# Management of Partial Hydatidiform Mole and Subsequent Intrauterine Adhesions: A Case Report and Literature Review

*Dor Partosh, BPharm; Genevieve Hale, PharmD, BCPS, BCCP*
*Nova Southeastern University College of Pharmacy*

**Abstract**

***Background:*** *Gestational trophoblastic disease (GTD) originates from placental tissue and is among rare human tumors that can be cured even in the presence of widespread metastases. The most common form of GTD is hydatidiform mole (HM), commonly referred to as molar pregnancy. Molar pregnancies have the potential to locally invade the uterus and metastasize and result as a result of gestational trophoblastic neoplasia. Intrauterine adhesions (IUAs) is a condition where scar tissue develops within the uterine cavity, often following a procedure. Hysteroscopy has been established as the criterion standard for the diagnosis of IUAs, although the optimal adjuvant treatment after surgical intervention remains unclear.*

***Case:*** *A 35-year-old-female underwent suction curettage a week after the detection of a molar pregnancy. Two months later, she suffered from amenorrhea and hormonal therapy was initiated. Saline-infusion sonogram was tried and failed due to cervical stenosis. IUAs leading to scar tissue developed along with uterine polyps. Hysteroscopy successfully lysed IUAs and uterine polyps. The patient conceived two months after stopping hormonal therapy and proceeded to a pregnancy which resulted in a healthy live birth.*

***Conclusion:*** *Although the etiology of the patient's molar pregnancy is still unknown, this report demonstrates the need to utilize hysteroscopy as a primary and early mode of treatment if IUAs are found in patients along with providing adjuvant treatment while utilizing clinical judgement in order to prevent IUAs recurrence. The patient conceived four months after the hysteroscopy resulting in a healthy live birth.*

**Key words**: hysteroscopy; intrauterine adhesions; molar pregnancy

## Background

Gestational trophoblastic disease (GTD) originates from placental tissue and is among rare human tumors that can be cured even in the presence of widespread metastases. The pathogenesis of GTD is unique because the maternal tumor arises from gestational rather than maternal tissue. The most common form of GTD is hydatidiform mole (HM), commonly referred to as molar pregnancy. Molar pregnancies have the potential to locally invade the uterus and metastasize. This invasion causes a malignant disease, otherwise known as gestational trophoblastic neoplasia (GTN).[1]

Molar pregnancy comprises two distinct entities, partial and complete mole, which can be distinguished by means of gross morphologic and histopathological examination and according to chromosomal patterns. Complete moles usually have a 46,XX karyotype, and the molar chromosomes are derived completely from the father. Most complete moles are homozygous and appear to arise from an anuclear empty ovum that has been fertilized by a haploid (23X) sperm, which then replicates its own chromosomes.[1,2] Partial moles usually have a triploid karyotype that develops after the fertilization of an apparently normal ovum by two spermatozoa leading to congenital anomalies associated with triploidy, such as syndactyly and cleft lip.[33]

**Corresponding author**: Dor Partosh, BPharm
Nova Southeastern University College of Pharmacy
1850 South Ocean Drive, 1101
Hallandale Beach, FL 33009
Phone: 954-815-9692; Email: dorpa89@gmail.com

Intrauterine adhesions (IUAs) occur when scar tissue develops within the uterine cavity, often in response to a uterine procedure. Intrauterine adhesions can be either primary after pregnancy-related curettage or after hysteroscopic surgery, or secondary after adhesiolysis has been performed.4 IUAs are a result of trauma to the basalis layer of the endometrium and may lead to clinical sequelae such as miscarriage, infertility, and menstrual irregularities.[1] Risk factors that have been associated with the development of IUAs are recurrent miscarriage and dilation and curettage (D&C) procedures, multiple pregnancies, high negative pressure suction evacuation and long suction evacuation time following induced abortions.[6,7]

Patients with suspected IUAs should be assessed based on history of symptoms (i.e., menstrual change, infertility, or dysmenorrhea), prior pregnancies, and prior uterine procedures. If amenorrhea is present, lab tests should include a thyroid panel and prolactin to rule out secondary amenorrhea.8 Hysteroscopy has been established as the criterion standard for diagnosis, although the optimal adjuvant treatment after surgical intervention remains unclear.[9] Hysteroscopy provides a real-time view of the uterine cavity, enabling accurate description of the location and degree of adhesions, classification, and concurrent treatment of IUAs. Another screening tool, hysterosalpingogram (HSG), has a high false-positive rate (up to 39%) and does not detect endometrial fibrosis or the nature and extent of IUAs. Alternatively, the use of saline-infusion sonogram (SIS) is as effective as HSG.[10]


