

Successful treatment of a persistent mole with myometrial invasion by direct injection of methotrexate

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Summary

For patients with persistent or invasive gestational trophoblastic disease (GTD), systemic injection of chemotherapy is the treatment of choice if fertility is to be preserved. To prevent serious adverse effects after systemic use and possibly achieve better effects, direct local injection of chemotherapy into the tumor site, especially when in the myometrium, seems a reasonable alternative.

A patient with a persistent molar pregnancy with myometrial invasion is presented. A plateau of β -hCG (human chorionic gonadotropin) level around 550 mIU/mL was noticed for three weeks though systemic methotrexate (MTX) injection and repeat suction curettage had been performed. During the same period, a well-defined invasive complex with multiple vesicles in the myometrium was documented using transvaginal ultrasound (TVUS). Sonar-guided injection to the tumor using 50 mg MTX was performed uneventfully. An obvious shrinkage of the mass and declining β -hCG level were demonstrated after the procedure. The patient restored her menses after the operation and a fertility evaluation including serial β -hCG levels and hysterosalpingography showed them to be within the reference ranges.

The successful outcome of this case encouraged us to treat localized invasive GTD using direct injection of MTX with the guidance of TVUS. Since no identical cases were found in our review of the English literature, more cases and similar regimens are needed to establish the safety and efficacy of this procedure.

Key words: Gestational trophoblastic disease; Ultrasound-guided injection.

Case Report

A 38-year-old, G3P3, woman visited our outpatient department with the chief complaint of vaginal spotting for two days. To re-establish her fertility, she had received reanastomosis of ligated tubes at our hospital about 18 months prior to this visit. A six-week intrauterine pregnancy was diagnosed using transvaginal ultrasound. Three doses of 200 mg oral progesterone were given each day; however, vaginal spotting persisted during the two weeks following the diagnosis. Transvaginal ultrasound at the eighth gestational week revealed an empty sac with internal hetero-echogenic complex. Incomplete abortion was impressed and a suctional curettage was done. The pathologic report showed the product of gestation without other abnormal findings such as hydropic or malignant change. After surgery, the patient still suffered from persistent vaginal bleeding and unexplained lower back pain. A follow-up ultrasound two weeks after suctional curettage revealed a retained intrauterine gestational tissue complex which consisted of multiple vesicles (Figure 1-a). A molar pregnancy was suggested. Serial β -hCG levels were 29,323 and 64,069 mIU/mL, respectively, and serial ultrasound showed progressive enlargement of the tumor (Figures 1-b). A repeat suctional curettage was performed. Grossly, the specimen consisted of multiple vesicles, which were compatible with molar pregnancy under a microscope. Her β -hCG level dropped to 11,261 and an echolucent complex near the fundal area was found using transvaginal ultrasound (Figure 2-a). An adjuvant intramuscular injection of 50 mg MTX with 5 mg folinic acid rescue was given. The β -hCG level dropped to the nadir of 560 mIU/mL, although the previously mentioned mass became larger and larger (Figures 2-b, 2-c, 2-d). The β -hCG level failed to decrease for the next three weeks and remained around 550 mIU/mL (Figure 3). We used a transvaginal ultrasound guided 21-gauge one-way ovum

