

Exploring the real cause of hemoptysis: A case of pulmonary tumor embolism in a young woman with accompanying pulmonary metastasis of gestational trophoblastic neoplasia

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Abstract

We report a case of pulmonary embolism caused by gestational trophoblastic neoplasia (GTN) accompanied by pulmonary metastasis to improve the recognition ability of the disease in young female patients with pulmonary embolism and hemoptysis.

KEYWORDS

choriocarcinoma, gestational trophoblastic neoplasia (GTN), hemoptysis, pulmonary embolism, pulmonary metastasis

CLINICAL PRESENTATION

A 25-year-old Tibetan woman was admitted to our hospital presenting with hemoptysis accompanied by right chest pain for 5 days. She had no fever, wheeze, joint pain, or hematuria and denied a history of tuberculosis, menoxenia, or pregnancy. Suspecting the diagnosis of pulmonary thromboembolism (PTE), computed tomography pulmonary angiography (CTPA) was performed and revealed an intraluminal filling defect in the right pulmonary artery and its branches (Figure 1a). Also, it showed scattered patches and consolidation in both lungs, especially on the lower right side (Figure 1b). Laboratory tests showed the level of D-dimer was 4.78 mg/L FEU

(normal < 0.55 mg/L FEU), with increased WBC ($12.96 \times 10^9/L$) and Neu% (88.4%). The color doppler flow imaging ultrasonography of lower limbs showed no deep venous thrombosis (DVT). The diagnosis of acute PTE with pulmonary infarction and pneumonia was made, and anticoagulation therapy by low molecular weight heparin according to the body weight per 12 h was prescribed with other treatments such as oxygen therapy and antibiotics. Her symptom of hemoptysis was relieved transiently and then got worse with an increasing amount of hemoptysis. Simultaneously, further screening examinations for thrombophilia, including immunological antibodies (anti-cardiolipin antibody, anti-2-glycoprotein antibody, and lupus anticoagulant), protein C, protein S,

Abbreviations: CTPA, computed tomography pulmonary angiography; DVT, deep venous thrombosis; GTN, gestational trophoblastic neoplasia; PTE, pulmonary thromboembolism; WBC, white blood cell; β -HCG, serum- β human chorionic gonadotropin.

