Case Report

Integrating High-intensity Focused Ultrasound with Chemotherapy for the Treatment of Invasive Hydatidiform Mole in Reproductive-age Women

Yongmiao Pan[1], Kaiqing Lin[2], Ying Hu[3], Xiaohong Song[1]*, Linjun Xu[3], Zhenfeng Zhou[4], Di Xie[5], Yuan Xue[5]

Departments of [1]Obstetrics and Gynecology and [4]Anesthesiology, Hangzhou Women's Hospital, [2]Department of Obstetrics and Gynecology, Hangzhou Red Cross Hospital, [3]Department of Surgery, Hangzhou Women's Hospital (Hangzhou Maternity and Child Health Care Hospital), Hangzhou, [5]Department of Gynecological, Chengdu Focused Ultrasound Hospital, Chengdu, China

Abstract

Invasive hydatidiform mole, a form of gestational trophoblastic neoplasm in reproductive-age women, poses a significant threat to life due to its associated signs and symptoms. This case report details the management of a 24-year-old Chinese woman with no prior pregnancy history, who presented at our hospital 23 days postcurettage, experiencing persistent vaginal bleeding for 3 days. While two rounds of chemotherapy effectively reduced human chorionic gonadotropin levels, a subsequent magnetic resonance imaging (MRI) revealed suspicious growth lesions in the uterus. High-intensity focused ultrasound (HIFU) treatment was administered under ultrasound guidance, resulting in notable grayscale changes to optimize the efficacy of chemotherapy and restrict lesion progression. Subsequent ultrasound and MRI assessments during follow-up demonstrated a transparent texture in the muscle layer at the lesion site. This case suggests that the combination of chemotherapy and HIFU, guided by ultrasound, may represent a promising therapeutic approach for managing invasive hydatidiform mole.

Keywords: Chemotherapy, high-intensity focused ultrasound ablation, invasive hydatidiform mole

Introduction

Malignant invasive staphyloma is a gestational trophoblastic neoplasm (GTN) characterized by an abnormal proliferation of trophoblastic tissue with a documented incidence of 0.01/1000.[1,2] Invasive hydatidiform mole is a type of abnormal growth of placental tissue that can spread to the uterus, blood vessels, and other organs.[3]

Diagnosis and risk stratification are guided by the International Federation of Gynecology and Obstetrics (FIGO) criteria established in 2000.[4] FIGO staging categorizes patients into low- and high-risk groups based on disease extent and a scoring system. Those with FIGO stage I and II-III disease and a score <7 are classified as low risk for GTN. Low-risk GTN can be effectively treated with single-agent chemotherapy, including methotrexate (MTX) or actinomycin-D (Act-D), with primary remission rates ranging from 50% to 90%, dependent on the dose administered.[5,6] In contrast, patients with a FIGO score ≥7 are deemed high risk, necessitating the use of combination chemotherapy regimens such as etoposide, MTX, Act-D, cyclophosphamide, and vincristine.[5,6]

High-intensity focused ultrasound (HIFU) emerges as a noninvasive surgical modality utilizing ultrasound to induce coagulation and cellular necrosis in pathological tissues.[7] Extensive studies have showcased the efficacy and safety of HIFU in treating various solid tumors, including

Article History:
Submitted: 14-Jul-2023
Revised: 26-Nov-2023
Accepted: 08-Dec-2023
Published: 18-Jul-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/gmit

DOI: 10.4103/gmit.gmit_86_23

Address for correspondence: Dr. Xiaohong Song, Department of Obstetrics and Gynecology, Hangzhou Women's Hospital, Hangzhou, China.
E-mail: songxh8866@163.com

How to cite this article: Pan Y, Lin K, Hu Y, Song X, Xu L, Zhou Z, *et al*. Integrating high-intensity focused ultrasound with chemotherapy for the treatment of invasive hydatidiform mole in reproductive-age women. Gynecol Minim Invasive Ther 2024;13:184-8.

