# Solitary lung metastasis from gestational choriocarcinoma resected six years after hydatidiform mole: A case report

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**ABSTRACT**

INTRODUCTION: Recently, the opportunity to encounter lung metastasis from choriocarcinoma has become very rare for thoracic surgeons, since chemotherapy works very well and the operative indications for lung metastasis are limited.

PRESENTATION OF CASE: A 45-year-old woman with a past history of hydatidiform mole six years previously was found to have a nodulous chest shadow in the right middle lung field on a chest radiography. She was also suspected of having an ovarian tumor and underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy. No malignancy was detected in the ovaries or uterus. A thoracoscopic partial pulmonary resection was then performed for the right lower lung nodule. The pathological diagnosis was choriocarcinoma. Her preoperative serum beta-human chorionic gonadotropin value was high (482.8 mIU/mL). Thus, she was diagnosed as having a pulmonary metastasis from gestational choriocarcinoma arising six years after a complete hydatidiform mole.

DISCUSSION: The possibility of choriocarcinoma arising as a solitary lung tumor should be considered regardless of the interval from the preceding molar pregnancy. The patient's medical history and high concentration of β-hCG in preoperative residual serum were helpful in arriving at a diagnosis of metastatic gestational CCA.

CONCLUSION: We presented pulmonary metastasectomy for very unique and rare metastatic choriocarcinoma arising six years after hydatidiform mole.

## 1. Introduction

Gestational choriocarcinoma (CCA) is the most aggressive trophoblastic disease, and 50% of gestational CCA arise from hydatidiform mole (HM) during a prior pregnancy [1]. HM occurs in about 1 in 1000 pregnancies in Western countries and is somewhat more frequent in Asian countries [2]. CCA affects approximately 1 in 40,000 pregnancies and 1 in 40 HMs in Western countries, whereas in Southeast Asia and Japan the gestational CCA rates are higher at 9.2 and 3.3 per 40,000 pregnancies [3]. The incidence of molar pregnancy has declined worldwide [4], with a resulting sharp decrease in the incidence of gestational CCA [5]. Moreover, because of the

high cure rate of gestational trophoblastic neoplasia (GTN) using chemotherapy, the indication for surgical therapy for lung metastasis is limited. Here, we report a rare case of a lung metastasis from gestational CCA arising six years after a complete HM.

## 2. Presentation of case

A 45-year-old woman who complained of irregular vaginal bleeding was suspected of having an ovarian tumor. She had a past history of HM. A nodulous chest shadow in the right middle lung field had also been pointed out on a chest radiography performed during a health examination at about the same time. The right lung nodule could not be diagnosed by transbronchial biopsy, and she was referred to the Department of Gynecology at our hospital. A total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. A benign ovarian cyst was diagnosed, and no malignancies in the ovaries or uterus were found upon histopathological examination. She was then referred to our department for the diagnosis of the lung nodule. She had no respiratory symptoms, and her physical examination showed

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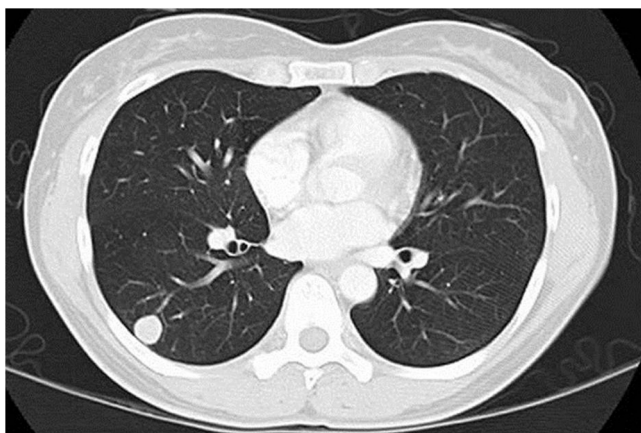
**Fig. 1.** Radiological findings. A CT scan shows a well-circumscribed nodule in S6 of the right lung.

