

Case Report

Successful treatment of choriocarcinoma with multiple organ metastases after term delivery: a case report

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Abstract: We describe a case of choriocarcinoma with multiple organ metastases after term delivery. A 43-year-old female was diagnosed as choriocarcinoma with metastases to the liver, lungs, marrow cavity, thoracic vertebra and brain, based on serum levels of β -human chorionic gonadotrophin (β -hCG), clinical symptoms, gynecological examination, PET/CT examination and medical histories. Fourteen courses of FAV (5-fluorouracil (5-FU), dactinomycin and vincristine) and three courses of intrathecal methotrexate chemotherapy were administrated, accompanied with panhysterectomy, cholecystectomy and partial resection of the right liver lobe. After 30 months of hospital discharge, brain, lung, liver and bone metastases were not found, and blood β -hCG stayed within the normal range. Choriocarcinoma should be taken into consideration in reproductive-age women when associated symptoms and significantly elevated blood levels of β -hCG were identified. Combined chemotherapy accompanied with surgical resection is an effective strategy to treat choriocarcinoma patients with multiple organ metastases.

Keywords: Choriocarcinoma, reproductive-age, β -hCG, chemotherapy, bone metastasis, surgical resection

Introduction

Choriocarcinoma is the most severe form of the gestational trophoblastic neoplasia (GTN) which originate in the chorionic villi and the extravillous trophoblast [1, 2]. Choriocarcinoma most often follows a molar pregnancy but may ensue after a normal pregnancy, ectopic pregnancy or abortion, and other gestational event [3]. It is a rare disease and commonly occurs in women of reproductive age with an incidence of 1 in 40,000 pregnancies [4]. Additionally, the incidence of choriocarcinoma after complete hydatidiform mole is about 1000 times greater than after a normal pregnancy [5]. Since gestational choriocarcinoma contains paternal DNA, it is exquisitely sensitive to chemotherapy [3]. GTN produces excessive amounts of β -human chorion gonadotropin (β -hCG). Since the definitive diagnosis cannot be obtained by histology in most cases, the disease can be diagnosed by elevated serum levels of β -hCG from the growth of syncytio trophoblastic cells. β -hCG plays an important role in diagnosis and monitoring the therapeutic effects [6].

Choriocarcinoma is a rapidly growing, and potentially metastatic cancer which spreads distantly via the bloodstream and metastasizes to the lung, liver, and, less frequently, brain [8, 9]. Some researches show that the pulmonary metastasis rate is about 70%, the vagina metastasis 30%, the pelvic cavity metastasis rate 20%, and the brain and liver metastasis rate 10% [11]. It is reported that metastases of choriocarcinoma to the bone, kidney, bladder, and digestive track rarely occur [12]. Herein, we report one choriocarcinoma case with multiple organ metastases after term delivery.

Case report

A 43-year-old female (G₂P₁A₁, term gestation in 2008) with normal menstruation had been diagnosed as ectopic pregnancy based on lower abdominal pain, large amounts of effusion in pelvic cavity, detected blood by culdocentesis and urine hCG(+), and the patient underwent laparoscopic right salpingectomy in another hospital on July 22, 2011. A crater-like lesion (3.0 cm in diameter) near the right anterior lobe of liver was found during the surgery;