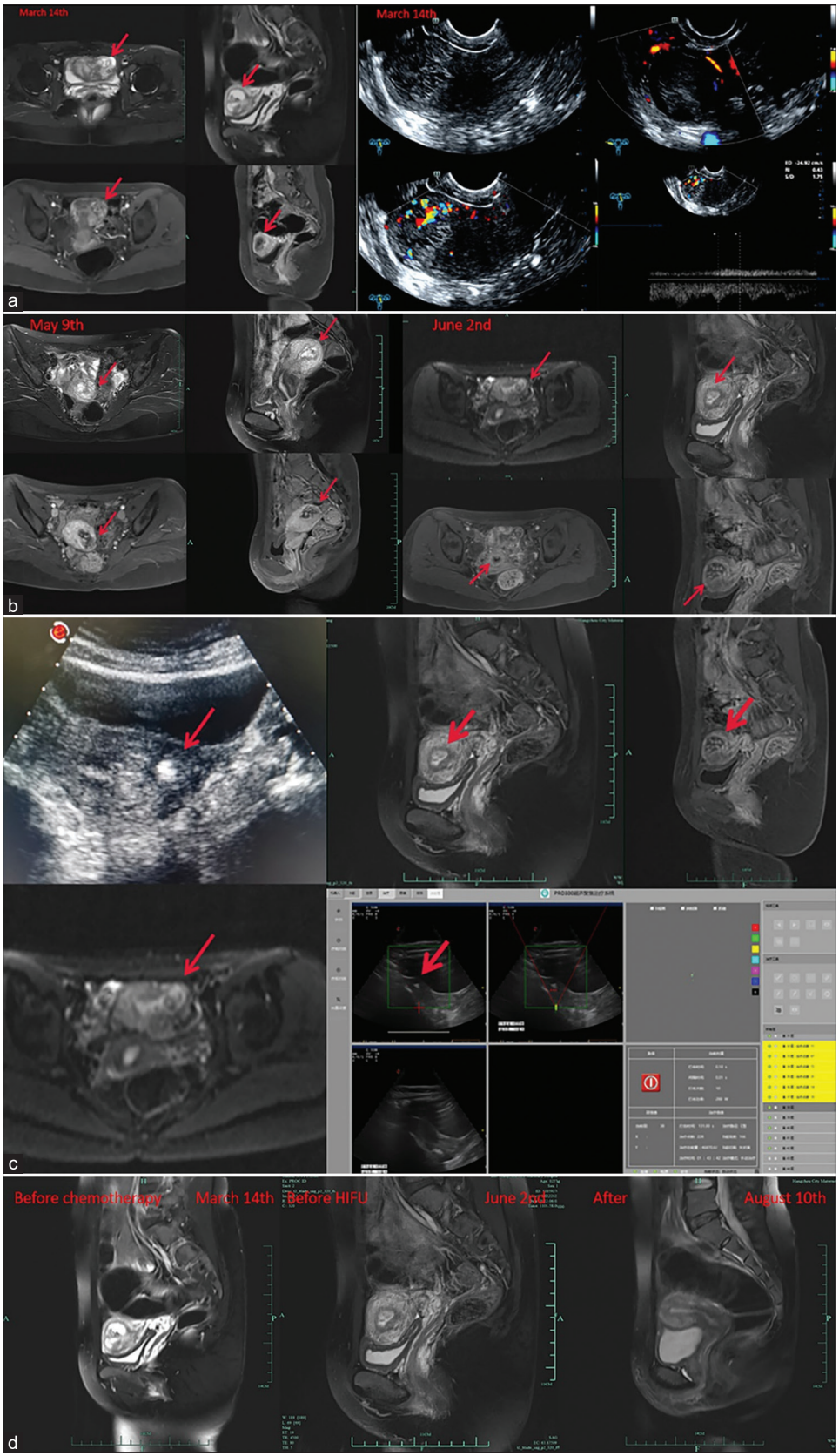

Figure 1: Imaging changes in the uterus of the woman during treatment. Red arrows indicate lesions. (a) The image before the treatment. (b) The image after chemotherapy and before high-intensity focused ultrasound. T2 shouws visible lesion approaching the serosal layer. (c) Images during the treatment process. The area with increased grayscale is consistent with the location of the magnetic resonance imaging (MRI) lesion. (d) The changes of uterus in the MRI during the treatment process. HIFU: High-intensity focused ultrasound

