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Case Report

An invasive mole localized in the fallopian tube with ovarian metastasis

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Abstract

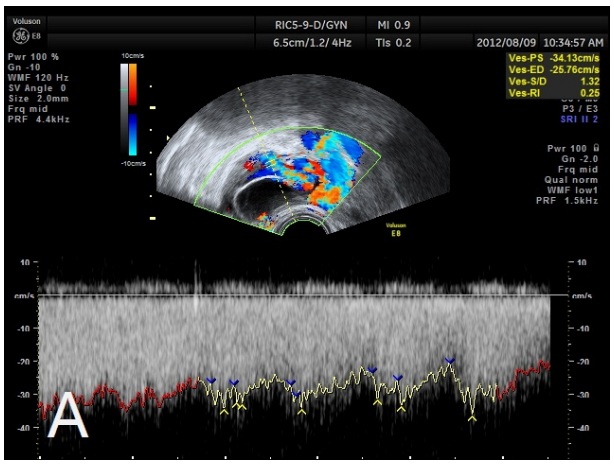
Objective: To present a case of an invasive mole localized in the fallopian tube with ovarian metastasis.
Design: Case report.
Setting: Department of Obstetrics and Gynecology, the First Affiliated Hospital of Xi'an Jiaotong University.
Patient: A 30-year-old woman with amenorrhea sixty-four days with a little bit of vaginal bleeding. The serum levels of β-hCG was significantly increased but no gestational sac was observed in the uterus cavity by ultrasound examination. She once had a dilation and curettage 5 months ago.
Intervention(s): The patient underwent laparoscopic operation with right salpingo-oophorectomy and left theca-lutein cysts puncture under general anesthesia and received chemotherapy after the operation.
Main Outcome Measure(s): The serum β-hCG level of the patient fell into the normal range after the 2nd cycle of chemotherapy and transvaginal ultrasonography reexamination showed no abnormalities. The patient is well at one year follow-up.
Conclusion(s): An invasive mole in fallopian tube with ovarian metastasis was diagnosed and the patient was successfully treated by laparoscopic operation and chemotherapy.

Gestational trophoblastic disease (GTD) is a group of rare tumors originating from the trophoblast, which surrounds the blastocyst and develops into the chorion and amnion. GTD often arises after molar pregnancies but can also occur after any gestational event including miscarriages and term pregnancies. The main types of GTD are hydatidiform mole (complete or partial); invasive mole; choriocarcinoma; and placental site trophoblastic tumor. GTD is known to be associated with increased maternal age and is more common in Asia[1]. An invasive mole is also called malignant mole due to its aggressive growth characteristics. There is invasion of the myometrium, parametrial tissues and blood vessels by hydropic chorionic villi, accompanied by proliferation of trophoblast. The risk factors for developing invasive moles are 1) a prior mole; 2) maternal age greater than 40 years or less than 20 years; and 3) a previous spontaneous abortion. Overall, invasive moles occur at an estimated rate of 1 in 15,000 pregnancy[2].A total of 10-17% of hydatidiform moles resulted into invasive moles with approximately 15% of lung or vagina metastasis[3]. Invasive moles are more common in complete molar pregnancies than in partial molar pregnancies. In a review of 2100 cases of GTD at the New England Trophoblastic Disease Centre, 16 patients (0.76%) were identified affecting the fallopian tube[4]. The tubal pregnancy is often degenerated or surgically removed before villi changed, so the incidence of invasive mole in fallopian tube is very low and metastasis to ovary is extremely rare, which even much lower than that of gestational primary ovarian choriocarcinoma with an estimated incidence of 1 in 3.7 x 10^8 pregnancies[5]. Up to now, there is no report of the incidence of invasive mole in fallopian tube from our hospital. Herein, we repot a case of an invasive mole in the fallopian tube with ovarian metastasis.