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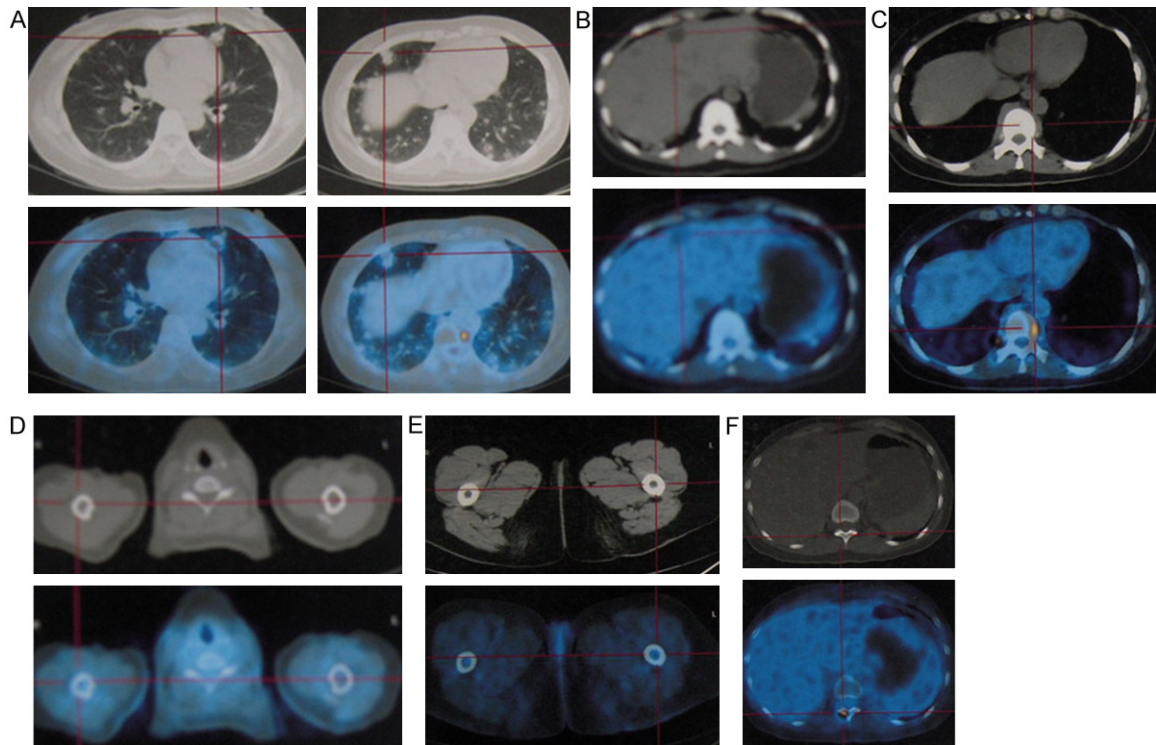


Figure 1. PET/CT imaging on admission. A. Bilateral lungs could be seen with multiple soft tissue nodular shadows and increased FDG uptake. Maximum standardized uptake value (SUV_{max}) = 3.4; B. Intense FDG uptake in the right liver lobe, SUV_{max} = 4.6; C. Increased FDG uptake around the 10th thoracic vertebra, SUV_{max} = 6.4; D-F. The increased uptake FDG of the right humerus's and left femur's marrow cavity and the 11th thoracic vertebra, SUV_{max} = 6.1.

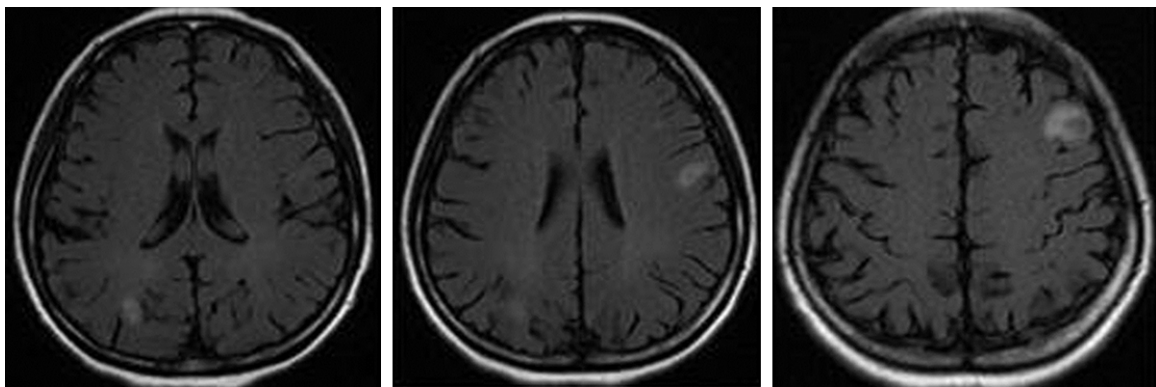


Figure 2. The brain's MRI imaging after one course of chemotherapy. MRI imaging showed multiple abnormal signal area in bilateral cerebral hemispheres and right cerebellar hemisphere, which suggested mixed low T1W1 signal and slight increase in T2W1 signal and there was edema around the nidus.

large areas of hemorrhage, fibrinoid substance and a few white blood cells were detected in tubal epithelium by postoperative pathology. Positron emission tomographic/computed tomographic (PET/CT) examination (**Figure 1**) on August 5, 2011 showed that multiple soft-tissue shadows located in the double lungs and low-density shadows in the right liver lobe, the

right humerus, the left thighbone's marrow cavity, as well as the 10th and the 11th vertebrae. However, the biopsy and pathological examination of lung showed the absence of cancer cells.

