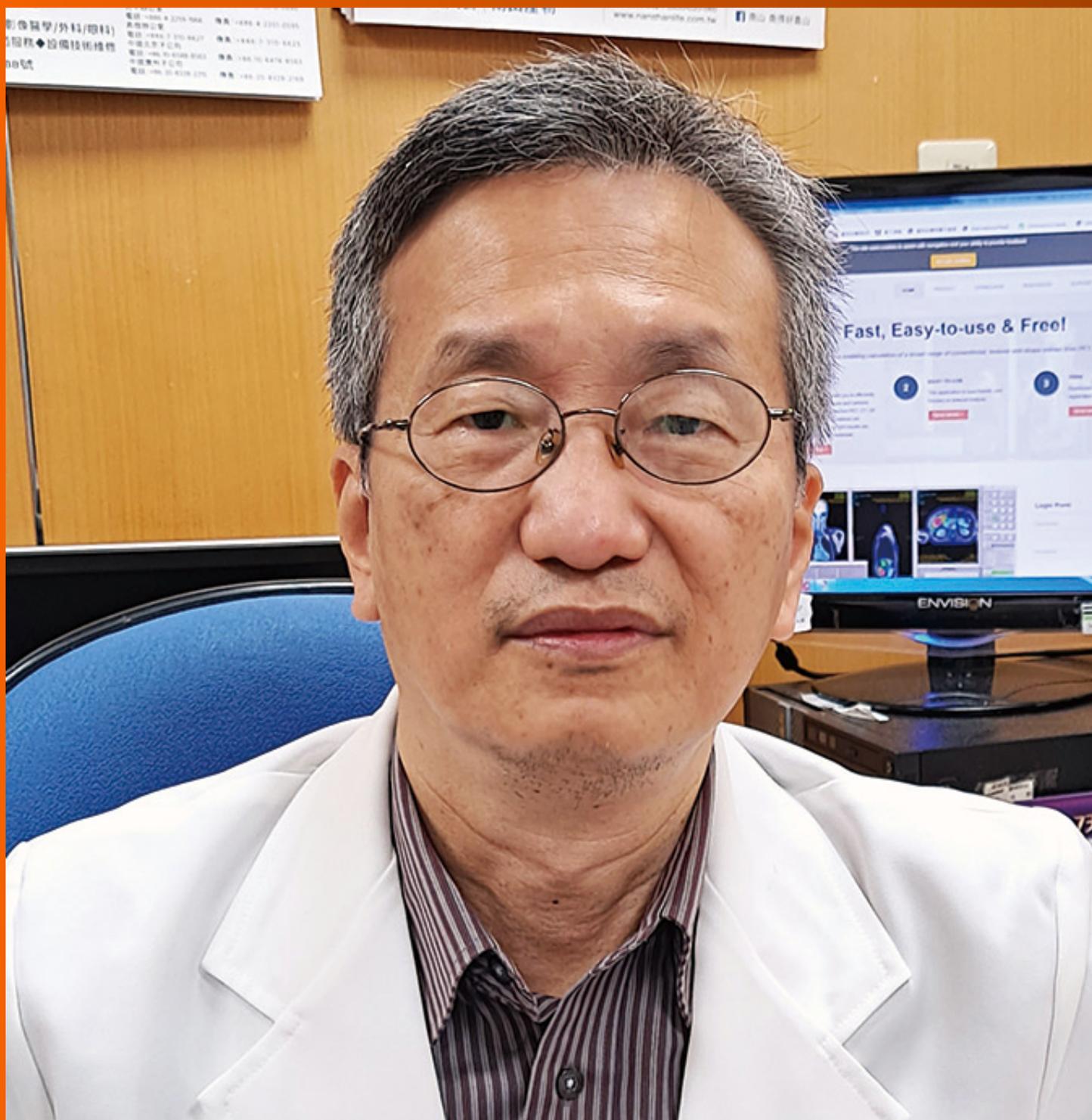


World Journal of *Clinical Cases*

World J Clin Cases 2022 April 16; 10(11): 3321-3638



REVIEW

- 3321 Encouraging specific biomarkers-based therapeutic strategies for hepatocellular carcinoma
Yao M, Yang JL, Wang DF, Wang L, Chen Y, Yao DF