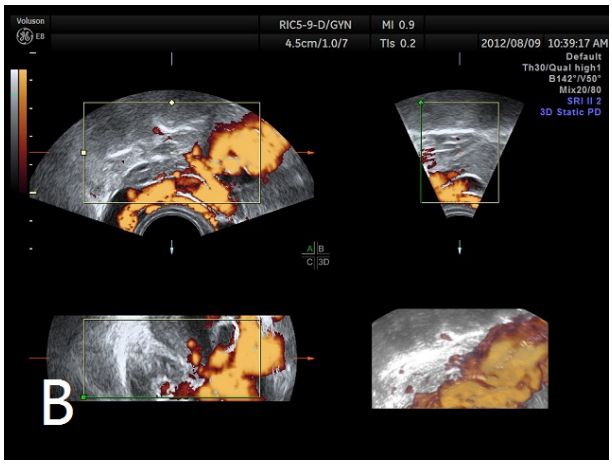
Case report

A 30 years old woman, gravida 2 para 1, was transferred from a local hospital for amenorrhea sixty-four days and found GTD. The patient had no significant past medical or surgical history. Her menarche occurred at the age of 15 and subsequent menses were regular at 30-day intervals, lasting for 5-6 days. She hadn't taken normative contraception. She had a dilation and curettage at gestational age of more than seven weeks five months ago. Her menstrual cycle was recovery postoperation. She had a positive pregnancy test by herself at thirty-six days of amenorrhea and underwent ultrasound examinations at a local hospital at forty-two and fifty days of amenorrhea, respectively. No gestational sac in the uterus cavity was visualized by ultrasound. There was a little bit of vaginal bleeding at fifty-

eight days of amenorrhea. The blood is bright red and there was no tissue discharge. The serum level of human chorionic gonadotropin (β-hCG) was 13411 mIU/ml. She went to another hospital in Xian to seek treatment at fifty-nine days of amenorrhea. The gynaecological ultrasound examination revealed normal uterus, a left adnexa nonneoplastic cysts and right adnexa with a size of 5.0 cm × 4.8cm × 5.3 cm irregular anechoic surrounding by abundant blood flow signal and diagnosis of GTD was suggested. The second test of serum β-hCG was 12051 mIU/ml three days later, which the level of β-hCG didn't obviously decrease compared to the previous test. The patient was admitted to our hospital for evaluation. The patient had no symptoms of cough, hemoptysis or dizziness etc. The vital signs were within normal limits and physical examination was unremarkable. The pelvic examination revealed normal vulva and vagina. The cervix pain was suspiciously positive. The uterus was retroverted position with normal size. A diameter of 5 cm cystic mass in the right adnexa could be touched and it was mobile and tender. No abnormality was observed in the left adnexa. The repeated transvaginal ultrasound depicted myometrium with heterogenous echoic and blood flow resistance index (RI) of 0.48. The size of right ovary was 2.4 cm x 1.7cm, with a 4.5 cm x 2.0 cm cystic mass in irregular shape around abundant blood flow signals with RI of 0.25. The size of left ovary was 2.5 cm x 2.0 cm, with a 1.9 cm x 1.8 cm anechoic area inside. The ultrasound suggested GTD. The color Doppler flow imaging showed that there were multilocular cystic structures with obvious vasodilation and the envelope with burr sign, RI of 0.25 (Figure 1A). The energy diagram showed "Fire sign" of blood flow in right adnexa (Figure 1B). Chest radiography has no abnormality (Figure 2A) and computed tomography (CT) revealed a small nodule (5.3 mm x 4.8 mm) in the left upper lobe of the lung and the patient may have lung metastases (Figure 2B). The patient was stage III according to invasive mole FIGO 2000. The serum level of β-hCG was 11125 mIU/ml (within normal limit ≤ 4.9 mIU/ml) and CA-125 was 7.22 U/ml (within normal limit < 35.00 U/ml).



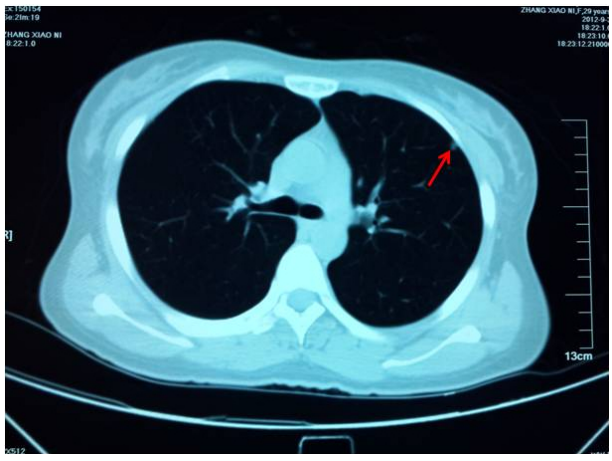
1A



1B

Figure 1 Color Doppler flow imaging (A) and energy diagram (B) of blood flow in right adnexa.