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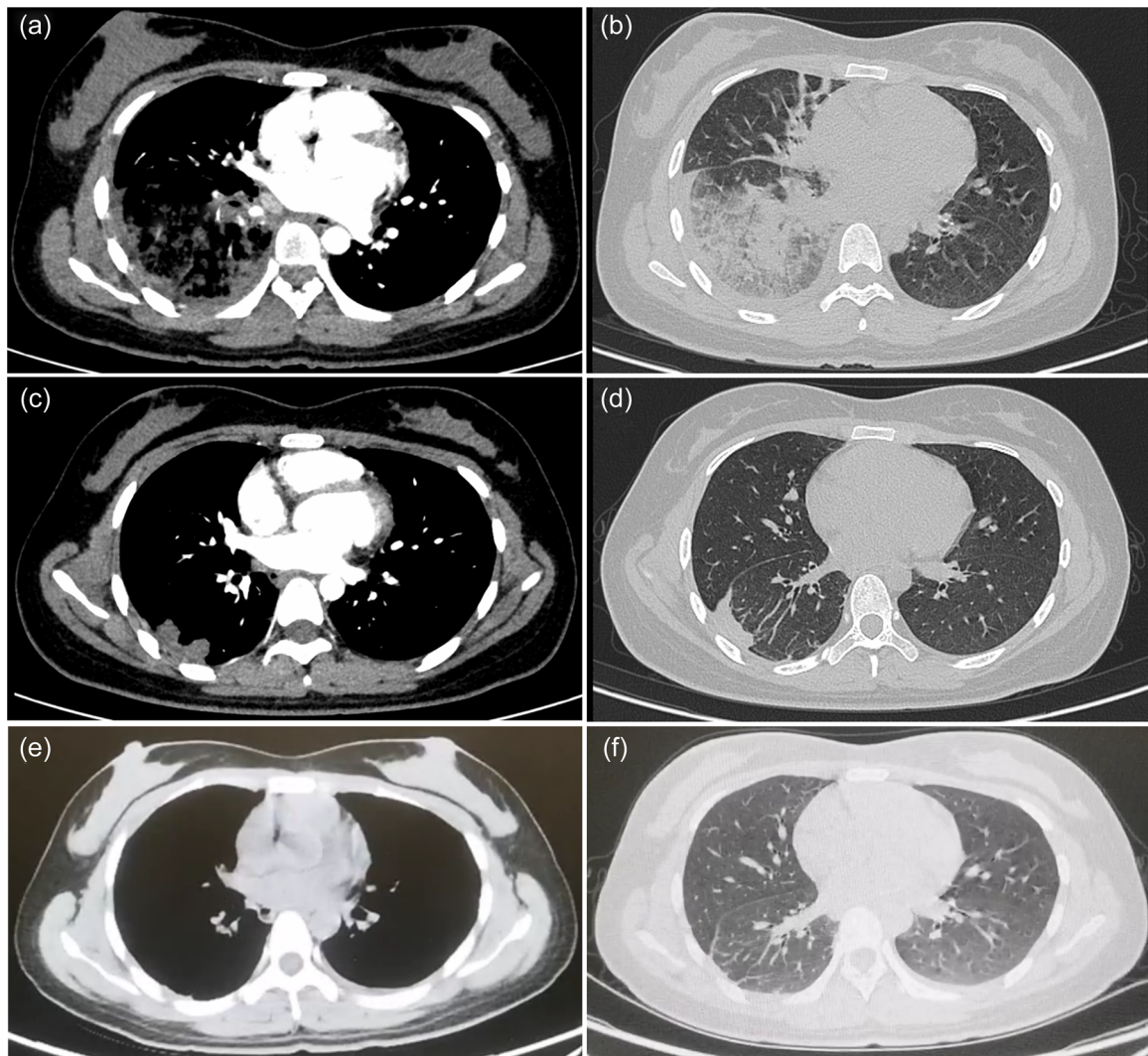


FIGURE 1 CTPA showed an intraluminal filling defect in the right pulmonary artery (white arrow, a). CT scan showed scattered patches and consolidation on the lower right side (b). The review of CTPA showed the absorption of embolism in the right lower pulmonary artery (c). CT scan showed that the right lower lung lesions were also significantly absorbed (d). Reexamination of chest CT scan during the negative β -HCG period showed the previous lung lesions were almost completely absorbed (mediastinal window e; lung window, f). CTPA, computed tomography pulmonary angiography.

antithrombin III, and tumor markers related to lung cancer and gastroenteric tumor were all negative.

The poor effect of anticoagulation indicated the possibility of non-thromboembolism. Although the patient denied a reproductive history, considering she was of childbearing age, we also tested the level of serum- β human chorionic gonadotropin (β -HCG). Unexpectedly, her β -HCG level was 195,550.00 mLU/mL (normal < 5 mLU/mL), significantly higher than the normal range. The patient then admitted that she experienced a history of curettage because of a hydatidiform mole 2 years ago in a local hospital without regular follow-up. A further contrast-enhanced CT scan of the abdomen and pelvis showed no remarkable abnormalities. Gynecologic ultrasound revealed uterine solid

nodules, which were suspected to be hystero myoma. The gynecological bimanual examination was normal. GTN with lung metastasis and pulmonary tumor embolism was diagnosed by the gynecologist. According to the latest treatment recommendations,¹ she received a chemotherapy regimen of EMA-CO (etoposide, methotrexate, and actinomycin-D alternating with cyclophosphamide, and vincristine). Anticoagulation was continued in case of secondary in situ pulmonary thrombosis. Four periods of chemotherapy produced a rapid clinical response. The symptoms of hemoptysis and chest pain were released, and the level of her serum β -HCG fell rapidly to 3175.4 mLU/mL. The review of CTPA showed absorption of embolism in the right lower pulmonary artery (Figure 1c). The right lower lung lesions were also

significantly absorbed (Figure 1d). After sequential eight periods of chemotherapy, her β -HCG value was less than 2.0 mLU/mL. The lung lesions of the chest CT images were almost completely absorbed (Figures 1e,f). The patient was followed up by a monthly test of β -HCG level for 1 year as a plan.