ORIGINAL ARTICLE**Clinical and Translational Research**

- 3334 Autophagy-related long non-coding RNA prognostic model predicts prognosis and survival of melanoma patients
Qiu Y, Wang HT, Zheng XF, Huang X, Meng JZ, Huang JP, Wen ZP, Yao J
- 3352 Identification of circ_0000375 and circ_0011536 as novel diagnostic biomarkers of colorectal cancer
Yin TF, Du SY, Zhao DY, Sun XZ, Zhou YC, Wang QQ, Zhou GYJ, Yao SK

Retrospective Study

- 3369 Echocardiography in the diagnosis of Shone's complex and analysis of the causes for missed diagnosis and misdiagnosis
Li YD, Meng H, Pang KJ, Li MZ, Xu N, Wang H, Li SJ, Yan J
- 3379 Predictors and prognostic impact of post-operative atrial fibrillation in patients with hip fracture surgery
Bae SJ, Kwon CH, Kim TY, Chang H, Kim BS, Kim SH, Kim HJ
- 3389 Added value of systemic inflammation markers for monitoring response to neoadjuvant chemotherapy in breast cancer patients
Ke ZR, Chen W, Li MX, Wu S, Jin LT, Wang TJ
- 3401 Washed microbiota transplantation reduces serum uric acid levels in patients with hyperuricaemia
Cai JR, Chen XW, He YJ, Wu B, Zhang M, Wu LH

Clinical Trials Study

- 3414 Concurrent chemoradiotherapy using gemcitabine and nedaplatin in recurrent or locally advanced head and neck squamous cell carcinoma
Huo RX, Jin YY, Zhuo YX, Ji XT, Cui Y, Wu XJ, Wang YJ, Zhang L, Zhang WH, Cai YM, Zheng CC, Cui RX, Wang QY, Sun Z, Wang FW

META-ANALYSIS

- 3426 Effect of enhanced recovery after surgery on inflammatory bowel disease surgery: A meta-analysis
Peng D, Cheng YX, Tao W, Tang H, Ji GY
- 3436 Accuracy of ultrasound elastography for predicting breast cancer response to neoadjuvant chemotherapy: A systematic review and meta-analysis
Chen W, Fang LX, Chen HL, Zheng JH

- 3449 Association of chronic obstructive pulmonary disease with mild cognitive impairment and dementia risk: A systematic review and meta-analysis

Zhao LY, Zhou XL

CASE REPORT

- 3461 Circulating tumor DNA genomic profiling reveals the complicated olaparib-resistance mechanism in prostate cancer salvage therapy: A case report

Yuan F, Liu N, Yang MZ, Zhang XT, Luo H, Zhou H

- 3472 Difference and similarity between type A interrupted aortic arch and aortic coarctation in adults: Two case reports

Ren SX, Zhang Q, Li PP, Wang XD

- 3478 Combination therapy (toripalimab and lenvatinib)-associated toxic epidermal necrolysis in a patient with metastatic liver cancer: A case report

Huang KK, Han SS, He LY, Yang LL, Liang BY, Zhen QY, Zhu ZB, Zhang CY, Li HY, Lin Y

- 3485 Unusual glomus tumor of the lower leg: A case report

Wang HY, Duan P, Chen H, Pan ZY

- 3490 Pulmonary *Cladosporium* infection coexisting with subcutaneous *Corynespora cassiicola* infection in a patient: A case report

Wang WY, Luo HB, Hu JQ, Hong HH

- 3496 Preoperational diagnosis and management of breast ductal carcinoma *in situ* arising within fibroadenoma: Two case reports

Wu J, Sun KW, Mo QP, Yang ZR, Chen Y, Zhong MC

- 3505 Reconstruction of complex chest wall defects: A case report

Huang SC, Chen CY, Qiu P, Yan ZM, Chen WZ, Liang ZZ, Luo KW, Li JW, Zhang YQ, Huang BY

- 3511 Young children with multidrug-resistant epilepsy and vagus nerve stimulation responding to perampanel: A case report

Yang H, Yu D

- 3518 Intramedullary nailing for pathological fractures of the proximal humerus caused by multiple myeloma: A case report and review of literature

Xu GQ, Wang G, Bai XD, Wang XJ

- 3527 Double tracheal stents reduce side effects of progression of malignant tracheoesophageal fistula treated with immunotherapy: A case report

Li CA, Yu WX, Wang LY, Zou H, Ban CJ, Wang HW

- 3533 Ankylosing spondylitis complicated with andersson lesion in the lower cervical spine: A case report