The patient came to the Hepatopancreatobiliary Surgery Department of our hospital on August

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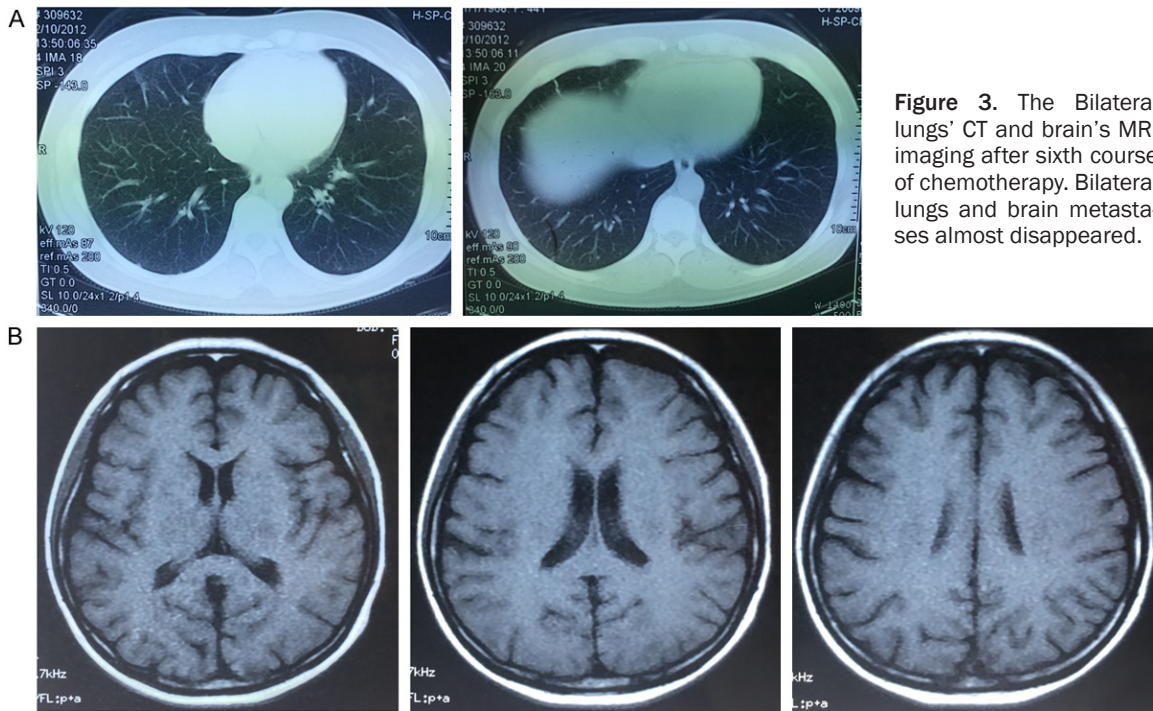


Figure 3. The Bilateral lungs' CT and brain's MRI imaging after sixth course of chemotherapy. Bilateral lungs and brain metastases almost disappeared.

8, 2011 for hepatic biopsy. The patient was with a low-grade fever, cough, hemoptysis, and chest pain. Though no cancer cells were found, serum levels of β -hCG were detected to be as high as 4677 IU/L. The patient was transferred to the Gynecology Department. Gynecological examination showed no abnormality. Based on the clinical symptoms as well as her medical history and the β -hCG values, the patient was diagnosed as choriocarcinoma with metastases to the liver, lungs, marrow cavity and thoracic vertebra. Thus, FAV [5-fluorouracil (5-FU), dactinomycin and vincristine] chemotherapy program was administrated. After one course of chemotherapy, the patient's general condition was improved, serum β -hCG level was decreased to 3075 IU/L, and other symptoms such as cough, hemoptysis, and chest pain were slightly alleviated.

