Hydatidiform mole in a perimenopausal and primary infertility patient: case report

M. Li, M.Y. Wu, Y. Han, R. Li

Department of Minimally Invasive Gynecology, Central Hospital of Fengxian District, Shanghai (China)

Summary

We present a case of a 56-year-old woman with primary infertility who complained of amenorrhea for five months and vaginal bleeding for two months. Initially she was misdiagnosed with endometrial cancer due to her disease history and older age, but eventually a diagnosis of complete hydatidiform mole was confirmed and then laparoscopic total hysterectomy was performed. The patient has been followed-up as an outpatient for more than one year, and hads an excellent prognosis. To our knowledge, this is the first case of hydatidiform mole in a woman with primary infertility during the perimenopausal stage. Even though hydatidiform mole is rare in primary infertility patients during perimenopause, it should always be considered in case of misdiagnosis.

Key words: Gestational trophoblastic disease; Hydatidiform mole; Perimenopausal women; Primary infertility.

Introduction

Gestational trophoblastic diseases (GTD) encompass a diverse group of lesions that include hydatiform mole (HM), invasive mole, choriocarcinoma and placental site trophoblastic tumor [1]. Grossly HM is composed of various sizes of grape-like vesicles. Microscopic examination demonstrates hydropic degenerated villi with circumferential trophoblastic cell proliferation, without structure normal embryonic. It is divided into a complete and partial mole. HM is the most frequently occurring GTD [2]. GTD generally occurrs in women of reproductive age and rarely presents in patients beyond that group age, and is especially rarer in those women who suffer from primary infertility at the same time. In China, the incidence of GTD is on average 0.78 per 1,000 pregnancies [3]. It generally occurs in women of reproductive age with an age range of 20 to 34 years [4]. When it occurs in women older than 50 years, it frequently represents a malignant disease. Until now there have been few series reported in the world literature of gestational diseases occurring in women older than 50 years. Even rarer are reports of benign trophoblastic disease in perimenopausal women combined with primary infertility. We present a rare case of complete HM in a perimenopausal woman with primary infertility.

HM is a difficult condition to diagnose in women past reproductive age due to its very low incidence. The most frequent symptom in patients with molar pregnancy is abnormal vaginal bleeding, which is usually related to endometrial tumor.

Numerous studies support the fact that benign GTD is extremely rare in perimenopausal and postmenopausal women. Patients in the sixth decade are not expected to be pregnant, and physicians may not even think of checking β-hCG levels. Therefore, the diagnosis of HM may be missed. On the other hand, in women of perimenopausal age, the possibility of GTD may be considered for those patients who have perimenopausal syndrome or endometrial tumor. These patients usually present with abnormal vaginal bleeding and excessive uterine size. Transvaginal ultrasound usually shows an enlarged uterus containing mixed material with minor blood flow within the uterine cavity.

In the world literature [5-7], it is well established that the occurrence of GTD in women older than 50 years is rare, and symptoms of the disease become more and more atypical. GTD is extremely rare in perimenopausal women with primary infertility, with no publications being reported either at home and abroad.

In 1997, Davidson *et al*. [8] described a case of a perimenopausal 60-year-old woman diagnosed with a molar pregnancy after only three months of amenorrhea. Rabczynski *et al*. [9] in 2000 reported a case of complete complete HM in a 59-year-old woman; however, the history of amenorrhea was not addressed. In the largest series, Ramondetta *et al*. [10] presented a case of a 60-year-old woman with evidence of a pelvic mass and pulmonary metastasis. Jequier and Winterton [11] reviewed 109 cases of GTD in women older than 50 years. They found malignant disease in 28.4% (31 patients), benign moles in 47.7% (52 patients), and an unclear pathologic diagnosis in the remaining 23.9%. The age of the patients with benign moles and malignant neoplasms ranged from 50 to 59 years (mean, 52.2 years) and 51 to 64 years (mean, 54.2 years).