Peng YJ, Zhou Z, Wang QL, Liu XF, Yan J

- 3541 Severe gastric insufflation and consequent atelectasis caused by gas leakage using AIR-Q laryngeal mask airway: A case report

Zhao Y, Li P, Li DW, Zhao GF, Li XY

- 3547** Hypereosinophilic syndrome presenting as acute ischemic stroke, myocardial infarction, and arterial involvement: A case report
Sun RR, Chen TZ, Meng M
- 3553** Cytochrome P450 family 17 subfamily A member 1 mutation causes severe pseudohermaphroditism: A case report
Gong Y, Qin F, Li WJ, Li LY, He P, Zhou XJ
- 3561** Patellar dislocation following distal femoral replacement after extra-articular knee resection for bone sarcoma: A case report
Kubota Y, Tanaka K, Hirakawa M, Iwasaki T, Kawano M, Itonaga I, Tsumura H
- 3573** Qingchang decoction retention enema may induce clinical and mucosal remission in left-sided ulcerative colitis: A case report
Li PH, Tang Y, Wen HZ
- 3579** Anti-nuclear matrix protein 2+ juvenile dermatomyositis with severe skin ulcer and infection: A case report and literature review
Wang YT, Zhang Y, Tang T, Luo C, Liu MY, Xu L, Wang L, Tang XM
- 3587** Ultrasound-guided local ethanol injection for fertility-preserving cervical pregnancy accompanied by fetal heartbeat: Two case reports
Kakinuma T, Kakinuma K, Matsuda Y, Ohwada M, Yanagida K, Kaijima H
- 3593** Successful apatinib treatment for advanced clear cell renal carcinoma as a first-line palliative treatment: A case report
Wei HP, Mao J, Hu ZL
- 3601** Del(5q) and inv(3) in myelodysplastic syndrome: A rare case report
Liang HP, Luo XC, Zhang YL, Liu B
- 3609** Papillary thyroid microcarcinoma with contralateral lymphatic skip metastasis and breast cancer: A case report
Ding M, Kong YH, Gu JH, Xie RL, Fei J
- 3615** Contrast-enhanced ultrasound manifestations of synchronous combined hepatocellular-cholangiocarcinoma and hepatocellular carcinoma: A case report
Gao L, Huang JY, Lu ZJ, Lu Q
- 3624** Thyrotoxicosis after a massive levothyroxine ingestion: A case report
Du F, Liu SW, Yang H, Duan RX, Ren WX
- 3630** Pleomorphic adenoma of the left lacrimal gland recurred and transformed into myoepithelial carcinoma after multiple operations: A case report
Huang WP, Li LM, Gao JB

ABOUT COVER

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Ultrasound-guided local ethanol injection for fertility-preserving cervical pregnancy accompanied by fetal heartbeat: Two case reports

Toshiyuki Kakinuma, Kaoru Kakinuma, Yoshio Matsuda, Michitaka Ohwada, Kaoru Yanagida, Hirotsune Kaijima

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Abstract

BACKGROUND

The incidence of cervical pregnancy is increasing due to the recent widespread application of assisted reproductive technology. Although hysterectomy has been a treatment option, high-sensitivity human chorionic gonadotropin testing and improved accuracy of transvaginal ultrasound imaging have increased possibility of uterine preservation. Dilation and curettage with methotrexate therapy and uterine artery embolization have been reported as treatments with fertility preservation; however, certain disadvantages limit their use.

CASE SUMMARY

In our two reported cases, we avoided massive bleeding and immediately resumed infertility treatment using ultrasound-guided local ethanol injection for cervical pregnancies with fetal heartbeats.

CONCLUSION

This treatment may be a new fertility-preserving option for cervical pregnancy.

Key Words: Ultrasonography; Ethanol; Infertility; Fertility preservation; Methotrexate; Case report

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Core Tip: We describe the use of transvaginal ultrasound-guided local injection of absolute ethanol as a new treatment method for cervical pregnancy that preserves fertility. In both cases, the patients had developed cervical pregnancy through assisted reproductive technology and sought fertility-preserving treatment. A local injection of absolute ethanol allowed resumption of menstruation 2 mo after treatment and early resumption of infertility treatment without any complications. We suggest that local injection of absolute ethanol for cervical pregnancy could be a safe and effective new treatment method.