no abnormalities. Her laboratory data including tumor marker levels such as carcinoembryonic antigen, squamous cell carcinoma antigen, carbohydrate antigen (CA) 19-9, and CA 125 were within the normal ranges. A computed tomography (CT) scan showed a well-circumscribed nodule in segment 6 (S6) of the right lung (Fig. 1). Whole body 2-deoxy-2-[$^{18}$F]-fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT imaging showed a maximal standardized uptake value of 7.39 during the early phase to 9.57 during the late phase only in the S6 nodule. A thoracoscopic partial resection of the right S6 nodule was scheduled and performed 6 weeks after the initial gynecologic surgery. Macroscopically, a white to reddish brown-colored, well-defined tumor was found within the resected specimen. A frozen section analysis revealed a tumor that was suspected to be a squamous cell carcinoma with significant keratinization, but it was very rare histology for a primary lung cancer. A metastatic tumor was thought to be a strong

possibility. The histopathological findings showed that the tumor was highly hemorrhagic and necrotic and consisted of an intimate admixture of atypical cytotrophoblasts and syncytiotrophoblasts arranged in nests without a villus structure (Fig. 2A and B). The immunohistological findings indicated that the tumor cells were strongly positive for human chorionic gonadotropin (hCG) (Fig. 2C) and positive for cytokeratin (CK) 7, but were negative for thyroid transcription factor-1, alpha fetoprotein, and CK 20. Other organs that could have been potential primary sites of the suspected malignancy could not be identified using CT and FDG-PET/CT examinations. However, she had a past history of dilation and curettage for a complete HM at the age of 39 years. Her preoperative serum beta-human chorionic gonadotropin (β-hCG) value was high at 482.8 mIU/mL and decreased to 23.1 mIU/mL on postoperative day 10, and it had returned to within the normal range at one month after the lung surgery. Thus, the patient was diagnosed as having a pulmonary metastasis from a gestational CCA arising six years after a complete HM. She underwent three cycles of chemotherapy with methotrexate postoperatively. She was followed for 7 years and 3 months and showed no signs of recurrence.

## 3. Discussion

Gestational CCA is a type of GTN. Gestational CCA is defined as a malignant neoplasm composed of large sheets of biphasic, markedly atypical trophoblasts without chorionic villi [6]. GTN is the unique tumor that arises from gestational rather than maternal tissue, and also it is highly curable in most patients with chemotherapy even when the disease has metastasized. Recently, the opportunity to encounter lung metastases of choriocarcinoma has become very rare for thoracic surgeons, because of the excellent outcome of chemotherapy, and the operative indications for lung metastasis are limited. The International Federation of Gynecology and Obstetrics (FIGO) defined criteria for the diagnosis of GTN, and also adopted a combined anatomic staging and the modified World
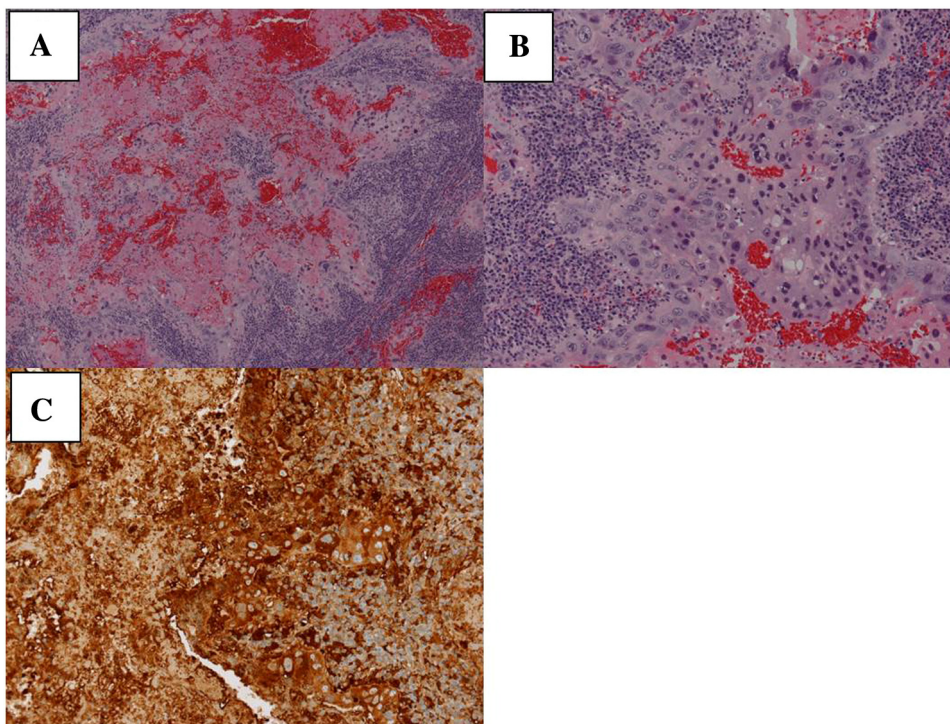