2A

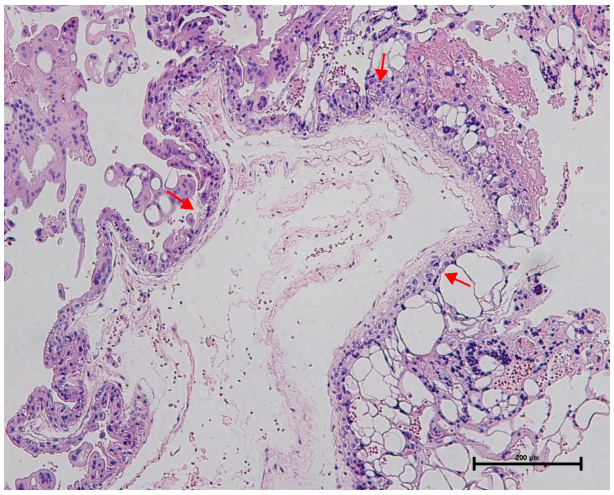


2B

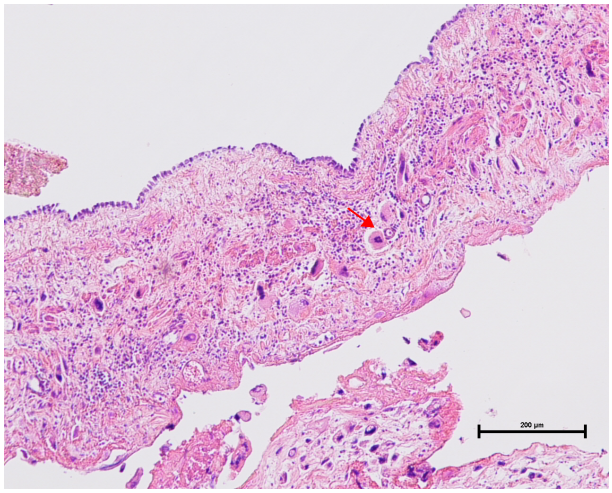
Figure 2 The chest radiography (A) and CT (B).

In order to conform the diagnosis of the patient, a laparoscopic surgical exploration under general anesthesia was performed. The uterus were

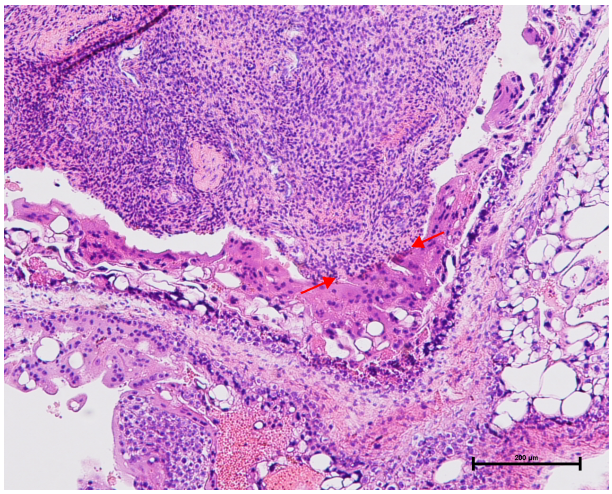
normal and the ampulla of right fallopian tube was enlargement and a mass of 4 cm × 3 cm × 2 cm with irregular shape, integrated membrane, purplish blue during intra-operation. There was no break and active bleeding in the surface of blood vessels, which was exposure and engorgement. The size of right ovary increased (4 cm × 4 cm × 3 cm) with congestion and dark red. The left ovary slightly enlarged and there were several cysts with a diameter of one centimeter on the surface. The cysts walls were transparent and thin and the fluid of cysts was yellow and clear. The left fallopian tube was normal. The right salpingo-oophorectomy and left theca-lutein cysts puncture were performed for the patient. The pathological studies revealed right annex gestational trophoblastic tumor (GTT) (a chorionic epithelial cancer) by intraoperative frozen-section and was confirmed as a malignant hydatidiform mole in the right fallopian tube with vascular and ovarian metastasis by paraffin section. The results of postoperative hematoxylin-eosin (H-E) staining samples are shown in Figure 3. The final diagnosis of the patient was an invasive mole in fallopian tube with ovarian metastasis. The patient received five days chemotherapy starting on the 2nd day postoperation with methotrexate (MTX) 10 mg/m^2/d plus 5-fluorouracil (5-FU) 800 mg/ m^2/d plus etoposide(VP-16) 60 mg/ m^2/d. The serum β-hCG level decreased to 51.95 mIU/ml after the first cycle of chemotherapy and fell into the normal range after the 2nd cycle of chemotherapy and still maintained within normal limits for more than 12 months (the 5^{th} measurement). The courses of serum β-hCG level are shown in Figure 4. The transvaginal ultrasonography (TVS) reexamination showed no abnormalities with the uterus and bilateral annex. The patient received consolidation chemotherapy for one cycle and responded the treatment well. The nodule in lung of the patient completely disappeared three months after the chemotherapy by CT examination and the patient is normal right now for more than one year follow-up.