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INTRODUCTION

Cervical pregnancies occur in approximately 1 in 9000 pregnancies[1,2]. They are believed to be more common in those with a history of abortion or cesarean delivery, and are more common with assisted reproductive technology than with natural pregnancies[3]. The cervix contains very little smooth muscle, and it is thought that the villi easily infiltrate the muscular layer and form a high degree of placenta accreta. Furthermore, careless intracervical curettage for cervical pregnancy may cause complicated massive bleeding. Therefore, hysterectomy should be considered for treatment.

However, the recent development of high-sensitivity human chorionic gonadotropin (hCG) testing and improved accuracy of transvaginal ultrasound imaging have allowed asymptomatic diagnosis and increased fertility preservation due to early intervention. Dilation and curettage with methotrexate (MTX) therapy[4] and uterine artery embolization (UAE)[5] have been reported as treatments for the preservation of fertility. However, in patients who wish to preserve fertility, MTX therapy poses problems that may include ovarian dysfunction and a delay in resumption of infertility treatment due to the washout period[6]. Furthermore, there are many reported cases of unsuccessful MTX administration in cases accompanied by fetal heartbeat or blood hCG concentration of ≥ 10000 mIU/mL[7]. Moreover, with UAE, the rate of preterm birth in subsequent pregnancies may increase, and placenta accreta may occur[8].

There have been reports on the efficacy and safety of ultrasound-guided local ethanol injection as an alternative to topical MTX therapy in ectopic pregnancy[9,10]. This therapy has the potential to become a treatment option, as it does not require a washout period and has fewer complications than UAE therapy. Nevertheless, reports on this topic are scarce. In this report, we present two cases of cervical pregnancy with fetal heartbeat and elevated blood hCG concentration, in which fertility was preserved using local ethanol therapy.

CASE PRESENTATION

Chief complaints

Case 1: A 39-year-old nulliparous woman achieved pregnancy *via in vitro* fertilization-embryo transfer (IVF-ET). Ultrasonographic images at 6 wk 2 d of gestation suggested cervical pregnancy; therefore, she was referred to our hospital for detailed examination and treatment.

Case 2: A 33-year-old woman, gravida 2, para 1 had achieved pregnancy *via* IVF-ET. Ultrasound imaging results at 7 wk 6 d of gestation suggested cervical pregnancy; therefore, she was referred to our hospital for further examination and treatment.

History of present illness

Cases 1 and 2: The patients were asymptomatic aside from the ultrasonographic images suggesting cervical pregnancy.

History of past illness

Cases 1 and 2: The patients reported no notable past illness.

Personal and family history

Cases 1 and 2: No notable personal or family medical history.

Physical examination

Case 1: Findings upon presentation included blood pressure of 128/72 mmHg, pulse rate of 72 beats/min, and body temperature of 36.8 °C.

Case 2: Findings upon presentation included a blood pressure of 104/79 mmHg, pulse rate of 78 beats/min, and body temperature of 36.9 °C.

Laboratory examinations

Case 1: Blood testing revealed an elevated hCG concentration of 16346 mIU/mL and no other abnormalities noted.

Case 2: Blood testing revealed an elevated hCG concentration of 26930 mIU/mL and no other noteworthy abnormalities.

Imaging examinations

Case 1: Transvaginal ultrasonography revealed no gestational sac (GS) within the uterine body; however, a 21-mm GS-like mass with a fetal heartbeat was found within the cervix (Figure 1).

Case 2: Transvaginal ultrasonography revealed a 30 mm cervical GS with fetal heartbeat, and blood flow was noted around the GS by color Doppler imaging (Figure 2).

FINAL DIAGNOSIS

In both cases, based on the findings, cervical pregnancy was diagnosed.