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**Case**

A 35-year-old-female presented to an obstetrics and gynecology (OB-GYN) clinic with a positive pregnancy test and elevated maternal serum beta-chorionic gonadotropin (β-hCG) levels. She denied menstrual bleeding, abdominal cramping, nausea, and vomiting. Her last menstrual period was eight weeks before the visit. Vitals were unremarkable. Her uterus had normal size and shape, and an irregular yolk sac shape was noted in a transvaginal ultrasound with a faint cardiac activity detected. The patient's past medical history included anxiety and mild depression. Clonazepam 0.5 mg was prescribed twice daily as needed for anxiety. She had one term live birth six months before this visit.

The patient was referred to check β-hCG levels and a follow-up ultrasound with a specialist. Transvaginal ultrasound showed suspected molar pregnancy based on an enlarged placenta as well as the mass of cysts only partially covering the uterus (Figure 1). Her first laboratory results showed β-hCG levels of 67,135 mIU/mL, corresponding to the normal range during early pregnancy (7,650-288,000 mIU/mL).

Suction curettage was performed under general anesthesia a week after the detection of the molar pregnancy. Prophylactic doxycycline 200 mg was administered in a single dose one hour before the procedure. A rigid size 8 curette was used and the endometrial material was removed via vacuum aspiration and an experienced surgeon had performed the procedure while under ultrasound guidance. The uterine size at that time was 4.66X3.16 cm. There were no complications and the patient was discharged several hours later. Surgical pathology confirmed a partial molar pregnancy based on the chromosomal and histopathological features (triploid karyotype) and the presence of embryonic tissue. Follow-up bloodwork revealed a steady decline in β-hCG levels: 3 weeks post-D&C 83 mIU/mL; 4 weeks post-D&C 17 mIU/mL; 5 weeks post-D&C 5 mIU/mL. Undetectable levels (<2 mIU/mL) after 6 weeks, consistent with a successful procedure. Follow-ups were done monthly afterward and showed undetectable levels for 2 months at which point the testing was stopped.

Four months post-D&C the patient returned to the OB-GYN clinic complaining of amenorrhea. The diagnostic evaluation started with laboratory testing to rule out secondary amenorrhea (β-hCG levels were still undetectable). Laboratory tests revealed thyroid stimulating hormone (TSH) levels of 1.25 mIU/L, prolactin 217 mIU/L, estradiol (E2) 217 pmol/L, luteinizing hormone (LH) 2.0 IU/L, follicle stimulating hormone (FSH) 4.4 IU/L (all within normal limits).

Following the laboratory tests, a progestin withdrawal test was done with a two-month trial using medroxyprogesterone (Provera®), followed by a three-month trial of estradiol valerate 2 mg and norgestrel 0.5 mg. No withdrawal bleeding was seen on either treatment. This treatment method was chosen to identify if the source of amenorrhea was due to primary ovarian insufficiency or related to fragile X, for which the patient is a carrier. After the estrogen/progestin withdrawal test, an SIS was scheduled but was unsuccessful due to cervical stenosis. The stenosis was partially opened with a dilator during an HSG that was performed a month after the SIS (Figure 2). At the time of HSG, IUAs were spotted. Hysteroscopy was scheduled for a month after the HSG and revealed moderate IUAs and uterine polyps (Figure 3). During the hysteroscopy, there was a successful removal of scar tissues and polyps, as well as a complete dilation of the cervical stenosis (Figure 4). Insertion of an intrauterine Foley catheter with an inflatable balloon tip after the hysteroscopy was placed for seven days to prevent recurrent adhesions by solid barrier technique. Postoperative treatment with ethinyl estradiol 0.03 mg and desogestrel 0.15 mg (Enskyce®) for 2 months was prescribed to the patient. One-month follow-up after hysteroscopy was done, and a SIS showed no evidence of IUA recurrence (Figure 5). The patient conceived two months after stopping hormonal therapy and proceeded to a pregnancy which resulted in a healthy live birth.