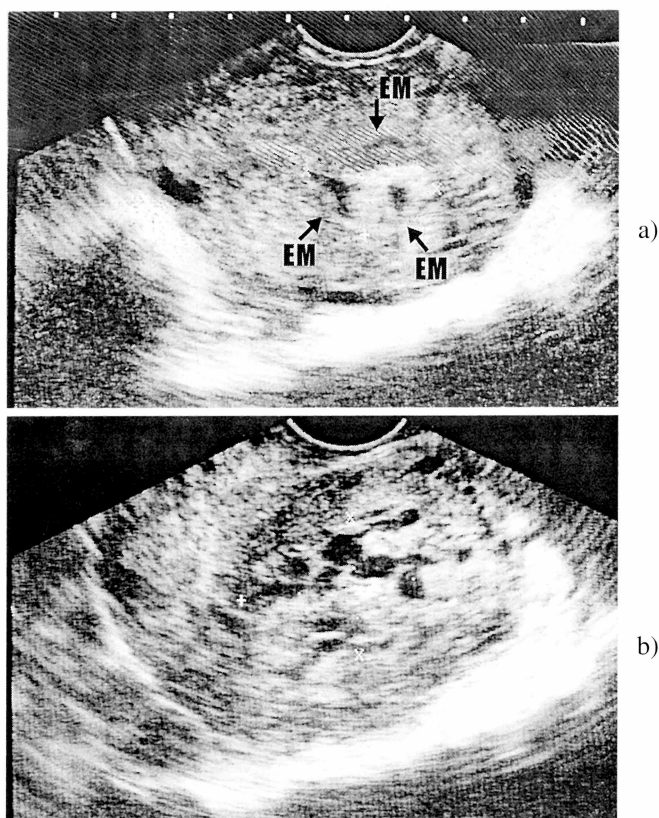


Figure 1. — Transvaginal ultrasound (TVUS) pictures of the intrauterine complex before the second uterine evacuation.

1-a. A small intrauterine complex, 2.0x2.3 cm, with multiple vesicles and an obvious uterine endometrial outline (EM).

1-b. Before the second suctional curettage, the complex was 3.8x2.7 cm and more vesicles were demonstrated.

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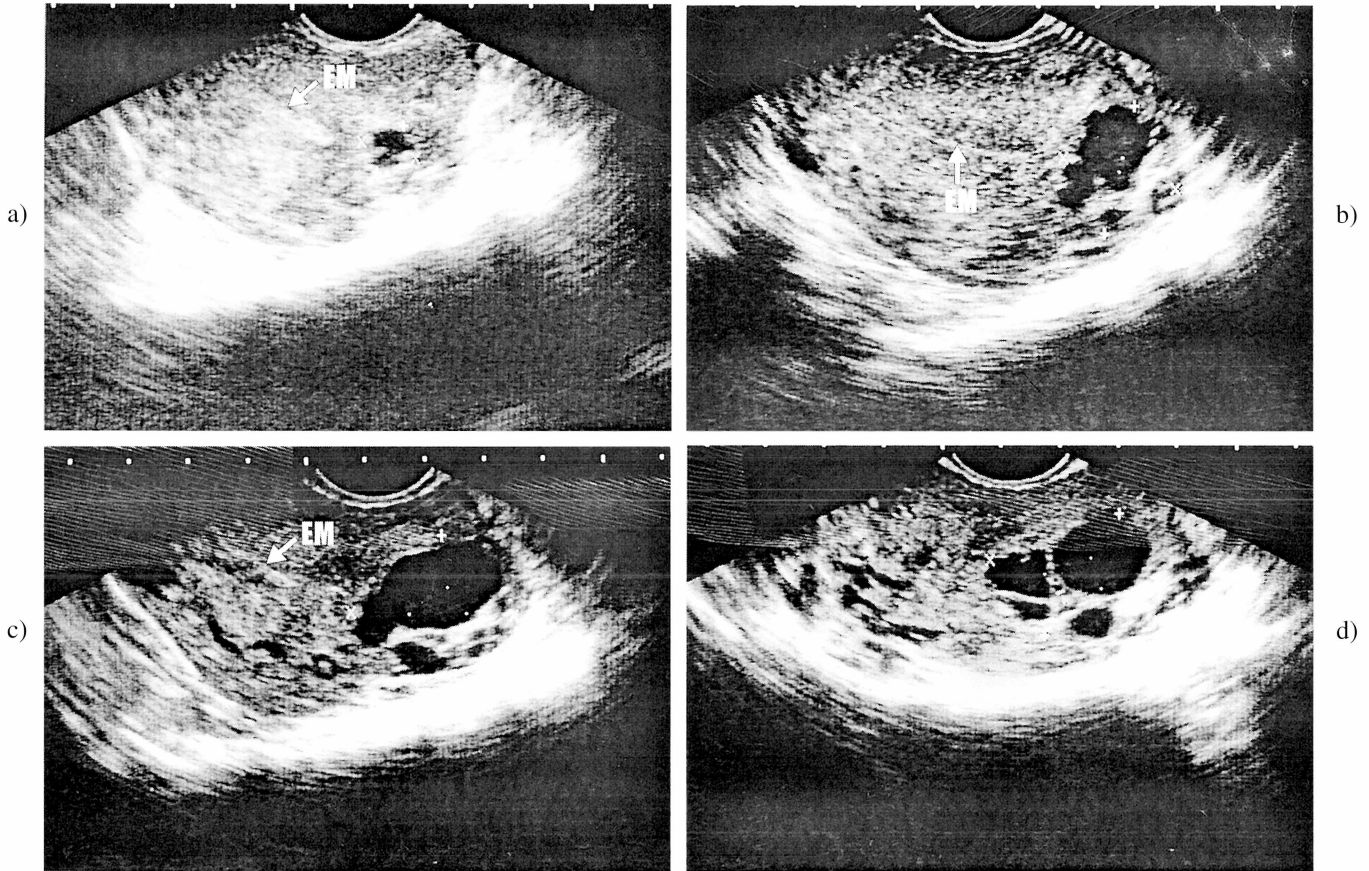