TREATMENT

Case 1

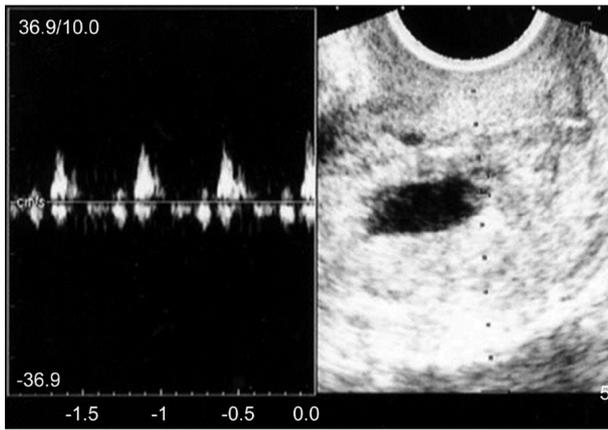
MTX therapy was offered as a treatment option because of the patient's desire to preserve fertility. The patient declined MTX therapy after learning that side effects may include ovarian dysfunction and that a course of contraception was required during MTX washout. Dilation and curettage with UAE were also presented as options; however, the patient declined these after understanding that UAE may affect subsequent pregnancies. As such, the patient sought other fertility-preserving therapies. Therefore, we offered transvaginal ultrasound-guided local absolute ethanol injection because it allows early resumption of infertility treatment and has little effect on ovarian function and subsequent pregnancy. We also emphasized its efficacy and safety in patients with ectopic pregnancies. We explained that the use of local absolute ethanol injection for cervical pregnancy is an off-label and unestablished treatment at this time. Upon explaining the above, the patient and her family chose this treatment.

The treatment involved local injection of 2.5 mL absolute ethanol around the cervical GS using a 23-gauge percutaneous transhepatic cholangiography (PTC) needle under transvaginal ultrasonic guidance (Hakko Co., Ltd., Nagano, Japan). The blood hCG concentration 2 h after treatment was decreased by 20% from the pretreatment value; therefore, the therapeutic effect was confirmed. However, the blood hCG concentration increased the next day to 18087 mIU/mL; therefore, 2.5 mL absolute ethanol was injected again in the same manner. Thereafter, the blood hCG concentration decreased steadily, and spontaneous passage of the GS was observed 7 d after the second local injection of absolute ethanol. Histopathological examination revealed decidua and chorionic villi.

Case 2

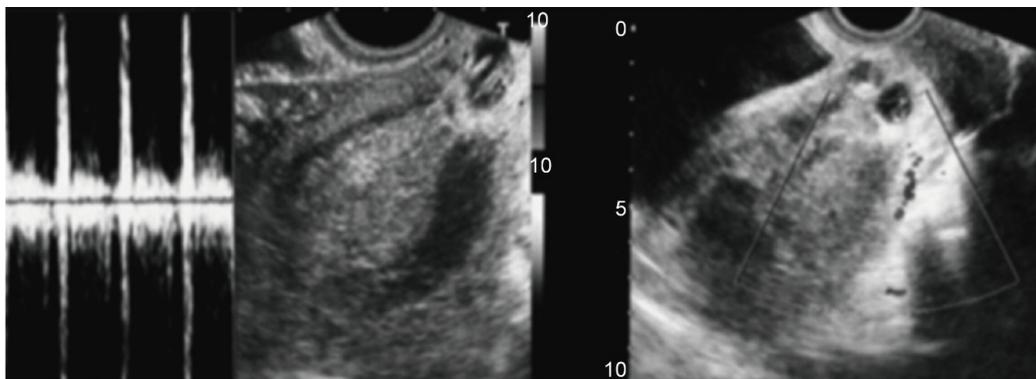
The patient and her family sought fertility-preserving treatment. As in Case 1, the patient chose transvaginal ultrasound-guided local absolute ethanol injection among the available fertility-preserving treatments.

Using a 23-gauge PTC needle, 4.0 mL absolute ethanol was locally injected around the cervical GS under transvaginal ultrasonic guidance (Hakko Co., Ltd.). The blood hCG concentration 2 h after treatment was 20% less than the pretreatment value, verifying the therapeutic effect. Thereafter, the blood hCG concentration decreased steadily, and the GS spontaneously passed 6 d after the local injection of absolute ethanol. Histopathological examination revealed decidua and chorionic villi.



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Figure 1 Transvaginal ultrasound findings in Case 1. A gestational sac with fetal heartbeat was found in the cervix.



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Figure 2 Transvaginal ultrasound findings in Case 2. A 30 mm gestational sac with fetal heartbeat was found in the cervix, and blood flow was noted around the sac by color Doppler imaging.

OUTCOME AND FOLLOW-UP

Case 1

On day 17, the blood hCG concentration had decreased to 198 mIU/mL, and no complications due to local ethanol injection were observed during follow-up. Two months after local ethanol therapy, menstruation had resumed, and infertility treatment was re-initiated.

Case 2

On day 10, the blood hCG concentration had decreased to 116 mIU/mL, and only a small amount of vaginal bleeding was noted during follow-up. In addition, no complications due to local ethanol injection were noted. Two months after local ethanol therapy, menstruation had resumed, and infertility treatment was re-initiated.