The patient was hospitalized on September 19, 2011 for the second course of chemotherapy. Head magnetic Resonance Imaging (MRI) was conducted because of her headache for one week, which showed multiple abnormal signals in bilateral cerebral hemisphere and right cerebellar hemisphere (**Figure 2**). Accompanied with high level of β -hCG in cerebrospinal fluid (1305 IU/L), diagnosis of the brain metastases of choriocarcinoma was made. FAV treatment accompanied with 15 mg of intrathecal metho-

trexate (MTX) was administrated for three times. After the second course of chemotherapy, the symptoms such as headache, cough, hemoptysis, and chest pain were disappeared, and the blood level of β -hCG decreased to 465 IU/L. The patient received additional seven courses of FAV chemotherapy, together with two courses of intrathecal MTX chemotherapy. The lung and brain metastases disappeared after the sixth courses of FAV chemotherapy (**Figure 3**); metastatic tumor in liver became smaller and serum level of β -hCG decreased to 3.74 IU/L after the eighth courses of FAV chemotherapy. Lesions in her brain and bilateral lungs disappeared after the ninth courses of FAV chemotherapy (**Figure 4**), except for some higher density shadow of nodules and schistose in the left ligule and in the right middle lobe of the lungs. Besides, the hypermetabolic lesions disappeared in marrow cavity of the right humerus and the left femur, and decreased in the right liver lobe. However, the local density in the ninth, tenth, and eleventh thoracic vertebra increased, and low metabolism was found in the tenth thoracic vertebra. FDG of the focus in the left adnexa showed radial pattern. These results indicated potential inflammation, metastatic tumor or endometrial hyperplasia. In addition, multiple stones were discovered in the gallbladder.

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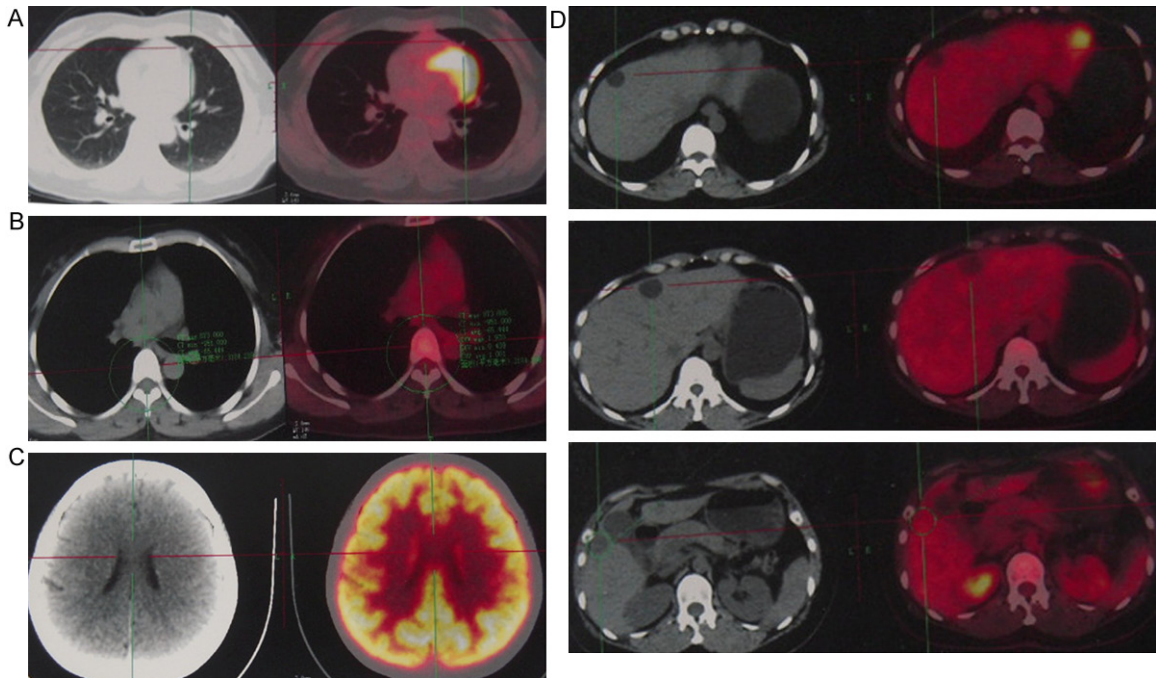