A few studies showed that ovarian cells of perimenopausal women had different levels of degeneration, and hazard of HM in women over 50 years of age was much higher in 20-35 year old patients [12]. The research by Feng *et al*. [13] pointed out that the diagnosis of pregnancy and pregnancy-related disease should be considered in older women presenting with abnormal vaginal bleeding. Once GTD in women aged 50 years or more is diagnosed, chemotherapy should be given as soon as pos-

Revised manuscript accepted for publication December 9, 2011

Fig. 1

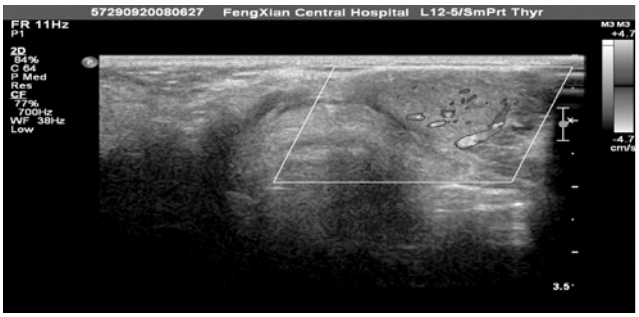

Fig. 2

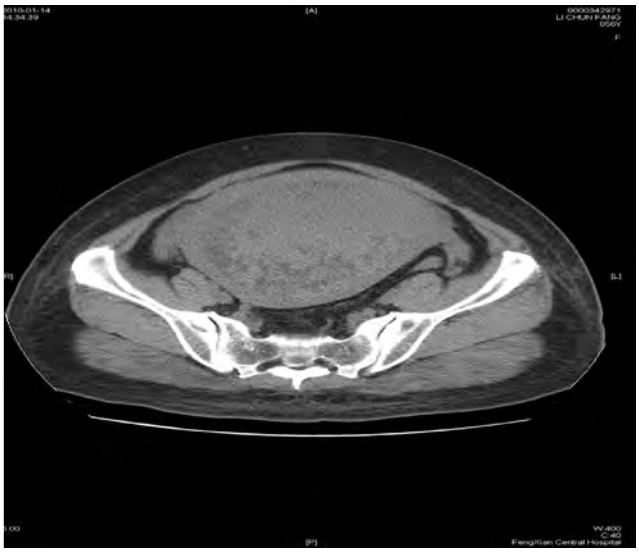

Fig. 3

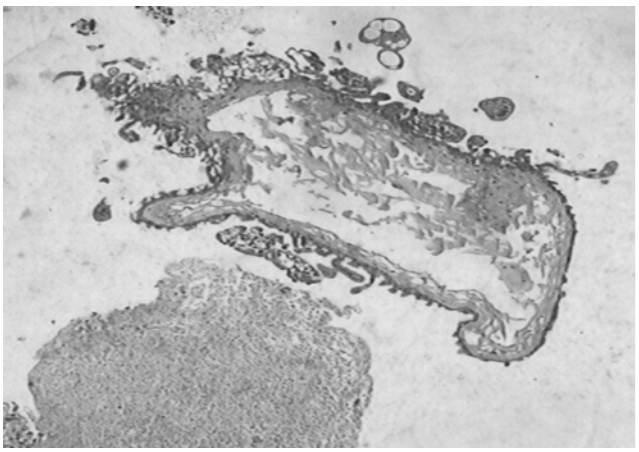

Figure 1. — Ultrasound showing enlarged uterus (19 × 10.7 × 19.3 cm), with complex echoes (18.9 × 10.6 ×1 9.2 cm) in the uterine cavity. CDFI: no blood signals.

Figure 2. — Computed tomography suspicious for malignant uterine disease.

Figure 3. — Histological pathology showing hydropic villi with circumferential hyperplastic trophoblasts (hematoxylin-eosin, original magnification × 100).

sible. Hysterectomy has frequently been required to improve the prognosis of GTM in older women.

