Fertility preserving treatment in a nulliparous with a molar pregnancy: a case report

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Abstract
Hydatidiform mole represents an abnormal form of conception that occurs in about one in 500–1000 pregnancies. It is a subtype of gestational trophoblastic disease. Hydatidiform moles should be regarded as premalignant lesions because 15–20% of complete hydatidiform moles (CHMs) and 1% of partial hydatidiform moles (PHMs) undergo malignant transformation into invasive moles, choriocarcinomas, or, in rare cases, placental-site trophoblastic tumors (PSTTs). We will illustrate the case of a 26-year-old nulliparous with a seven weeks amenorrhea, positive immunological pregnancy test, a β-HCG value of 136 000 mIU/mL and minor vaginal bleeding. The ultrasonographic examination showed an enlarged endometrium with adjacent hyperechoic material containing tiny anechoic spaces and an anembryonic pregnancy, distended endometrial cavity containing innumerable, variably sized anechoic cysts with intervening hyperechoic material (“snowstorm” appearance). The CT showed a uterine mass measuring 89/111/67 mm, inhomogeneous density, proliferative-infiltrative endocavitary tissue without exceeding the peritoneal serosa, and a few pulmonary micronodules with not certain origin on the left inferior lobe. In this case, due to the large infiltrative uterine mass, the risk of severe bleeding after curettage and the possibility of a necessity hysterectomy, we decided to apply first of all the Methotrexate protocol for molar pregnancy.

Keywords: hydatidiform mole, ultrasonography, trophoblastic disease, Methotrexate.

Introduction
Hydatidiform mole represents an abnormal form of conception that occurs in about one in 500–1000 pregnancies [1, 2]. It is a subtype of gestational trophoblastic disease. It can present like a complete or incomplete form. Hydatidiform mole, or molar pregnancy, results from overproduction of the tissue that is supposed to develop into the placenta.

Hydatidiform moles should be regarded as premalignant lesions because 15–20% of complete hydatidiform moles (CHMs) and 1% of partial hydatidiform moles (PHMs) undergo malignant transformation into invasive moles, choriocarcinomas, or, in rare cases, placental-site trophoblastic tumors (PSTTs) [3, 4].

Early diagnosis should be a prior onset on this pathology due to the risk of association with maternal pregnancy complications such as severe preeclampsia, and most important due to the risk of developing persistent trophoblastic disease or more seriously malignant trophoblastic disease such as choriocarcinoma [5].

The clinical findings in most of the cases of molar pregnancy presented in the second trimester are vaginal bleeding, a ‘large-for-dates’ uterus and passage of vesicles per vagina [6].

Patient, Methods and Results
We will illustrate the case of a 26-year-old woman with a history of one abortion two years ago, that presented to our clinic with a seven weeks amenorrhea, positive immunological pregnancy test, a β-HCG value of 136 000 mIU/mL and minor vaginal bleeding with red blood onset two days prior to the admission.

General examination revealed an obesity stage II women with a body mass index (BMI) 35.6 kg/m², no fever, hemodynamically stable (BP 110/70 mmHg, HR 87 bpm), with a pronounced nausea and vomiting for about one week, mobile and slender abdomen, painless spontaneously or to palpation, normal values for hemogram and urinary test.

Local examination revealed enlarged uterus like a 15 weeks pregnancy, soft consistent on palpation, supple recto-uterine pouch and a minor vaginal bleeding.

The ultrasonographic examination showed an enlarged endometrium with adjacent hyperechoic material containing tiny anechoic spaces and an anembryonic pregnancy, distended endometrial cavity containing innumerable, variably sized anechoic cysts with intervening hyperechoic material (“snowstorm” appearance). The surrounding myometrium was not clearly defined suggesting the presence of molar tissue (Figure 1, a–c).

At that time, the ultrasound examination raised the possibility of hydatidiform molar pregnancy.

Complete blood tests were made, the β-HCG level, repeated, increased in 24 hours from 136 000 to 226 968 mIU/mL. CT of chest, abdomen and pelvis was performed. The CT showed a uterine mass measuring 89/111/67 mm, inhomogeneous density, proliferative-infiltrative endocavitary tissue without exceeding the peritoneal serosa, and a few pulmonary micronodules with not certain origin on the left inferior lobe.

At that moment, we are confronting with a patient
with no children, with desire to conserve her fertility, strongly suspected of a molar pregnancy. The routine protocol would be first curettage and afterwards depending on the histopathological result a second step in treatment [7].

But, in this case, due to the large infiltrative uterine mass, the risk of severe bleeding after curettage and the possibility of a necessity hysterectomy, we decided to apply first of all the Methotrexate protocol for molar pregnancy. This decision was taken not only in order to decrease the mass volume and make curettage safer but also considering the pulmonary micronodules revealed by the CT imaging as a dissemination.

The treatment began with Methotrexate, dosage of 0.4 mg/kg/day for five days with monitoring of β-HCG values at two days and ultrasonography measuring the uterus and the endocavitary mass according to the Romanian Health Ministry Protocol in hydatidiform mole [7]. The β-HCG values decreased from 226 968 mIU/mL to 205 152 mIU/mL after two days, then to 71 186 mIU/mL in the day of curettage – the sixth day. The uterine mass also decreased from 11/9 cm to 4/6 cm, so the curettage was made in safer conditions. The macroscopic aspect of the mass extracted from the uterus was the same with a molar pregnancy, a mass of macroscopic clear vesicles. Those fragments were all sent to the Histopathology Department.