Figure 4. The PET/CT imaging after ninth course of chemotherapy. A. There are nodules in the left lung ligule, while it did not exhibit FDG uptake; B. The 10th thoracic vertebra showed evidence of hypometabolism, $SUV_{max} = 1.97$. C. There was not obvious low density shadow in bilateral brain; D. The right liver lobe, caudate lobe and the right liver next to the gallbladder could be seen with low density nidus, $SUV_{max} = 2.41$.

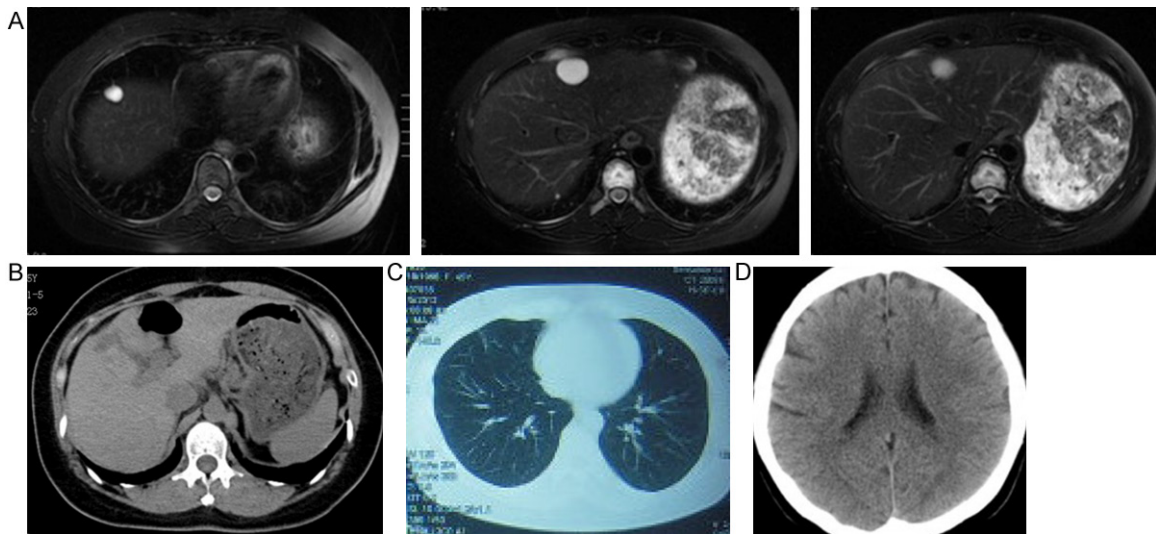


Figure 5. The enhanced MRI imaging for liver before operation and the images of rechecking post-operation. A. The liver's MRI imaging pre-operation. B. Postoperative liver CT imaging. C. CT imaging for bilateral lungs after operation. D. CT imaging for brain after operation. Bilateral lungs and brain metastases disappeared.

The patient was treated with additional four courses of FAV chemotherapy. Then, a nodular lesion (1.9 cm in diameter) was discovered in the liver next to the gallbladder by MRI imaging (Figure 5). The gynecological sonography showed anomaly and asymmetrical echo in the uterus. The patient underwent panhysterecto-

my, cholecystectomy and partial resection of the right liver lobe on September 21, 2012. Postoperative pathology showed focal necrosis, calcification and fibrous hyperplasia in liver while no abnormal constituent in the uterus. Thus, additional one course of FAV was administered. Blood level of β -hCG decreased to

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Table 1. Treatment outcome in the patient