prostate cancer, liver tumors, recurrent ovarian cancer, and metastatic pelvic tumors.[8-10] HIFU has also been used to treat uterine fibroids, adenomyosis, and abdominal wall endometriosis.[11-14] Notably, HIFU has demonstrated positive outcomes in preserving postoperative fertility in women treated for uterine fibroids, leading to successful pregnancies and shorter pregnancy cycles.[15-19]

This case report presents an illustrative example of a woman diagnosed with an invasive hydatidiform mole. Despite encountering suspicious growth lesions during chemotherapy, she retained both her intact endometrium and fertility following treatment with HIFU. This case emphasizes the potential of HIFU in preserving reproductive function amid the challenges posed by invasive hydatidiform mole.

This comprehensive exploration underscores the significance of integrating innovative and noninvasive approaches, such as HIFU, into the therapeutic landscape for GTN, particularly in cases with fertility preservation considerations.

Case Report

A 24-year-old Chinese woman with no previous pregnancy history underwent curettage on February 18, 2022. She presented to our hospital on March 15 of the same year, complaining of "Vaginal bleeding for 3 days, 23 days after the curettage."

T2-weighted fat suppression sequence magnetic resonance imaging (MRI) showed the lesions' range in the uterus's posterior wall on March 14, 2022. Transvaginal sonography of the uterus before chemotherapy showed lesions in the uterine cavity of the left rear uterine fundus. The size of the lesion was about 3.6 cm × 2.8 cm × 3.0 cm. Doppler Ultrasound blood flow signal showed extensive vascular organization within the lesion. RI = 0.43 indicates rich blood flow and low resistance. Figure 1a shows that nuclear magnetic resonance has advantages in image resolution, while color Doppler ultrasound has more advantages in blood flow signals.

From March 14, 2022, to May 24, 2022, blood human chorionic gonadotropin (HCG) levels were tested weekly. After two phases of chemotherapy, there were significant gastrointestinal reactions and mouth and lip ulcers, so the dose of MTX was adjusted to 15 mg intramuscularly. After changing the MTX dose, the woman underwent four additional phases of chemotherapy.

However, on May 9th of the same year, MRI revealed a significant reduction in the size of the lesion in the uterine compared to before chemotherapy, with a length of 1.95 cm × 1.89 cm × 3.11 cm. However, on the June 2nd follow-up MRI, the lesion size in the uterine cavity showed a slight increase compared to the May 9th MRI, with a length of 2.6 cm × 2.6 cm × 1.8 cm. It also indicated that the lesion was invading and growing toward the serous layer, with the thinnest part of the serous membrane being about 0.10 cm [Figure 1b].

To limit lesions' growth and enhance MTX's effectiveness, it was decided to undergo focused ultrasound ablation treatment. The HCG decline curve is shown in Figure 2a.

MRI in this woman suggested a shortened distance between the lesion and the plasma layer. MRI indicated that the lesion boundary was unclear from the plasma boundary, so HIFU treatment was feasible. The Cobot HIFU System Pro300 (Shenzhen PRO HIFU Technology Co.) was used for the June 2 treatment. It has a frequency of 1.25 MHz. depth of focus 13 cm. acoustic power 220w-350W. ultrasonic emission parameters: pulse duration Pulse duration: T1: 0.1 seconds, interval time T2: 0.1 seconds. The woman lies supine on the HIFU surgical bed, and a circular transducer containing bubble-free water is placed close to her lower abdomen to keep the intestines away from the pathway.

