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Tuberculosis Infected T Lymphocyte Spot as a Differential Diagnosis of Pulmonary Tuberculosis and Choriocarcinoma Recurrence: A Case Report and Review of the Literature

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Abstract

Introduction: Choriocarcinoma is an aggressive tumor, whose incidence is 0.18 per 100,000 women between the ages of 15 and 49 years [1]. Although its prognosis has improved with the development of chemotherapy regimens, the mortality rate of patients with brain metastases is reportedly 29.7% [2]. After chemotherapy, most often, the reappearance of masses in pulmonary is considered to be a sign of relapse. **Case Presentation**: The patient was a 32-year-old Asian Chinese female who delivered a dead male infant at 33 weeks gestation. The placenta appeared to be normal. The major presentation was a haemorrhage of the vagina. The patient received combined treatment with systematic multi-agent chemotherapy and whole-brain radiation therapy at the General Hospital of Hebei Province and achieved complete remission. Two years after remission, a chest CT scan revealed a mass in the right lung that had become larger over 6 months. The patient's serum β-human chorionic gonadotropin (β-HCG) level was normal, and the tuberculosis infected T lymphocyte spot (T-SPOT.TB) tests were positive. The patient was started on anti-tuberculosis therapy, after which the size of her right lung mass decreased. **Conclusion**: Lung masses after choriocarcinoma require extensive laboratory and imaging exams to exclude recurrence. This case highlights the importance of differential diagnoses of lung masses in patients with choriocarcinomas. Imaging studies, β-HCG and local lesion resection should be employed to rule out choriocarcinoma recurrence.

Keywords

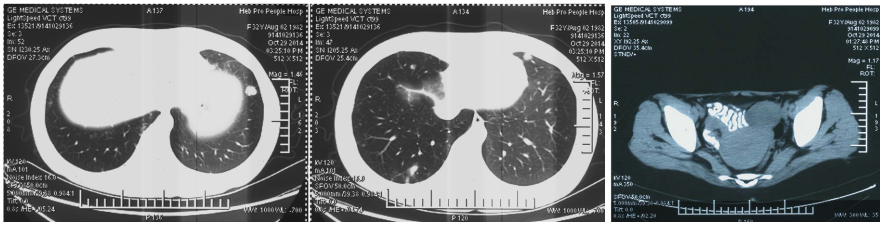
Choriocarcinoma, Tuberculosis

1. Introduction

Choriocarcinoma is a highly aggressive malignant tumour, and metastases to the lung and brain usually occur. Brain metastases are found in 10% - 20% of choriocarcinoma cases, most often manifesting as intracerebral or subdural haematomas, and are known to be poor prognostic factors [3]. The aim of the current report was to present the case of a 32-year-old female with International Federation of Gynaecology and Obstetrics (FIGO) (15) stage IV gestational choriocarcinoma. The patient received combined treatment with systematic multi-agent chemotherapy and achieved complete remission. Two years after remission, pulmonary tuberculosis was initially misdiagnosed as a choriocarcinoma recurrence.

2. Case Report

A 32-year-old female initially presented to an outpatient clinic with vaginal bleeding, which had lasted for 3 months. Three months previously, the patient delivered a dead male infant at 33 weeks gestation. Her last pregnancy had occurred 5 years before, with a full-term vaginal delivery. The pelvic exam showed a 2-cm friable mass on the left side of the vagina. Routine laboratory examinations were performed. β-HCG was 52,155,300 mIU/mL (normal level, <5.3 mIU/mL). She underwent transvaginal ultrasound at our institution demonstrated heterogeneity of the endometrium and a mass on the left ovary. A CT scan of the chest, abdomen, and brain revealed irregular multiple bilateral pulmonary nodules and multiple haemorrhagic masses in the frontal lobe of the right cerebrum, the left side of the thalamus and the right hemisphere (**Figure 1**). Based on the clinical findings and imaging results, gestational choriocarcinoma with pulmonary and cerebral metastasis [FIGO stage IV; World Health Organization score, 15] was diagnosed [4]. Systemic multi-agent chemotherapy (EMA/CO) was administered after written informed consent was obtained. Two weeks after chemotherapy, the patient became drowsy and developed vision deficits. MRI of the brain indicated that in addition to the lesion detected by CT, there were multiple metastases in the meninges (**Figure 2**). Therefore, the patient underwent whole-brain irradiation and intrathecal chemotherapy (methotrexate). The EMA/CO regimen was highly effective for the treatment of this patient, as it exhibited good efficacy and was well-tolerated. The brain metastases were controlled rapidly by the administration of immediate whole-brain irradiation and intrathecal chemotherapy. After 11 cycles of chemotherapy, the β-HCG level was within the normal range. The patient achieved complete remission. Transvaginal ultrasound after treatment completion was negative for uterine and ovarian lesions. A CT scan of the chest and an MRI of the brain showed disease resolution.



(A) (B)

Figure 1. (A) Chest computed tomography shows multiple high-density clear boundary nodules in both lungs. (B) Pelvic computed tomography shows high-density mass in left ovary.

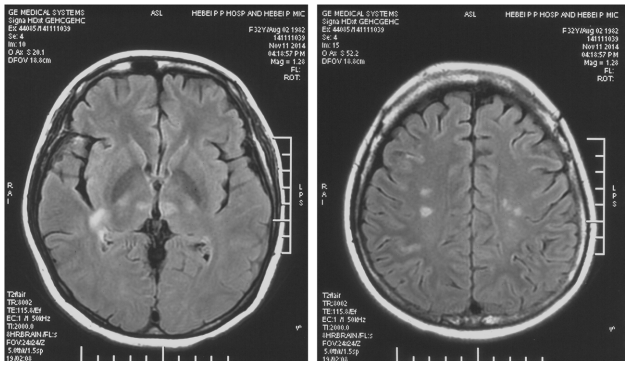


Figure 2. MRI images showing multiple metastases within the brain.