**Discussion**

Suction curettage is the preferred method of HM evacuation regardless of uterine size in patients who desire to preserve fertility. Electric and manual suction evacuation are comparable in terms of their effectiveness for complete evacuation and in side effects.[11] Since trophoblastic cells (which produce β-hCG) are hyperplastic in molar pregnancy, the presence of a complete mole is strongly suggested by markedly elevated β-hCG values.[3] Because of this, HM follow-up treatment consists of measurement of serial serum β-hCG levels until an undetectable level is reached and is maintained for several months. Based on the American College of Obstetricians and Gynecologists (ACOG) guidelines, once β-hCG undetectable levels are shown every week for three weeks, the testing should be done monthly for six months. During the testing period patients should not try to conceive. At the end of the β-hCG testing period, patients may resume trying to become pregnant if they wish.[12]

Treatment for secondary amenorrhea, depending on the cause, may include medical or surgical treatments or a combination of the two13. Certain oral contraceptives may help restart the menstrual cycle. Estrogen replacement therapy (ERT) may help balance hormonal levels and restart the menstrual cycle in women with a primary ovarian insufficiency (POI) or Fragile X-associated primary ovarian insufficiency (FXPOI).[14]

The true prevalence of IUAs is difficult to establish, in part because the condition is uncommon in the general population, often asymptomatic, and requires an invasive procedure for diagnosis. There is a link between termination of pregnancy (TOP) and adhesion formation, however, the relationship between the methods of TOP and IUA formation remains unclear.[15]


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Hysteroscopic lysis of adhesions by direct vision and a tool for adhesiolysis is the recommended approach for symptomatic IUAs. Women with IUAs who do not want an intervention but still want to conceive can choose to avoid surgical lysis. Expectant management (watchful waiting) may result in a subsequent pregnancy, however, the time interval may be prolonged and IUAs recurrence occurs in 30 to 66% of women.[16]

Methods to reduce recurrence include a variety of solid and semi-solid (gel) barriers. Traditional solid barrier techniques of separating the uterine walls following adhesiolysis include the use of an intrauterine device (IUD), amnion graft or stent, typically comprising an intrauterine catheter with an inflatable balloon tip. The use of an IUD, stent or catheter appears to reduce the rate of postoperative adhesion reformation. There is limited data regarding subsequent fertility outcomes when these barriers are used.[10]

The lack of a universal classification system for IUAs and the use of variable outcomes to measure the success of adjunctive treatment pose challenges in generating standard treatment recommendations.[1] Although, some results show that auto-cross-linked hyaluronic acid (ACP) plus a balloon and freeze-dried amniotic agents plus a balloon were most likely to reduce IUA recurrence and IUA scores after adhesiolysis.[9]

The likelihood of pregnancy following adhesiolysis appears to vary directly with the severity of disease. The pregnancy rates after adhesiolysis are 61% (mild disease), 53% (moderate disease), and 25% (severe disease).17 It is difficult to assess the implications of long-term fertility and reproductive outcomes following IUAs as data on the link is lacking.[7]

**Conclusion**

This case report described a woman with HM who underwent suction curettage with subsequent amenorrhea by unknown causes. She later received hormonal therapy, had a failed SIS, and eventually developed IUAs that were successfully lysed by a hysteroscopy. The patient was then able to conceive and deliver at term with no further complications. Although the etiology of the patient's molar pregnancy is still unknown, this report demonstrates the need to utilize hysteroscopy as a primary and early mode of treatment if IUAs are found in patients along with providing adjuvant treatment while utilizing clinical judgement in order to prevent IUAs recurrence.

**List of abbreviations:** IUAs - intrauterine adhesions; GTD - gestational trophoblastic disease; HM - hydatidiform mole; GTN - gestational trophoblastic neoplasia; D&C - dilation and curettage; HSG – hysterosalpingogram; SIS - saline-infusion sonogram; OB-GYN - obstetrics and gynecology; β-hCG - beta-chorionic gonadotropin; ERT - estrogen replacement therapy; POI - primary ovarian insufficiency; FXPOI - Fragile X-associated primary ovarian insufficiency; TOP - termination of pregnancy; IUD - intrauterine device

**Conflict of Interest**: We declare no conflicts of interest or financial interests that the authors or members of their immediate families have in any product or service discussed in the manuscript, including grants (pending or received), employment, gifts, stock holdings or options, honoraria, consultancies, expert testimony, patents and royalties.