In combination with ultrasound and MRI, the location of the lesion was determined, and the dose was used as W: 280 w, T1: 0.1 s, T2: 0.1 s. The lesion in the uterine with necrosis was evident, where the gray value increased significantly, and

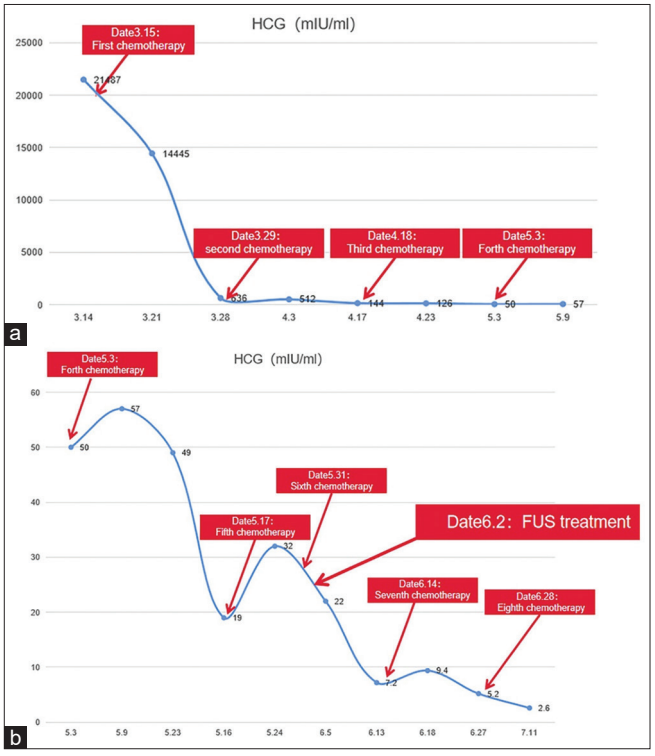

Figure 2: The woman's serum human chorionic gonadotropin (HCG) changes during treatment. Red arrows indicate lesions. (a) Satisfactory decrease in serum HCG value. (b) Surem HCG change after high-intensity focused ultrasound. HCG: Human chorionic gonadotropin, FUS: Focused ultrasound

the mission had a massive internal echo. The area where the ultrasound grayscale value increases is consistent with the location of the MRI lesion, as shown in Figure 1c.

Significant strong echogenic graying occurred at only 131 s. The lesion was ablated at about 151 s, and the treatment was stopped, for the lesion was ablated to a satisfactory extent.

After HIFU treatment, MTX treatment continued, and the woman was rechecked for HCG every week until 6–27 when her HCG had decreased to 5.2 mIU/mL. The HCG decline curve is shown in Figure 2b.

After 3 months of HIFU treatment, an MRI reexamination showed that the lesion had further shrunk, and there was no significant internal perfusion. Six months after HIFU treatment, MRI reexamination showed no abnormal signal in the uterine cavity, the movement in the myometrium was expected, and color B ultrasound showed that the texture of the myometrium at the focus was clear. Figure 1d shows the changes in the MRI uterus during the treatment process.

Discussion and Conclusions

While HIFU has been employed in certain cases of gestational trophoblastic tumors with persistent lesions, particularly in instances of impaired liver function and intrauterine damage to the ovarian reserve hindering continued chemotherapy,[20] our case represents a unique scenario of invasive hydatidiform mole. To our knowledge, there are no reported instances in the literature of invasive hydatidiform mole with satisfactory results in chemotherapy and lesions exhibiting suspicious growth being successfully treated with HIFU.