	Blood β -hCG (IU/L)	Liver metasta- ses (mm ²)	Brain metasta- sis (mm ²)	Pulmonary metastasis (mm ²)
On admission	7.45	52 * 40	None	23 * 19
1 st chemotherapy	5241	58 * 29	7 * 12	24 * 18
4 th chemotherapy	16.36	37.6 * 25.7	8 * 5	13 * 5
6 th chemotherapy	7.92	36.9 * 21.8	None	None
8 th chemotherapy	3.74	29.2 * 18	None	None
9 th chemotherapy	0.685	22.7 * 14.2	None	None
13 th chemotherapy (operation)	1.73	19.1 * 13.4	None	None
14 th chemotherapy (1 month after the operation)	1.33	11.0 * 9.9	None	None
2 month after the operation	0.17	None	None	None

0.17 IU/L and none metastases were found in liver, brain or pulmonary after two months of the last chemotherapy (**Table 1**).

The patient discharged from our hospital after two month of surgery, and a 30-month follow-up visit was performed. Serum β -hCG level was found to be less than 0.1 IU/L and no evidence of neoplasm recurrence was found after 3 month of surgery.

Discussion

Choriocarcinoma is a trophoblastic tumor that is characterized by high metastatic potential. A study reported that a 31-year-old woman in genital activity were diagnosed with choriocarcinoma companied with pulmonary metastases [13]. Besides, a 33-year-old woman who was diagnosed to have choriocarcinoma with pulmonary and cerebral metastases was reported in another study [14]. Recently, a report outlined a case of high-risk choriocarcinoma in a postmenopausal female with multiple lung, skull and skin metastases.

Patients with choriocarcinoma may develop corresponding acute symptoms and be misdiagnosed due to multiple organ metastases. For example, tumor emboli may infiltrate to the pulmonary vessels, grow in the lung tissue and cause some respiratory symptoms, such as cough, expectoration, hemoptysis and chest tightness, which are easily misdiagnosed as lung cancer or pulmonary tuberculosis. The liver metastasis of choriocarcinoma has a low incidence, but it is usually complicated with other organ metastases such as lung, vagina, and brain, and the syndromes resulting from the liver metastasis are often considered as indicators of poor prognosis [15]. Because of

the characteristics of choriocarcinoma cells, brain metastasis is prone to cause intracranial hemorrhage and some neurological symptoms such as headache, convulsions, hemiplegia, even the life-threatening cerebral hernia, so patients often go to hospital for headache or neurologic changes [16]. It is also reported that there may be a surprising variation in the morphologic appearance of choriocarcinoma, and bervical punch biopsy accompanied with curettage may reveal a polymorphic tumor and be diagnosed as poorly differentiated squamous cell cancer of the cervix [17]. It is therefore easy to induce the negligence of choriocarcinoma and miss the best time for treatment. In the present study, the patient was initially misdiagnosed as suspected ectopic pregnancy and underwent right salpingectomy during which a crateriform neoplasm was found in her right anterior lobe of liver. Diagnosis of choriocarcinoma with metastases to the liver, lungs, marrow cavity, thoracic vertebra and brain was finally confirmed based on comprehensive information including PET/CT examination, clinical symptoms, head MRI and especially the high values of serum β -hCG.

The principle treatment for choriocarcinoma is polychemotherapy, combined with surgery and radiotherapy [18]. More than 90% choriocarcinoma patients can be cured if the chemotherapy program is properly performed [19]. Many chemotherapy programs are suitable for choriocarcinoma management, among which EMA-CO (etoposide, MTX, actinomycin D, cyclophosphamide and vincristine) and combined treatments dominant with 5-FU are the most commonly used ones. Surgery is only needed for a small number of patients when chemotherapy is poor on the metastasis foci. For the

case in our study, the FAV program, combined with the MTX intrathecal chemotherapy for brain metastasis, was administered. After fourteen courses of FAV chemotherapy and three courses of MTX, the brain, lung, liver and even bone metastases in the case almost disappeared, and blood β -hCG also returned to normal range.

In conclusion, this experience suggests that choriocarcinoma should be taken into consideration when reproductive-age women with delivery history appear associated symptoms accompanied with elevated serum β -hCG level. The synergism of combined chemotherapy and surgical resection is an effective pathway to treat these patients.

Acknowledgements

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Disclosure of conflict of interest

None.

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