**Fig. 2.** Microscopic findings. (A) The tumor was highly hemorrhagic and necrotic. H.E. stain, ×10. (B) An intimate admixture of atypical cytotrophoblasts and syncytiotrophoblasts arranged in nests without a villus structure is visible. H.E. stain, ×20. (C) Tumor cells were strongly positive for hCG. Immunohistochemistry against β-hCG, ×20.

Health Organization (WHO) prognostic scoring system for GTN in 2002 [7,8]. Treatment is based on classification into risk groups defined by the stage and scoring system. Single-agent chemotherapy, usually methotrexate or actinomycin D, was performed for the patients with non-metastatic GTN (FIGO stage I) and low-risk metastatic GTN (FIGO stage II–III, modified WHO score < 7). Patients with high-risk metastatic GTN (FIGO stage IV or stage II–III of modified WHO score $\geq$ 7), are treated with multi-agent chemotherapy with or without adjuvant radiation or surgery [8]. The overall cure rate with treatment is currently over 90%.

Gestational CCA frequently undergoes distant hematogenous metastasis to various organs. The most common metastatic sites are the lungs (80%) and vagina (30%) [9]. Metastasis to other sites, such as liver and brain, are rare without pulmonary metastases. Up to 40% of patients with negative findings for lung metastases on a chest radiograph will have metastases diagnosed on a chest CT scan [10]. Pulmonary wedge resection has been shown to be effective for treating patients with low-risk GTN who develop resistant pulmonary nodules after exhausting primary and secondary chemotherapy. The criteria that predict a favorable outcome include the following [11]: 1) absence of other systemic metastases, 2) presence of a unilateral solitary nodule, 3) no uterine involvement, and 4) a serum level of hCG < 1500 mIU/mL.

CCA of the lung could represent metastases that arises from unknown trophoblastic disease, which might undergo a spontaneous regression sometimes leaving only the uterus [12,13]. This phenomenon, so-called "burned out" hypothesis, would represent a unique and specific feature of choriocarcinoma that is likely to become metastatic before detection of the primary lesion. In the present case, despite gynecologic surgery for an ovarian tumor, we could not detect the primary site of the lung metastasis. Before a thoracotomy, we considered the possibility of metastasis because of the history of HM; however, we could not make a diagnosis of metastasis from gestational CCA because the interval was relatively long (6 years). Tomoda et al. reported that the median interval between a preceding molar pregnancy and the diagnosis of choriocarcinoma was approximately 36.5 months (range, 5–247 months), and the longest reported interval was 20 years and 7 months [14]. The possibility of choriocarcinoma arising as a solitary lung tumor should be considered regardless of the interval from the preceding molar pregnancy. The patient's medical history and high concentration of $\beta$-hCG in preoperative residual serum were helpful in arriving at a diagnosis of metastatic gestational CCA.

## 4. Conclusion

We presented pulmonary metastasectomy for very unique and rare metastatic choriocarcinoma arising six years after hydatidiform mole.

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