Patients have an excellent prognosis; it is necessary to evaluate the disease before treatment, evaluation includes serum hCG level, pelvic examination, chest radiography, ultrasound sonography and computed pelvic tomography. Suction curettage is the method of choice to treat HM. Hysterectomy may be indicated as part of the management of older patients who have no desire for children, moreover, it can not prevent distant metastasis and replace careful follow-up.

Even though HM is rare in women older than 50 years with a history of primary infertility, it really does occur. Therefore, a high level of suspicion must be maintained to establish the correct diagnosis.

Case Report

A 56-year-old perimenopausal woman with primary infertility in Shanghai Province of China who complained of amenorrhea for five months, irregular vaginal bleeding for two months, and abdominal distension for two weeks ", who was diagnosed with endometrial carcinoma and then admitted to our hospital. The patient was also diagnosed as primary infertility (gravida 0, para 0), who had no extra-marital sexual relations, and had no history of surgery. On admission, pelvic examination revealed that the uterus was enlarged as seven gestational weeks with tenderless, moderate consistency and poor mobility. The lab revealed mild anemia (haematocrit 25.5%, haemoglobin 96.0 g/l), high level of estrogen and progesterone (reproductive hormone PRL = 124.18 ng/ml, FSH = 0.06 mIU/ml, LH = 0.21 mIU/ml, E2 1000 pg/ml, PROG 60 pg/ml, T = 2.65 nmol/l), tumor markers negative (AFP = 1.79 ng/ml, CEA = 1.32 ng/ml, CA125 = 31.45 u/ml, and CA199 = 3.10 u/ml). A pelvic ultrasound showed an enlarged uterus with complex echoes in the uterine cavity. CDFI: no blood signals (Figure 1). Computed tomography of the pelvis indicated malignant uterine disease (Figure 2).

Due to the high level of sexual hormone determination, urine human chorionic gonadotropin (hCG) level was checked and showed mild positivity, so we suspected that the mass might be related with pregnancy. Accordingly, serum hCG level was determined, which was greater than 200,000 mIU/ml; finally GTD was diagnosed.

The patient underwent suction curettage which grossly revealed a large amount of vesicular tissue, mixed with blood clots; a total of 3000 ml. Considering the huge size of the uterus, suction curettage was incomplete and had to be repeated after one week. We extirpated a total amount of 30 g product; histology showed blood clots and decidual tissue with hydropic trophoblastic cell proliferation (Figure 3). Serum β-hCG was reduced to 4309.5 mIU/ml four days after curettage. The pathology confirmed the diagnosis of benign molar pregnancy.

The patient was classified as high risk according to the WHO Prognostic Scoring System for GTD. She had no desire for further pregnancies, so laparoscopic hysterectomy was subsequently performed five days after curettage. During the operation, we found that uterine size corresponded to three gestational months, was soft in consistency, and there were two fibroid nodules 4 x 3 cm in size extruding from the surface of the anterior wall and fundus of the uterus. No abnormalities were found in bilateral adnexal tissue and the operation was successful. Serum β-hCG was reduced to 1330.4 mIU/ml seven days after operation. Histological pathology showed fibrinous exudate of the uterine cavity, a few pieces of endometrial tissue and uterine leiomyoma. Since the patient had high risk factors for hydatidi-

form mole, prophylactic chemotherapy was proposed, but the patient refused due to personal reasons. She was discharged on the 10th day after the operation, and ultrasound showed no abnormality.

The patient received careful follow-up of hCG as an outpatient, and it took seven months after hysterectomy for serum hCG to regress to normal levels. Up to today symptoms like vaginal bleeding, cough, hemoptysis and metastasis signs have not appeared, and gynecological examinations have shown no abnormalities.