DISCUSSION

According to the symptoms of hemoptysis and chest pain, and the filling defect of the pulmonary artery on CTPA, the patient has been diagnosed with pulmonary thromboembolism at the beginning. Fortunately, the unsatisfactory treatment performance of anticoagulation, deficiency of deep vein thrombosis, and unilateral embolism of pulmonary arteries lead to the consideration of nonthrombotic pulmonary embolism, such as neoplastic embolism. Considering her reproductive age, the embolism caused by GTN was taken into account in the differential diagnosis, even though she denied a history of pregnancy at first. Although we did not get the histopathological evidence, the highly elevated level of serum β -HCG combined with the history of the hydatidiform mole was sufficient for making the diagnosis in this case, which shortened the time of diagnosis and avoided the risk of biopsy.

GTN refers to a group of malignant gestational trophoblastic diseases originating from the placenta. GTN contains four types of tumors, including invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor, of which invasive mole and choriocarcinoma are the most common and aggressive types.¹ Invasive moles usually occur after a hydatidiform mole pregnancy and are diagnosed histologically by the identification of direct myometrial invasion by hydropic villi with trophoblastic proliferation.^{2,3} Choriocarcinoma could be a consequence of live birth or nonmolar abortion and easy to develop hematogenous metastasis.⁴

The previous study has shown that hemorrhagic necrotic metastases in one or more organs are the typical manifestation of metastatic GTN, among which the most common site is the lung (83.3%).⁵ GTN could also metastasize to pulmonary arteries and cause pulmonary tumor embolism by hematogenous spreading.^{6,7} By summarizing 30 similar previously reported cases, we found that 80% of cases were choriocarcinoma,⁸ 66.7% presented only respiratory symptoms,⁹ and 36.7% manifested as hemoptysis.¹⁰ Imaging examination or autopsy indicated that 60.9% of trophoblastic embolization can involve bilateral pulmonary arteries, while 39.1% were unilateral, 62.1% were located in the pulmonary trunk or left/right main pulmonary arteries.^{8,11,12} Metastatic GTN

lacking vaginal bleeding and other primary manifestations are easily misdiagnosed. Some cases could not be diagnosed until by surgical procedure^{9,13,14} or autopsy,^{6,15} which account for 23.3% and 36.7%, respectively. Early detection of serum β -HCG in these patients can reduce misdiagnosis.

GTN can be classified into four stages according to the site of metastasis and divided into low-risk or high-risk groups. When pulmonary metastases are found, the disease is at stage III at least. The prognostic scoring system was used to allocate patients to high or low risk by the sum of all the actual risk factor scores such as age, antecedent pregnancy, site of metastases, and so on.¹⁶ With the confirmed efficacy of chemotherapy,¹⁷ GTN has become highly curable nowadays, and the overall survival rate almost approaches 100% in low-risk patients, and 80~90% in the high-risk group.¹⁸ The presence of lung metastases before treatment was found to be associated with an increased risk of disease recurrence and resistance to first-line multidrug chemotherapy but did not affect overall survival.^{19,20} The summarized data in GTN patients with pulmonary metastasis and pulmonary tumor embolism showed that the proportion of only chemotherapy after diagnosis was 73.7%, chemotherapy combined with anticoagulant therapy 26.3%.²¹ The overall mortality rate was 55.2%.

In conclusion, when dealing with fertile women manifested by hemoptysis and radiologically confirmed with unexplained pulmonary embolism and lung consolidation, the diagnosis of GTN with neoplastic embolism of the pulmonary artery and lung metastasis should be taken into consideration.

AUTHOR CONTRIBUTIONS

Hu, Qun: Writing—original and revised draft, searching the literature, data curation, and analysis. **Li, Meiqian:** Searching the literature, patient follow-up, and obtaining the imaging data. **Liu, Yu:** Writing—original draft, searching the literature. **Xie, Min:** Conceptualization, providing the case. **Wang, Lan:** Writing—review & editing, supervision, funding acquisition.

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CONFLICTS OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ETHICS STATEMENT

The patient signed informed consent for use in an anonymous form of clinical data for research.

PATIENT CONSENT

Written informed consent was obtained from the patient.

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