DISCUSSION

The patients in this report developed cervical pregnancy through assisted reproductive technology. Under these circumstances, many patients wish to preserve their fertility. Such patients often choose MTX therapy or UAE, both of which have high rates of treatment success[4,5] and postoperative pregnancy[11]. However, MTX therapy and UAE also have disadvantages for patients who desire fertility preservation. In a study of 35 patients with a history of MTX treatment for cervical pregnancy, oocyte yields during *in vitro* fertilization were 10.1 ± 3.9 before treatment and 7.8 ± 3.6 after treatment, suggesting that MTX therapy caused a decrease in the number of oocytes. It has been reported that a decrease in oocyte count leads to a decrease in the number of collected eggs[6], and because MTX therapy affects the ovaries, it may also affect fertility preservation. Furthermore, when MTX is used, a 4–6-mo contraception period is required after surgery for washout[12,13], which delays the resumption

of fertility treatment. Because patients under infertility treatment are becoming older, the best treatment method should allow early resumption of infertility treatment.

In UAE, postoperative fever is the most common complication, and pain, endometritis, intrauterine adhesions, uterine necrosis, and ovarian dysfunction may also occur[14-16]. According to Hardeman *et al*[17], 14 of 53 patients who underwent UAE for obstetrical bleeding desired subsequent pregnancy (all gelatin embolization cases), and 12 of these patients conceived and had successful delivery. These results indicate relatively high rates of postoperative fertility. However, in post-UAE pregnancies, there have been reports of significant increases in miscarriage rate, postpartum bleeding, preterm birth rate, and fetal position abnormalities, and there have been case reports of intrauterine growth restriction[8]. This emphasizes the need for strict perinatal management in post-UAE pregnancies.

In this report, transvaginal ultrasound-guided local injection of absolute ethanol was performed as a new treatment method replacing MTX therapy and UAE. Previously, we reported the efficacy and safety of transvaginal ultrasound-guided local absolute ethanol injection in ectopic pregnancies[9,10]. This treatment method involves the local injection of absolute ethanol around the implantation site under ultrasonic guidance. Its therapeutic effect can be determined earlier than in MTX therapy since a 10%-30% decrease in blood hCG concentration can be confirmed within 2 h of injection. We believe that absolute ethanol dehydrates and denatures the villous tissue, and that acute tissue changes reduce the blood hCG concentration within a short period of time. Therefore, we believe that these mechanisms are effective in patients such as ours, who had high blood hCG concentrations and fetal heartbeats – factors associated with unsuccessful MTX therapy. Furthermore, because no massive bleeding was observed after local injection of absolute ethanol, we believe that these mechanisms are hemostatic and may also be an effective treatment for cervical pregnancy accompanied by genital bleeding in patients who desire fertility preservation.

Absolute ethanol administration may also be effective in other transvaginal procedures, as there is a low possibility of iatrogenic infection. The therapy requires no anesthesia because the small needles cause less bleeding and pain, and the procedure is also more affordable than MTX therapy. This mitigates the physical and financial burdens of patients. In addition, when repeated administration is required for persistent ectopic pregnancy, side effects of anticancer drugs, such as MTX, also become a problem. However, injection of absolute ethanol causes only a local effect, which means that it can be repeated for persistent ectopic pregnancies. In Case 1, two local injections of absolute ethanol were administered for persistent ectopic pregnancy; however, no side effects were observed with this treatment.

In our two reported cases, blood hCG concentration was high and fetal heartbeat was present, which are risk factors for unsuccessful MTX therapy. However, the local injection of absolute ethanol was still able to preserve fertility. In both cases, local injection of absolute ethanol allowed resumption of menstruation 2 mo after treatment and early resumption of infertility treatment without any complications. Based on these results, we suggest that local injection of absolute ethanol for cervical pregnancy could be a safe and effective new treatment method.

CONCLUSION

In this report, we presented two cases of cervical pregnancy with elevated blood hCG concentrations and fetal heartbeats. Each underwent fertility-preserving treatment with local ethanol injection. The outcomes suggested that this treatment method may avoid the complications of MTX therapy and UAE and may be an option for patients who desire fertility preservation.

FOOTNOTES

Author contributions: Kakinuma T designed the research study and wrote the manuscript; Kakinuma T, Kakinuma K, Ohwada M and Yanagida K performed the research; Matsuda Y and Kaijima H provided help and advice on the study protocol; All authors read and approved the final manuscript.

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