3A



3B



3C

Figure 3 Histopathological image of invasive mole in the fallopian tube.

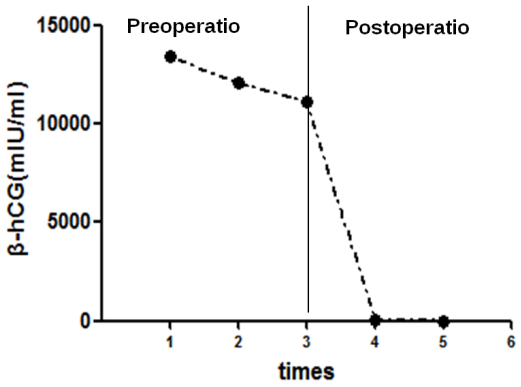


Figure 4 The courses of serum β-hCG level from five tests.

Discussion

Invasive mole in the fallopian tube is rare and often misdiagnosed as ectopic pregnancy because the clinical symptoms of both diseases are extremely similar including amenorrhea, irregular vaginal bleeding, adnexa mass, abdominal pain and occurrence of hemorrhagic shock when a massive intra-abdominal hemorrhage. Therefore, a definite diagnosis needs by pathological examination after

operation. However, the diagnosis of an invasive mole is often based on the clinical symptoms of the patient rather than by pathological examination[6]. This patient had presented a little bit of vaginal bleeding for almost two months after a dilation and curettage five months ago. The serum β-HCG is the most important and valuable diagnosis and treatment marker of GTD. When tubal pregnancy, because of fallopian tube muscle weakness and insufficient blood supply, trophoblast cells are underdeveloped, syncytiotrophoblast synthesis of hCG quantity significantly reduced, the serum β-HCG doubling time extended to about 3-8 days[7]. Therefore, the serum levels of β-hCG are significantly lower than that of the same gestational week of the normal pregnancy. The invasive mole can secrete abundant hCG, so the levels of β-HCG in peripheral blood increased significantly compared with normal intrauterine pregnancy at the same gestational week. Thus, the serum levels of β-hCG of invasive mole in fallopian tube are significantly higher than tubal pregnancy[8]. However, sometimes the serum levels of β-hCG in ectopic pregnancy also increased significantly, so it can't be distinguished tubal pregnancy and tubal hydatidiform mole only based on to the serum levels of β-hCG. The gestational sac in the uterus cavity of the patient was not found by three times of ultrasound examination, but the serum levels β-hCG were higher at all the times and it's the clues to diagnosis of the invasive mole in fallopian tube.