Post curettage we administrate the patient three perfusions/day with Ergomet and Oxytocin, for about three days and Folinic Acid (Figure 2, a and b).

![Figure 1](image1.png)  
**Figure 1** – (a–c) Enlarged uterus containing a large echogenic mass with anechoic cystic spaces – the typical “snowstorm” appearance.

The treatment began with Methotrexate, dosage of

![Figure 2](image2.png)  
**Figure 2** – (a and b) Post curettage images showing free uterine cavity.

We continued monitoring β-HCG values at three days and we observed a diminution: 71 186 mIU/mL in the day of curettage to 5310 mIU/mL after three days, than 1634 mIU/mL, 975 mIU/mL and 258 mIU/mL at two weeks. At that point, the decision was to repeat the Methotrexate for another five days.

After the second series of five days Methotrexate, the β-HCG levels were 100 mU/mL in day 1 post Methotrexate administration and 0 after three weeks. β-HCG levels were monitored once a week for the next three weeks and then once a month for the next six months.

After one month, a second CT examination was made and the images revealed by the first examination disappeared.
Histopathological findings were: multiple tissue fragments representing chorionic membrane and villositary elements with marked morphological changes: non-uniform villi dimension, prominent stromal cysterns, mucoid/myxoid stroma in the majority of the villi, prominent stromal apoptosis, incomplete circumferential trophoblast in the majority of the villi, minimal trophoblastic atypia, trophoblastic pseudoinclusions.

The conclusion was that the aspect in conjunction with the β-HCG values, clinical and paraclinical panel sustained the diagnosis of a complete molar pregnancy (Figures 3–6).

Figure 3 – Stromal apoptosis. HE staining, ×400.

Figure 4 – Prominent stromal cysterns and circumferential trophoblast. HE staining, ×100.

Figure 5 – Prominent stromal cysterns and circumferential trophoblast. HE staining, ×100.

Figure 6 – Trophoblastic pseudoinclusions. HE staining, ×200.

Discussion

Although some molar pregnancies may be detected by pre-evacuation ultrasound examination, the majority manifest sonographically simply as missed or incomplete miscarriage, and false positive sonographic diagnosis may also occur. The gold standard for the diagnosis of molar pregnancy therefore remains at present routine histopathological examination of products of conception following uterine evacuation [6].

After confirming the diagnosis and if the patient is hemodynamically stable, the most appropriate method of molar evacuation should be decided upon [8, 9]. Suction evacuation and curettage is the preferred method of evacuation of a hydatidiform mole, independent of uterine size, for patients who wish to maintain their fertility [9, 10]. Hysterectomy is an alternative to suction curettage if childbearing has been completed. In addition to evacuating the molar pregnancy, hysterectomy provides permanent sterilization and eliminates the risk of local myometrial invasion as a cause of persistent disease. Because of the potential for metastatic disease even after hysterectomy, the risk of postmolar GTN still remains at 3–5%, thereby requiring continued β-HCG follow-up [10].

Prophylactic administration of either Methotrexate or Actinomycin D chemotherapy at the time of or immediately after evacuation of a hydatidiform mole is associated with a reduction in incidence of postmolar GTN from approximately 15–20% down to 3–8%. The use of prophylactic chemotherapy should be limited, however, to special situations in which the risk of postmolar GTN is much greater than normal or where adequate HCG follow-up is not possible, as essentially all patients who are followed up with serial HCG testing after molar evacuation and found to have persistent GTN can be cured with appropriate chemotherapy [11–13].

Follow-up after evacuation of a hydatidiform mole is essential to detect trophoblastic sequelae (invasive mole
or choriocarcinoma), which develop in approximately 15–20% with complete mole and 1–5% with partial mole [8, 14, 15]. Definitive follow-up requires serial serum quantitative HCG measurements every 1–2 weeks until three consecutive tests show normal levels, after which HCG levels should be determined at three months interval for six months after the spontaneous return to normal [7]. More than half of patients will have complete regression of β-HCG to normal within two months after evacuation.

Contraception is recommended for six months after the first normal β-HCG result, to distinguish a rising β-HCG because of persistent or recurrent disease from a rising β-HCG associated with a subsequent pregnancy. The use of oral contraceptive pills is preferable because they have the advantage of suppressing endogenous LH, which may interfere with the measurement of β-HCG at low levels and studies have shown that they do not increase the risk of postmolar trophoblastic neoplasia [16, 17].

Conclusions

The particularity of this case consists in the mole’s dimensions, the uterus’ thin walls and the therapeutic management applied successfully based on ultrasound and biological diagnostic with the main aim to preserve fertility. The accurate and early diagnosis of molar pregnancy is a major clinical aim due to the predisposition for infertility. The accurate and early diagnosis of molar pregnancy may interfere with the measurement of β-HCG at low levels and studies have shown that they do not increase the risk of postmolar trophoblastic neoplasia [16, 17].

References


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