IRB exemption granted

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**Figure legends**

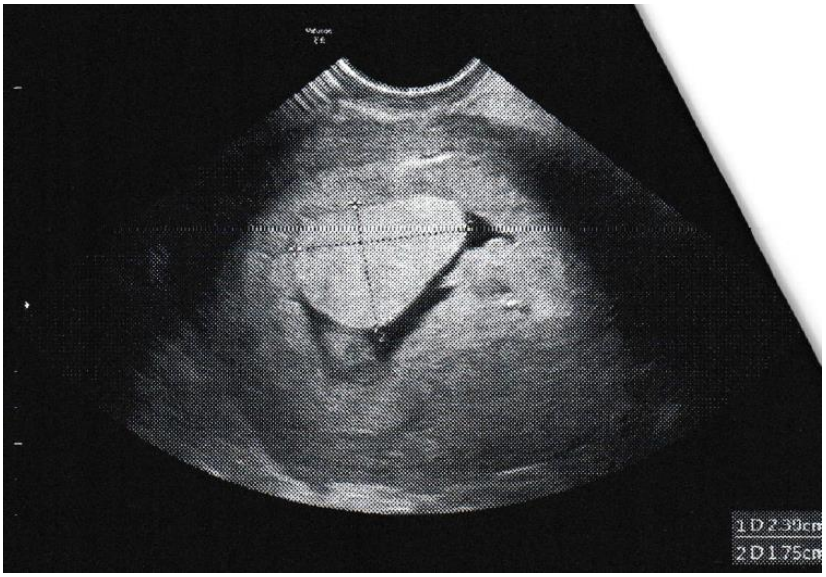


**Figure 1** Transvaginal ultrasound showing enlarged placenta with dimensions of 44X38 mm and an echogenic mass of 24X17 mm.

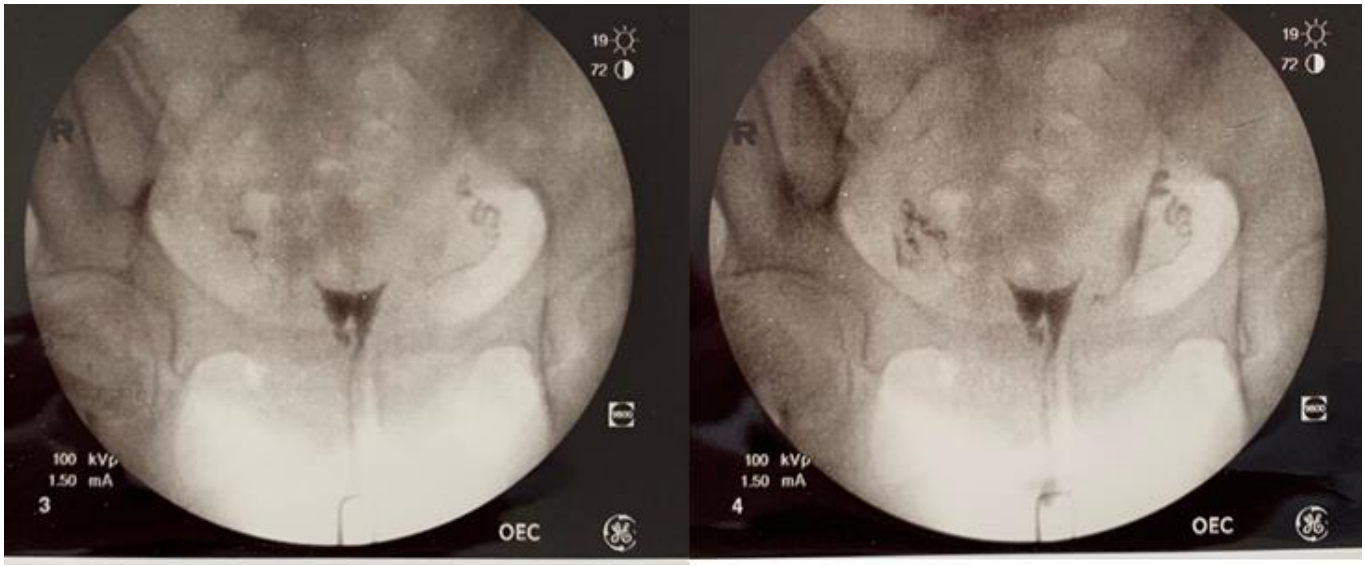


**Figure 2** HSG showing the uterus and ovaries with pre (left) and post (right) cervical stenosis opening as well as demonstrating IUAs in the uterine cavity