With the development of the ultrasonic technology and experience of ultrasound workers, sonograms of TVS could provide reliable information to help making the right diagnosis for clinical doctors. The ectopic invasive mole has the characteristics of abundant blood flow and shown up with color Doppler ultrasound: (1) Cystic low echo or anecho: invasion of tumor cells often lead to the damage of local vessel wall and blood sinus formation around the tumor tissues. The local blood vessels are rich and expansion to manifest "beam (bundles)". Visible blood vessels are distortion, deformation, and expansion and lead to arteriovenous fistula formation with multilocular cystic structures. The cysts have different size and irregular form; (2) "Colorful Mosaic" phenomenon: color ultrasonography showed cystic structure for the expansion of blood vessels which mainly affected the veins, and the formation of arteriovenous fistula; the existence of eddy current and high-speed flow making the tonal unusually bright so the local lesions appeared a variety of color mass at the same time by color ultrasonography called the "colorful Mosaic" phenomenon; (3)"Burr sign": It's the characteristics of blood vessels were aggressively invaded by GTT, extremely low resistance and arteriovenous fistulas in spectrum can appear buzzer sound. The local lesions and peripheral blood flow spectrum diagram for bimodal high speed and low resistance form low amplitude of broadband and unsmooth envelope; (4) Low RI: uterine artery and local blood vessels of lesions have fast systolic steep peak and high diastolic blood flow velocity, the RI of lesions is extremely low, mostly for 0.2 to 0.4 and different from the general corpus luteum cyst, about 30%-50% of patients with hydatidiform mole have corpusluteum cyst. Under the stimulation of endogenous hCG, the granulosa and theca cells in atresia follicle of bilateral ovarian often react to theca-lutein to form cysts which are multilocular, uneven, and lobulated. The ovarian cysts could by visible by ultrasound on both sides of the uterus. The capsule is clear and smooth. The internal separation of cysts often assumes the radial distribution, visible blood flow, and a clear liquid area. The ultrasound examination can provide important information with different signals of blood flow in invasive mole and ectopic pregnancy in the fallopian tube and it is valuable for their differential diagnosis. Ultrasonographic diagnosis of an ectopic pregnancy was based on the following grey-scale appearances: (1) "blob sign": an inhomogeneous mass adjacent to the ovary and moving separately; (2) "bagel sign": hyperechoic ring around gestational sac in adnexal region; (3) a gestational sac with a fetal pole with or without cardiac activity, i.e. a viable extra-uterine pregnancy[9]; (4) higher levels serum β-hCG of the patient fluctuated from 11125 to13411 mIU/ml. For the characteristics of cystic mass of GTT, ultrasound examination of the patient showed a cystic mass beside the right ovary, about 4.5 cm × 2.0 cm with rich blood flow and RI of 0.25 and energy diagram showed "Fire sign" of blood flow in right adnexa (Fig. 1). Magnetic Resonance Imaging (MRI) can also be used to diagnose the GTD[10].

The GTT often has erosion blood vessels to burst and rupture hemorrhage of primary lesions or metastases. Hemorrhage in the fallopian tubes is prone to disaster and bring great difficulties for clinical treatment. The invasive mole in fallopian tube is easy to be misdiagnosed as ectopic pregnancy and often as the reason for surgery. It's recommended to completely remove the lesions and control hematogenous dissemination through operation. Hysterectomy may need to be performed when the diagnosis is confirmed to avoid massive breeding due to rich blood sinus. In addition, chemotherapy can be administered to the patients to control disease and reduce surgical complications before surgery. An invasive mole is highly sensitive to chemotherapy and a single chemotherapeutic agent can cured the most of the disease (70-80% of the cases) after definite diagnosis[11–14]. This patient has been suspected of GTT based on the information of Doppler ultrasound, but it still could not be completely eliminated the possibility of ectopic pregnancy. Therefore, the patient underwent surgical exploration directly without preoperative chemotherapy. The chemotherapy was used on 2nd postoperative day and achieved satisfactory therapeutic effect. The reason for us to choose three drugs combination chemotherapeutic regimen for the patient is because the patient was suspected choriocarcinoma by pathological examination with intraoperative frozen section.

However, the final diagnosis of the patient was an invasive mole in fallopian tube with ovarian metastasis by pathological examination with H-E staining samples. We would use single-agent chemotherapy if I knew the diagnosis when the chemotherapy was initiated. Chest radiography and/or CT should be considered to detect pulmonary metastases. The patient's first chest CT revealed a nodular in the left lung, therefore, she may have lung metastases even without symptom such as cough, hemoptysis, and/or respiratory problems, etc. The patient responded the treatment well and the nodule in lung completely disappeared three months after the chemotherapy by CT examination. Follow-up is very important for GTD patients, this patient is still fine for more than one year after the chemotherapy.

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