therapy, which could make the *in vitro* low-energy ultrasound to be focused selectively on target tissues in the body, and induce coagulative necrosis through thermal, cavitation, and mechanical effects, sparing the adjacent normal tissues.

The rhesus monkey model at the middle to late stage of pregnancy was tested initially with high intensity focused ultrasound irradiation on the uterus, and a repeat pregnancy induction was attempted and studied by Zhibiao et al.^[18] It was confirmed that HIFU could terminate early pregnancy with no obvious adverse effects on the repeat pregnancy. However, since the current methods employed in clinical practice for termination of normal pregnancy are adequate with the advantages of easy operation, safety, and high effectiveness, there is no report

assessing the use of HIFU for termination of normal pregnancy. On the other hand, HIFU ablation was performed to treat 20 cesarean scar pregnancies by Xiao et al.,^[19] all the patients were cured, with complications such as persistent bleeding or uterine rupture. These studies indicated the feasibility of HIFU for the treatment of pregnancy lesions, although no report of its application for patients with cornual pregnancy is available.

In the current report, HIFU ablation was performed for the treatment of cornual pregnancy. The diagnosis was confirmed by both the preoperative B ultrasound examination and MRI. The particularity of this case was the concurrent adenomyosis, which was located at the right posterior wall of the uterus. This distant location of the cornual pregnancy lesion leads to the failure of uterine aspiration with ultrasound monitoring. Meanwhile, it was noticed that the cornual pregnancy lesion was wrapped within the adenomyosis; thus neither B ultrasound nor MRI could indicate the presence of the pregnancy lesion protruding to the uterine serosal surface. At this stage, performing open abdominal surgery or laparoscopic surgery was difficult and not highly recommended, because it could induce large injury to the uterus. Therefore, HIFU was selected as an alternative treatment for this patient. A 2 months follow-up examination was suggested, and postoperative serum HCG levels were significantly decreased and returned to the nonpregnant levels within 60 days. The menstrual cycle was restored one month after operation, and dysmenorrhea was ameliorated. MRI performed after 3 months confirmed complete recovery without any obvious

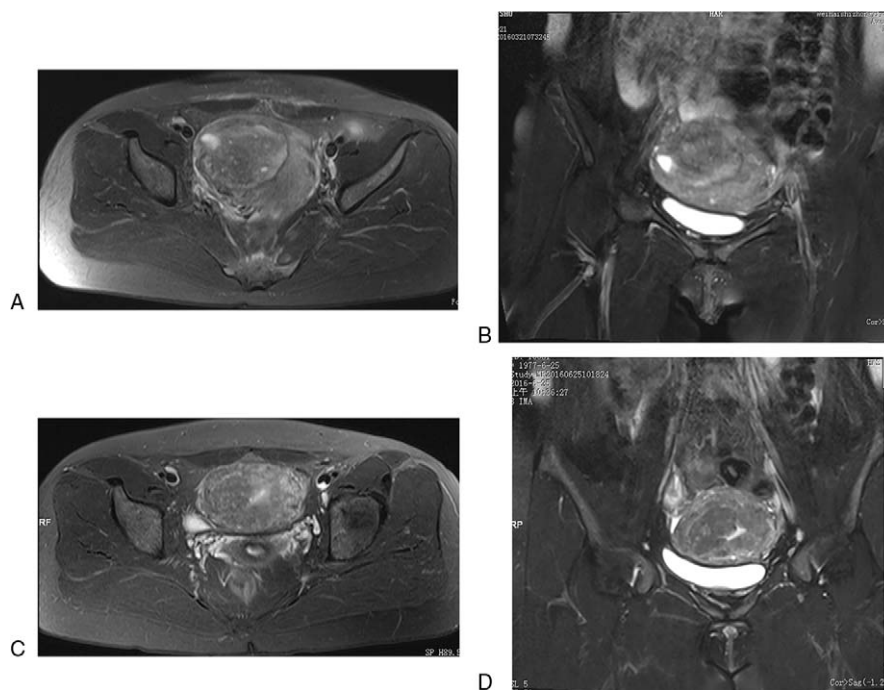


Figure 2. MR image obtained from the adenomyosis patient with cornual pregnancy after HIFU treatment. (A) Transverse and (B) coronal views of postoperative T2-weighted images showing the effects of local and whole intensity perfusion at the site of adenomyosis and cornual pregnancy. (C) Transverse and (D) coronal views of post procedural T2-weighted images showing no obvious blood supply at the site 3 months after HIFU. HIFU=high-intensity focused ultrasound, MR=magnetic resonance.

sign of cystic structure at the right uterine horn, indicating the effectiveness of HIFU treatment in this case.

As cornual pregnancy with adenomyosis is very rare, a comparative analysis was not possible. Moreover, as the current patient did not want to conceive again, the real study outcome regarding the restoration of patient's ability for child bearing could not be evaluated, even though the normal menstrual cycle was restored after the intervention.

4. Conclusion

There are multiple therapeutic methods for the treatment and management of cornual ectopic pregnancy, which could lead to diverse therapeutic effects in patients. Currently, there is lack of unified treatment guidelines in clinical practice toward cornual ectopic pregnancy with adenomyosis. The treatment method is usually determined by clinical practitioners, according to their comprehensive analysis of specific clinical manifestations and the results of relevant examinations, with the requirement for future childbearing ability. HIFU is a novel noninvasive therapeutic method, and the feasibility of this technique in treating cornual ectopic pregnancy complicated with adenomyosis was successfully demonstrated through this case. However, long-term post-treatment follow-up for sustainable efficacy and safety profile is required with a large sample size study.

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