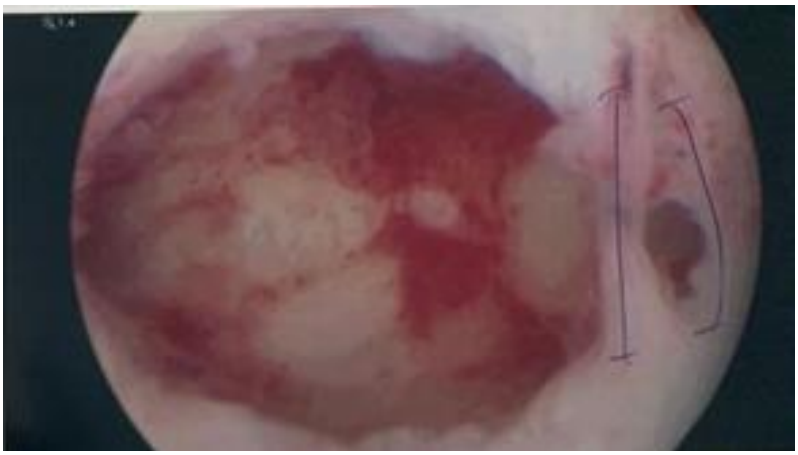

**Figure 3** Hysteroscopic image of the uterus before surgical removal of IUAs

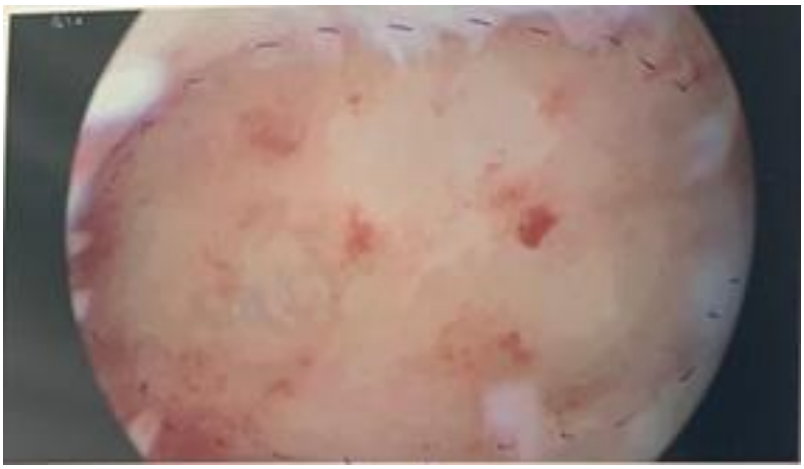

**Figure 4** Hysteroscopic image of the uterus at the end of the procedure with successful removal of IUAs and uterine polyps

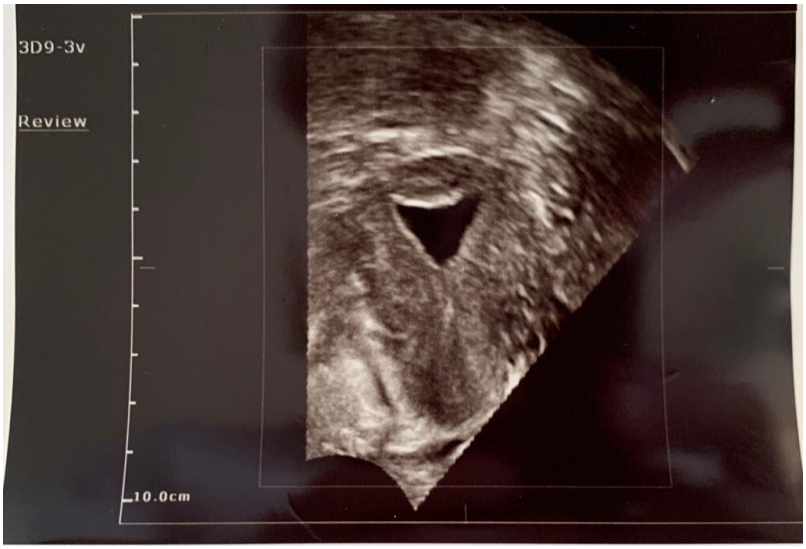


**Figure 5** A SIS with no evidence of IUA recurrence, showing normal endometrial cavity