The patient, in this case, classified as FIGO stage I with a score <7, underwent an intramuscular chemotherapy regimen of MTX at 20 mg, staged for 5 days at a time. However, data suggest that intramuscular MTX may be less effective than intravenous administration, with remission rates ranging from 49% to 74%.[21] Moreover, a prospective study of 147 women with low-risk GTN revealed that a FIGO score ≥4 was associated with an increased risk of 5-day MTX tolerance,[22] possibly explaining the observed growth of the intrauterine lesion in our case.

Invasive hydatidiform mole typically exhibits cystic characteristics with visible flow-controlled vascular shadows on MRI due to high hormone secretion by trophoblast cells, resulting in substantial vascular heterogeneity. Despite a satisfactory decrease in HCG levels and the gradual collapse of the MRI lesion, suspicious invasive growth behavior persisted at the lesion border. This observation prompted the consideration of HIFU treatment, aiming for disease prevention and the preservation of the patient's fertility.

HIFU therapy, chosen in this case due to the patient's nulliparity, offered the advantage of complete ablation of the solid portion of the lesion while ensuring the integrity of the patient's endothelium. Although HIFU alone can address solid lesions, the combination with prior MTX treatment created favorable conditions for subsequent HIFU lesion ablation.

Our findings suggest that HIFU therapy emerges as a viable alternative for patients with invasive hydatidiform mole who present challenges such as chemoresistance or suspicious lesion growth. Notably, the coagulative necrosis of the ablated lesion holds significant implications for enhancing patient prognosis, facilitating disease recovery, and, crucially, preserving the complete endometrium and the fertility of patients with reproductive aspirations. This case, with its high repeatability potential, underscores the need for further exploration and investigation into applying HIFU in similar cases, contributing to the evolving landscape of therapeutic options for GTN.

Declaration of patient consent

This study is approved with waived informed consent by the Research Ethics Committee by Hangzhou Women's Hospital (approval no.092).

Author Contributions

Yongmiao Pan – Study protocol, literature review, data collection, results analysis, and manuscript drafting. Kaiqing – Study protocol, data collection. Ying Hu manuscript drafting. Xiaohong Song – Study protocol, data collection, manuscript drafting, and corresponding author. Zhenfeng Zhou – Study protocol, data collection, statistical analysis, drafting manuscript drafting Linjun Xu, and Zhenfeng Zhou – Bias evaluation, manuscript review, and study supervision. Di Xie – Bias evaluation, manuscript review, and study supervision. Yuan Xue – Bias evaluation, manuscript review, and study supervision. All authors have read and agreed to the published version of the manuscript.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Seckl MJ, Sebire NJ, Fisher RA, Golfier F, Massuger L, Sessa C, *et al.* Gestational trophoblastic disease: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24 Suppl 6:i39-50.
2. Lok C, Frijstein M, van Trommel N. Clinical presentation and diagnosis of gestational trophoblastic disease. Best Pract Res Clin Obstet Gynaecol 2021;74:42-52.
3. Abu-Rustum NR, Yashar CM, Bean S, Bradley K, Campos SM,