Figure 2. — TVUS pictures of the intramyometrial lesion before sonar-guided puncture.

2-a. A small echolucent lesion, 1.0 x 1.0 cm, was on the top of the collapsed endometrial lining (EM) with some distance.
 2-b, c. The lesion with multiple vesicles became larger at two weeks (b) and 4 weeks (c) after the second evacuation. The endometrial lining (EM) was seen and the size of the complex was 2.0 x 2.5 cm and 2.7 x 2.8 cm, respectively.
 2-d. Another view of the lesion on 2-c. The intramyometrial complex with multiple vesicles was similar to the previous intrauterine view (Fig. 1-b).

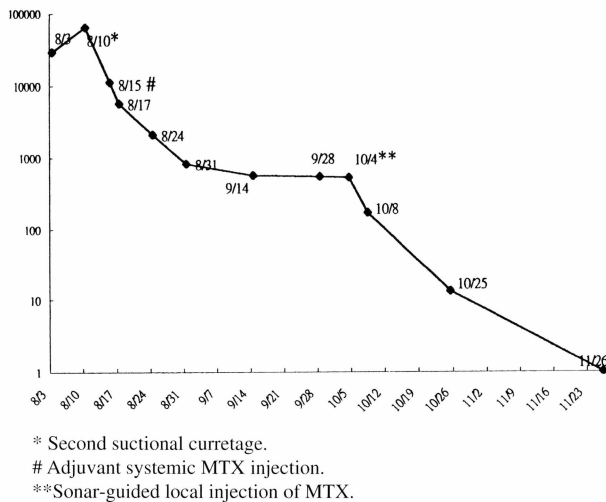


Figure 3. — β-hCG regression curve with a nadir around 550 mIU/mL for 3 weeks before the puncture procedure.

pick-up needle containing 50 mg MTX to treat the tumor. The patient tolerated the procedure well without any side-effects. After the procedure, the β-hCG level started to decrease, the mass shrank, and the patient achieved complete remission (Figure 4). Her menses returned three weeks after the procedure and she was told to use contraception for one year.

Discussion

The estimated incidence of complete mole is around one per 1,500-2,000 pregnancies whereas the incidence of partial mole is one in 700 pregnancies [1]. About 20% of patients with complete moles develop persistent gestational trophoblastic disease (GTD). The incidence of this complication after a partial mole has been stated to be between 4 and 11% but this figure is certainly lower since many partial moles are not diagnosed [1-3]. Before the advent of chemotherapy, myometrial invasion was reported in about 16% of patients with complete hydatidiform mole [4]. Invasive moles are rarely seen in patients with partial moles.

