

Diagnosis and Treatment of an Atypical Invasive Mole: A Case Report

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Gestational trophoblastic neoplasia (GTN) is spectrum of trophoblastic diseases that includes invasive mole, placental site trophoblastic tumor (PSTT), epitheloid trophoblastic tumor (ETT) and choriocarcinoma. The diagnosis of invasive mole is mostly based on clinical findings. In this paper, we report a 40-year-old woman with atypical presentation of invasive mole. She had no complaint, and was incidentally diagnosed after 9 months of amenorrhea during a hospital visit. Clinical diagnosis was difficult due to nonspecific ultrasound findings and low-level β -hCG. Dilatation and curettage failed to obtain sufficient pathologic information, and chemoresistance to methotrexate complicated the treatment. Hysterectomy was finally decided due to progressing uterine enlargement, even after the normalization of serum β -hCG.

Keywords: invasive; mole; trophoblast; methotrexate.

Gestational trophoblastic neoplasia (GTN) is spectrum of trophoblastic diseases that exhibit progression, invasion and metastatic potential. This terminology includes invasive mole, placental site trophoblastic tumor, and choriocarcinoma. Invasive mole is the most common form of post molar GTN.

GTN incidence varies from 0.6-1.1 per 1000 pregnancies in Europe and North America, to 1 in 77 pregnancies and 1 in 57 deliveries in Indonesia (Chhabra, 2007). GTN may arise after an episode of molar pregnancy (15-20% of patients with complete mole and 1-5% with partial mole), of which 50-70% are persistent or invasive mole (Barber, 2018). This accounts for 4-8% of all gestational trophoblastic disease (Chhabra, 2007).

About 10-17% of hydatidiform moles exhibit invasive properties and 15% progress to distant metastasis (Lurain, 2010).

Most of invasive moles can be diagnosed and treated based on clinical findings, without the need of pathological examination. History of mole in the antecedent pregnancy, combined with persistently high serum β -hCG and ultrasound finding of heterogenous mass infiltrating myometrium are the clinical features suggestive of invasive mole. Single agent chemotherapy is an effective measure, and it rarely needs combination chemotherapy or surgery (May, 2011). But in some clinical settings, the management of invasive mole may not be easy. In this paper, we report a

patient with atypical presentation of invasive mole, who was resistant to chemotherapy and finally underwent surgery.

Case report

A 40-year-old, P1A0, woman came with 9 months of amenorrhea with negative urine pregnancy test. She had no other complaint, and she thought it was the beginning of her menopause. Her vital signs were normal. Her general and obstetrics history was unremarkable. She had never used contraception before.

Gynaecologic examination revealed an enlarged uterus (appropriate for 16 wks), with no sign of cervix or adnexal pathology. Pelvic ultrasound showed a heterogenous ill-defined intrauterine mass causing the uterine enlargement. Inner mass neo-vascularization and increased underlying myometrial vascularization, were evident from colour doppler, suggesting a neoplasia (resistance index 0,311). Her serum β -hCG was 55.8 mIU/mL, while other laboratory panels were normal. At this point, gestational trophoblastic neoplasia (GTN) was diagnosed. Physical examination and radiologic survey did not suggest any sign of metastasis (low-risk GTN based on FIGO classification).

Two dose of chemotherapy using methotrexate (MTX, pulsed therapy, 30 mg/m² intramuscular, weekly) was given. Repeat doppler ultrasound showed a markedly reduced blood flow after the second dose of MTX. Dilatation and curettage was undertaken in the following week, but resulted in profuse bleeding. Pathologic examination only showed necrotic cells and blood clot. Third dose of MTX was given to ensure optimal resolution. Her serum β -hCG dropped to 20.4, 3, and 1.7 mIU/mL after the first, second, and third chemotherapy, respectively. Two after-course doses were given afterwards. Despite β -hCG normalization, uterine enlargement (18 wks) was noted during follow-up period, 1 week after the last dose of MTX. After discussing possible treatments with the patient, total hysterectomy + bilateral salpingectomy was decided.

Pathologic examination of the uterus specimen showed edematous chorionic villi with marked trophoblastic proliferation that invaded less than half of the myometrium, suggesting an invasive mole. Weekly follow-up including physical examination and β -hCG test was done

for 1 month, continued with 3-weekly β -hCG test for 3 months. Her serum β -hCG remained normal, and no complication was found.