Conclusions

The rarity of a molar pregnancy in a 56-year-old amenorrheic woman brings this patient's menopausal status into question. Serum luteinizing hormone and follicle-stimulating hormone levels are increased and the estradiol levels are decreased. One may not think of checking hCG in women older than 50 years with a 5-month history of amenorrhea. Even though this patient had amenorrhea for five months, she most likely was considered to be in a transitional period of progressive loss of ovarian function and sporadic ovulatory cycles. At first we almost misdiagnosed this case as endometrial carcinoma, which was attributed to the older age and history of primary infertility. Hydatidiform mole should be suspected in any woman with vaginal bleeding. Thus estimations of serum and urine human chorionic gonadotropin are necessary in perimenopausal patients with vaginal bleeding and history of primary infertility. Diagnosis in this age group depends on a high level of suspicion, and hysterectomy should be considered due to the high risk of postmolar gestational trophoblastic tumor after uterine suction evacuation. Effective procedures to prevent misdiagnosis lie in improving consideration of GTD in perimenopausal women and improving the level of diagnostic techniques.

References

[1] Noal S., Joly F., Leblanc E.: "Management of gestational trophoblastic disease". *Gynecol. Obstet. Fertil.*, 2010, *38*, 193.
[2] Kate-Booij M.J., Lok C.A., Verheijen R.H., Massuger L.F., van Trommel N.E.: "Trophoblastic diseases". *Ned. Tijdschr. Geneeskd.*, 2008, *152*, 2219.
[3] Feng Y.J., Sheng K.: "Obsterics & Gynecology", 2th edition, 2010, 366 (in Chinese).
[4] Shi Y.F., Li J.Q., Zheng W., Chen X.J., Qiao Y.H. Hao M. *et al.*: "Survey of gestational trophoblastic disease incidence among 3.6 million pregnancies in China". *Chin. J. Obstet. Gynecol.*, 2005, *31*, 76.
[5] Steigrad S.J.: "Epidemiology of gestational trophoblastic diseases". *Best. Pract. Res. Clin. Obstet. Gynaecol.*, 2003, *17*, 837.
[6] Lybol C., Thomas C.M., Bulten J., Dijck J.A., Sweep F.C., Massuger L.F.: "Increase in the incidence of gestational trophoblastic disease in The Netherlands". *Gynecol. Oncol.*, 2011, *121*, 334.
[7] Tham B.W.L., Everard J.E., Tidy J.A., Drew D., Hancock B.W.: "Gestational trophoblastic disease in the Asian population of Northern England and North Wales". *BJOG*, 2003, *110*, 555.
[8] Davidson S.A., Gottesfeld J., La Rosa F.G.: "Molar pregnancy in a 60-year-old woman". *Int. J. Gynecol. Obstet.*, 1997, *56*, 53.
[9] Rabczynski J., Kochman A., Prudlak E., Lewandowski M.: "Hydatidiform mole in 59-year-old woman: a case report". *Ginekol. Pol.*, 2000, *71*, 152.
[10] Ramondetta L.M., Silva E.G., Levenback C.F., Burke T.W.: "Mixed choriocarcinoma in a postmenopausal patient". *Int. J. Gynecol. Cancer*, 2002, *12*, 312.
[11] Jequier A.M., Winterton W.R.: "Diagnostic problems of trophoblastic disease in women aged 50 or more". *Obstet. Gynecol.*, 1973, 42, 378.
[12] Cao Z.Y.: "Norms and guidelines of diagnosis and treatment of trophoblastic disease". *Beijing People's Health Publishing House*, 2000, 61.
[13] Feng F.Z., Xiang Y., Wan X.R., Yin S.J., Yang X.Y.: "Clinical characteristics and management of gestational trophoblastic disease in women aged 50 years or more". *Chin. J. Obstet. Gynecol.*, 2005, *40*, 605.

Address reprint requests to:
Y. HAN, M.D.
No. 9588 Nanfeng Road
Nanqiao Town
Fengxian District of Shanghai
Shanghai 201499 (China)
e-mail: xjhy0519@163.com