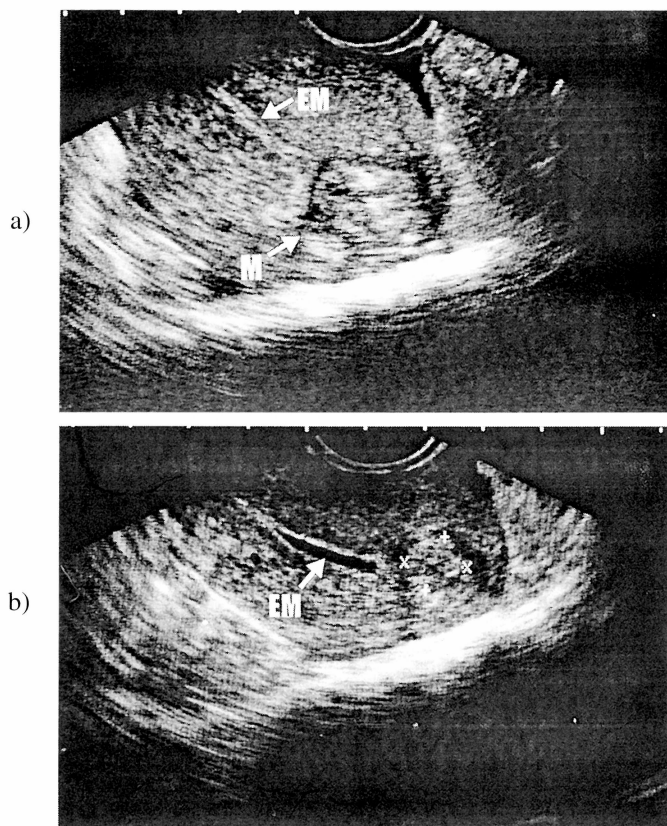


Figure 4. — TVUS pictures of the intramyometrial lesion after the puncture procedure.

4-a. On the 4th day after the procedure. The complex (M), in a diameter of 2 cm, became smaller. The appearance of multiple vesicles was replaced by multiple echogenic spots.

4-b. At 7 weeks after the procedure, the tumors had shrunk to 1.1 cm in diameter.

The classic sonographic appearance of a 'snowstorm' image of a complete mole using transabdominal ultrasound and various transvaginal ultrasound (TVUS) images, especially the appearance of multiple vesicles, help to establish the diagnosis [2, 5, 6]. However occasionally, physicians fail to make an accurate diagnosis of early molar pregnancies using ultrasound [5]. Weekly serial levels of serum β -hCG remain the most accurate, reliable, and definitive arbiters of diagnosis and treatment decision for patients with molar pregnancies [1, 6-11], though other tumor markers have been tested by some authors [7, 8].

Post-molar GTD is diagnosed using persistent or rising levels of β -hCG. Confirming the presence of visible diseases in the uterus using ultrasound helps to determine the correct management and follow-up of such cases [12]. However, different opinions about the correlation between the regression of tumors and declining serum β -hCG levels still exist [16-18]. To overcome this limitation, TVUS is used to assist in the diagnosing and monitoring of myometrial invasion after either complete or partial mole pregnancies have been reported [6, 10, 12,

13, 16]. When post-molar GTD fails to respond to chemotherapy, TVUS imaging helps confirm myometrial lesions in the uterus before hysterectomy is contemplated [6, 12].

Because of the excellent outcomes already reported, the systemic use of chemotherapy is the treatment of choice for patients with persistent molar pregnancy. However, the patients who fail to respond to conventional chemotherapy or even the standard high-risk regimens (EMA-CO: etoposide, methotrexate, actinomycin-D, cyclophosphamide, and oncovin) should be treated using the newer anticancer agents or newer procedures [4, 17]. Although the use of sonar-guided injection of MTX directly on the ectopic site has been used for years with few mentioned complications [18], to our knowledge this procedure on myometrial invasion in patients with post-molar GTD has never been reported in the English literature. To prevent the need for a hysterectomy or to decrease the incidence of serious adverse effects after using multiple doses of chemotherapy or multiple chemotherapy agents, a single dose injection of MTX directly on the tumor site seems to be a useful and safe alternative. With the advances of TVUS apparatus, similar procedures will become easier, safer, and more common. Based on this interesting case report, more studies are needed to establish and confirm the safety and efficacy of this procedure.

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