Two years after chemotherapy, a CT scan of the chest revealed a mass measuring 2.4 × 0.9 × 1.0 cm in the right lung. The patient's medical history indicated that metastases were present in the right lung 2 years previously. A comparison of the most recent image to that obtained 2 years ago showed that the mass had become larger. At first, the pulmonary mass was considered to be a choriocarcinoma recurrence. However, the patient's serum β-HCG and abdominal and pelvic ultrasound were negative. She immediately underwent PET-CT, which revealed a hypermetabolic mass in the right lung (**Figure 3**). The pulmonary mass was also considered to be a malignant lung tumour. However, the lung tumour markers were normal. MRI of the brain indicated that the metastases in the meninges had disappeared. Multiple laboratory examinations were performed, and the tuberculosis infected T lymphocyte spot (T-SPOT.TB) test was positive. Subsequently, an anti-tuberculosis regimen comprising isoniazid, rifampicin and ethambutol was administered for 3 months. Her follow-up is ongoing.

3. Discussion

Choriocarcinoma is a highly malignant neoplasm. Generally, choriocarcinoma is secondary to a hydatidiform mole and to abortion, ectopic pregnancy, preterm pregnancy or term pregnancy. The incidence of choriocarcinoma in China is high, at approximately one case per 2882 pregnancies [5]. Usually, the disease presentation in patients with choriocarcinoma is abnormal uterine bleeding with

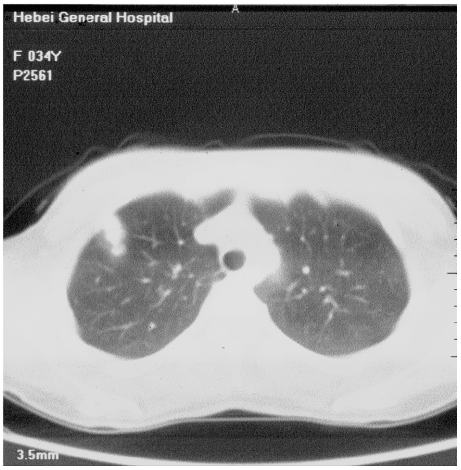


Figure 3. Lung image of PET-CT showing a mass measuring 2.4 × 0.9 × 1.0 cm in the right lung.

high β-HCG levels. Approximately 30% of choriocarcinoma patients exhibit metastases at the time of diagnosis, which may be attributable to the high affinity exhibited by trophoblastic cells for blood vessels [6] [7]. The most common metastatic sites of choriocarcinoma are the lungs (80%), vagina (30%), pelvis (20%) and liver (10%). Cerebral metastases occur in 10% of cases. The mortality rate of patients with brain metastases is significantly high and is reported to be 29.7%, in contrast to the overall death rate from gestational trophoblastic neoplasia (GTN), which is 5% [2]. EMA-CO therapy has been shown to result in a survival rate of 88% for high-risk patients, with 75% of patients having no evidence of disease [8]. Metastatic sites in the brain require both additional therapy and alternative regimens, including high-dose methotrexate, by intravenous or intrathecal injection in the EMA-CO protocol to ensure adequate drug levels in the cerebrospinal fluid. Brain radiation combined with systemic chemotherapy is successful in controlling brain metastasis, with cure rates up to 75%, and is generally the standard of care in the US [9]. The choice of treatment modality for brain metastases should take into consideration the size of the tumour, number of metastases, and urgency of treatment. Whole-brain radiation, stereotactic radiation, intrathecal chemotherapy and excisional surgery are considered. Due to our patient's focal neurological deficits and concerns for multiregional meningeal metastatic nodules, intrathecal methotrexate and brain radiation were performed.

The recurrence rate of GTN is 3% - 13% [10]. Four recurrence-associated risk factors identified by multivariate analysis were clinical stage, an interval of more than 12 months between the end of antecedent pregnancy and the start of chemotherapy, a negative blood β-HCG titre after seven courses of chemotherapy, and less than two courses of consolidation chemotherapy [11]. At first, our patient's pulmonary mass was considered to be a choriocarcinoma recurrence. Lung metastases often appear as lumpy shadows on imaging and are associated with various symptoms, such as dyspnoea, cough and even respiratory failure.

Pulmonary metastasis of choriocarcinoma and pulmonary tuberculosis have many similarities in terms of respiratory symptoms and X-ray manifestations. Patients with tuberculosis can also have the aforementioned symptoms with concomitant afternoon fevers and weakness. The differential diagnosis between lung metastasis of choriocarcinoma and pulmonary tuberculosis, based on histology, is very difficult. When pulmonary tuberculosis is misdiagnosed as choriocarcinoma metastasis, both active tuberculosis therapy and the isolation of the source of infection are delayed. Interestingly, our case exhibited a marked absence of respiratory symptoms, especially afternoon fevers, dyspnoea and cough, which was inconsistent with the international literature. Pulmonary tuberculosis differs somewhat from choriocarcinoma recurrence, which is accompanied by an elevated β-HCG level, vaginal bleeding, chest pain, and neurological signs, such as seizures and stroke. Therefore, serum β-HCG, imaging examinations and local lesion resections should be employed to rule out choriocarcinoma recurrence.

4. Conclusion

When a choriocarcinoma patient achieves complete remission by chemotherapy, the following circumstances should alert healthcare providers to the possibility of tuberculosis (1): the appearance of inexplicable afternoon fevers (2): the reappearance of a lung shadow with normal serum β-HCG levels (3): and a clinical presentation that is inconsistent with the lung CT scan.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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