DISCUSSION

Invasive mole arises from myometrial invasion of hydatidiform mole via direct extension through tissue or venous system (Lurain, 2010). It is characterized by edematous chorionic villi with trophoblastic proliferation that invades directly into the myometrium (Barber, 2018). Most invasive mole is diagnosed clinically, before the pathologic examination result has been obtained. This approach is really helpful in determining the initial treatment. Patients mostly present with vaginal bleeding and markedly elevated serum β -hCG level (>1.000 mIU/mL). Unlike the other variants of GTN that may occur months or years after various type of pregnancies (term, abortion, or molar), invasive mole usually occurs immediately after a molar pregnancy (Shaaban, 2017). Diagnosis is based on the stability of serum β -hCG4 measurements in 3 weeks or more than 10% increase in 2 weeks, combined with ultrasonography findings (Akhavan, 2016; Shaaban, 2017). In this case, GTN diagnosis was made based primarily on persistently elevated serum β -hCG; pathologic examination confirmed our findings, after hysterectomy was undertaken.

There exist quiescent gestational trophoblastic disease, a term used to describe a persistent low level serum β -hCG (<200 mIU/mL) for 3 months without clinically detectable disease, after any gestational trophoblastic disease or spontaneous abortion (Lurain, 2010). An elevated serum β -hCG level may also found in normal patients, and is termed phantom GTN/ β -hCG. This phenomenon is caused by the presence of circulating heterophilic hCG antibodies. This antibody is not excreted to urine, thus, it can be confirmed from negative urine pregnancy test (May, 2011).

Invasive mole may appear as nonspecific heterogenous or hyperechogenic myometrial focal mass with cystic areas in grey-scale ultrasound (Alcazar, 2018). A high-resolution ultrasound is very useful in the assessment of myometrial invasion and molar residue after evacuation (Akhavan, 2016). In some cases, it may be difficult to differentiate invasive mole with fibroids,

adenomyomas, retained products of conception, or other pelvic malignancies (Shaaban, 2017).

The role of doppler ultrasound in the diagnosis of GTN is still controversial. It does not seem to increase the diagnostic performance of ultrasound for GTN (Alcazar, 2018). Although it is reported to be helpful in monitoring the course of disease and the response to chemotherapy, we found no benefit in this patient. Before commencing MTX therapy, we observed an increased neo-vascularization with high blood-flow into the myometrium. In this setting, any attempt to evacuate intrauterine mass may cause morbidity to patient. Thus, we decided to start MTX chemotherapy to decrease vascularization and prevent tumor progression. The markedly reduced vascular pattern in the repeat ultrasound after the second dose of chemotherapy lead us to think that it is safe to perform uterine evacuation, but unfortunately it turned into a profuse bleeding. Even after normalization of serum β -hCG and the absent of vascular pattern, the tumor progression continued. This suggests that colour doppler findings do not always correlate with the true nature of disease, and interpretation should be made wisely in conjunction with other clinical features. Magnetic resonance imaging (MRI) is helpful in the evaluation of tumor invasion, but may be non-specific in some cases. Computed tomography (CT) and positron emission tomography (PET) CT have important role for detecting metastatic disease, but should not be used as routine screening method (Alcazar, 2018).

Invasive moles may spontaneously resolve even without treatment, but this approach will increase the risk of uterine perforation, haemorrhage, and infection (Barber, 2018). They are highly sensitive to chemotherapy and it can be given without histopathologic diagnosis (Lurain, 2010). Invasive moles usually respond well to single-agent chemotherapy such as MTX or actinomycin D (Chhabra, 2007; May, 2011). Partial resection or hysterectomy can be considered in patients with uncontrolled vaginal bleeding, unstable general condition or sepsis due to intrauterine infection. Hysterectomy may be a preferred option for women who do not wish to preserve fertility, and patients with extensive uterine tumor (Lima, 2016; Aminimoghaddam, 2017). Follow up serum β -hCG examination should

be done every 1-2 weeks until 3 consecutive normal values, continued with every 3 months for 6 months after normalization of serum β -hCG (Lurain, 2010).

In our patient, we found a persistently elevated, low-level serum β -hCG with no clinical symptoms, other than secondary amenorrhea. Positive urine pregnancy test had excluded the presence of antibody. But, the progress of tumor did not correlate with the serum β -hCG level: uterine enlargement and tumor invasion progressed, in the absence of high level β -hCG. Hence, we think that "quiescent" may not be appropriate to describe this finding, although chemoresistance that she experienced is a common finding in a low-activity neoplasia. It is also similar to patients with PSTT or ETT, who exhibit low-level serum β -hCG in spite of tumor progression. Unexpectedly, pathologic result showed histology properties of an invasive mole. These contradicting features may add to the clinical spectrum of the disease. Whether it is an invasive mole variant or new clinical entity is a question for future studies.

CONCLUSION

Invasive mole is the most common form of gestational trophoblastic neoplasia. It can be diagnosed clinically, and treatment plan consisting of chemotherapy and/or surgery can be initiated in the absence of pathologic examination. In some clinical settings, conventional management may be insufficient. Monitoring strategy using both serum β -hCG and ultrasound should always be implemented, to exclude unexpected tumor progression.

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