Chon HS, *et al.* Gestational trophoblastic neoplasia, version 2.2019, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2019;17:1374-91.
4. FIGO Oncology Committee. FIGO staging for gestational trophoblastic neoplasia 2000. FIGO oncology committee. Int J Gynaecol Obstet 2002;77:285-7.
5. Seckl MJ, Sebire NJ, Fisher RA, Golfier F, Massuger L, Sessa C, *et al.* Gestational trophoblastic disease: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24 Suppl 6:i39-50.
6. Lurain JR. Gestational trophoblastic disease II: Classification and management of gestational trophoblastic neoplasia. Am J Obstet Gynecol 2011;204:11-8.
7. Cheung VYT. High-intensity focused ultrasound therapy. Best Pract Res Clin Obstet Gynaecol 2018;46:74-83.
8. Guillaumier S, Peters M, Arya M, Afzal N, Charman S, Dudderidge T, *et al*. A multicentre study of 5-year outcomes following focal therapy in treating clinically significant nonmetastatic prostate cancer. Eur Urol 2018;74:422-9.
9. Gu L, Shen Z, Ji L, Ng DM, Du N, He N, *et al.* High-intensity focused ultrasound alone or combined with transcatheter arterial chemoembolization for the treatment of hepatocellular carcinoma with unsuitable indications for hepatectomy and radiofrequency ablation: A phase II clinical trial. Surg Endosc 2022;36:1857-67.
10. Lei T, Guo X, Gong C, Chen X, Ran F, He Y, *et al.* High-intensity focused ultrasound ablation in the treatment of recurrent ovary cancer and metastatic pelvic tumors: A feasibility study. Int J Hyperthermia 2021;38:282-7.
11. Nguyen MD. Magnetic resonance imaging-guided high-intensity focused ultrasound ablation for endometriosis of the abdominal wall. Gynecol Minim Invasive Ther 2020;9:45-6.
12. Shun Wong FW, Li TK. Noninvasive high-intensity focused ultrasound surgeries for fibroids and adenomyosis during COVID-19 pandemic in Hong Kong: A gynecologist's viewpoint. Gynecol Minim Invasive Ther 2021;10:272-3.
13. Jindal S, Jung J, Lee K, Chern B. High-intensity focused ultrasound for the treatment of fibroids: A single-center experience in Singapore. Gynecol Minim Invasive Ther 2023;12:15-25.
14. Lee KW, Lee CL. An alternative treatment for uterine fibroids and adenomyosis: High-intensity focused ultrasound. Gynecol Minim Invasive Ther 2023;12:61-3.
15. Jiang Z, Li Q, Li W, Zhu X, Jiang J, Chen L, *et al*. A comparative analysis of pregnancy outcomes of patients with uterine fibroids after high intensity focused ultrasound ablation and laparoscopic myomectomy: A retrospective study. Int J Hyperthermia 2021;38:79-84.
16. Wu G, Li R, He M, Pu Y, Wang J, Chen J, *et al*. A comparison of the pregnancy outcomes between ultrasound-guided high-intensity focused ultrasound ablation and laparoscopic myomectomy for uterine fibroids: A comparative study. Int J Hyperthermia 2020;37:617-23.
17. Huang YF, Deng J, Wei XL, Sun X, Xue M, Zhu XG, *et al*. A comparison of reproductive outcomes of patients with adenomyosis and infertility treated with high-intensity focused ultrasound and laparoscopic excision. Int J Hyperthermia 2020;37:301-7.
18. Torres-de la Roche LA, Rafiq S, Devassy R, Verhoeven HC, Becker S, De Wilde RL. Should ultrasound-guided high frequency focused ultrasound be considered as an alternative non-surgical treatment of uterine fibroids in non-Asiatic countries? An Opinion Paper. J Clin Med 2022;11:839.
19. Yu PH, Wu YH, Chen TS, Kuo TC, Wu MH. Segmentation of *in vitro* fertilization with high-intensity focused ultrasound in repeated implantation failure with adenomyosis. Gynecol Minim Invasive Ther 2023;12:109-12.
20. Qu D, Chen Y, Jiang J, Shi Q, Zhou H, Wang Z. Long-term outcome of ultrasound-guided focused ultrasound ablation for gestational trophoblastic neoplasia in the cesarean scar: A case report. BMC Womens Health 2022;22:522.
21. Lawrie TA, Alazzam M, Tidy J, Hancock BW, Osborne R. First-line chemotherapy in low-risk gestational trophoblastic neoplasia. Cochrane Database Syst Rev 2016;2016:CD007102.
22. Qin J, Zhang S, Poon L, Pan Z, Luo J, Yu N, *et al.* Doppler-based predictive model for methotrexate resistance in low-risk gestational trophoblastic neoplasia with myometrial invasion: Prospective study of 147 patients. Ultrasound Obstet Gynecol 2021;57:829-39.