

A rare case of pulmonary artery embolism with choriocarcinoma: A case report and literature review

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Received May 25, 2023; Accepted September 7, 2023

DOI: 10.3892/ol.2023.14077

Abstract. Pulmonary embolism (PE) caused by malignant tumor is not uncommon, but pulmonary artery with choriocarcinoma is rare and difficult to timely diagnose and effectively treat. To the best of our knowledge, there are only 15 cases reported at present in the literature that present variable clinical characteristics and prognosis. In the current study reports a 21-year-old female with a history of chest pain and slight fever for 4 months who was treated as a case of pneumonia. Owing to the recurrence of the symptoms, a contrast-enhanced chest computer tomography scan was performed on the patient, which revealed complete occlusion of the right pulmonary artery. The patient was diagnosed to have pulmonary embolism (PE). However, no abnormalities were observed in D-dimer value, tumor antigen testing or ultrasonography. Positron emission tomography/computed tomography (PET/CT) was performed, which revealed the abnormal hyper-metabolic lesion of the right pulmonary artery. Following the laboratory report of a significantly elevated human chorionic gonadotropin β -subunit level combined with characteristic appearance of PET-CT, the diagnosis of primary pulmonary artery with choriocarcinoma was established based on guidelines of the European Society for Medical Oncology and the criteria formulated by the International Federation of Gynecology and Obstetrics. The patient underwent chemotherapy and responded well to the treatment. Although rare, choriocarcinoma should be considered for any fertile women who presents with a massive PE. These findings emphasize the importance of the early diagnosis and treatment of this disease.

Introduction

Pulmonary embolism (PE) is a common acute and potentially fatal cardiovascular disorder that needs immediate medical intervention (1). According to guidelines, PE should be diagnosed by a combination of clinical features (common symptoms include dyspnea, chest pain, hemoptysis and syncope), D-dimer levels and radiological detection. However, the diagnosis of PE is challenging and often delayed due to lack of specific clinical presentation. In the past 10 years, the increased sensitivity of imaging modalities has doubled rates of hospital admission for pulmonary embolism (1). The causes of PE consist of venous thromboembolism and non-thrombotic embolism, such as fat, air, amniotic fluid, septic and tumor embolism (2).

Choriocarcinoma is a highly malignant trophoblastic cancer that is characterized by secreting high levels of human chorionic gonadotropin β -subunit (β -hCG) and hematogenous spread to various organs, particularly to the lungs (3). Although the lungs are the most common metastatic site, pulmonary artery embolism by choriocarcinoma is extremely rare. Currently, to the best of our knowledge, the total number of case studies that have reported pulmonary artery embolism by choriocarcinoma in the literature is <15. The present study reports a case of pulmonary artery embolism with choriocarcinoma in a 21-year-old woman who was initially misdiagnosed with pulmonary pneumonia, and then successfully treated with chemotherapy and the β -hCG level normalized. Additionally, the existing literature was reviewed and the clinical features and treatment outcomes were summarized.

Case report

A 21-year-old female was admitted to the Pulmonary and Critical Care Medicine Ward at Qingdao West Coast Area Central Hospital (Qingdao, China) in January 2022 with complaints of chest pain and slight fever for 4 months. No cough, sputum production and dyspnea was present. At that time, the patient was diagnosed with acute pneumonia based on chest computed tomography (CT), which revealed several scattered shadows on both lungs. Acid-fast bacilli staining using bronchoalveolar lavage showed negative results. Antibiotic treatment (specific medication not available) was administered, and the condition of the patient improved during the antibiotics course.

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Key words: pulmonary embolism, human chorionic gonadotropin β -subunit, choriocarcinoma, chemotherapy

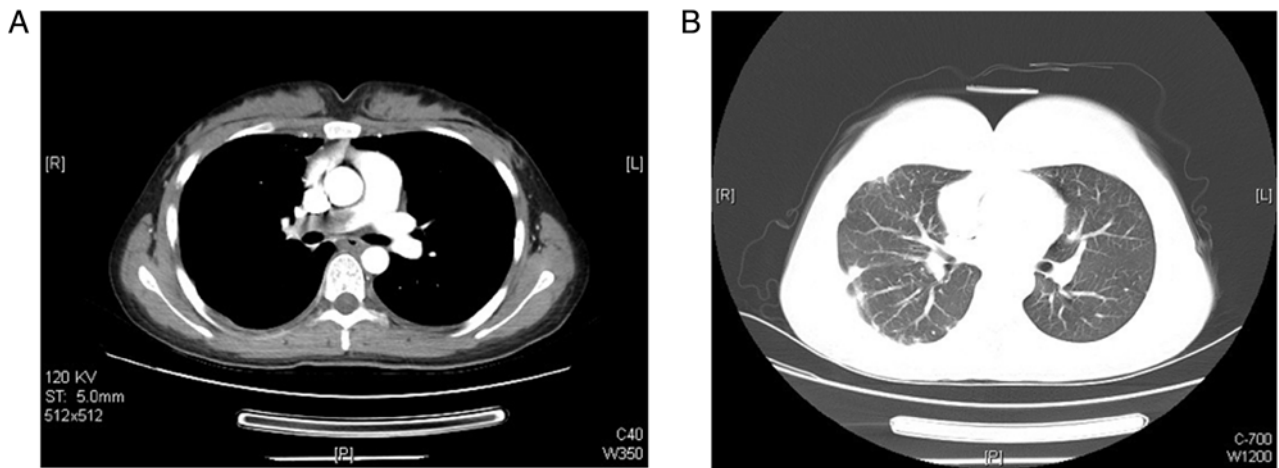


Figure 1. Contrast-enhanced chest CT images of a 21-year-old woman with chorio-carcinoma accompanied by a pulmonary embolism. (A) Contrast-enhanced chest CT (mediastinal window setting) scan image showing occlusion of the right pulmonary artery. (B) Chest CT (lung window setting) scan image showing multiple patchy, cordlike, nodular fuzzy shadows in the right lung. CT, computed topography.

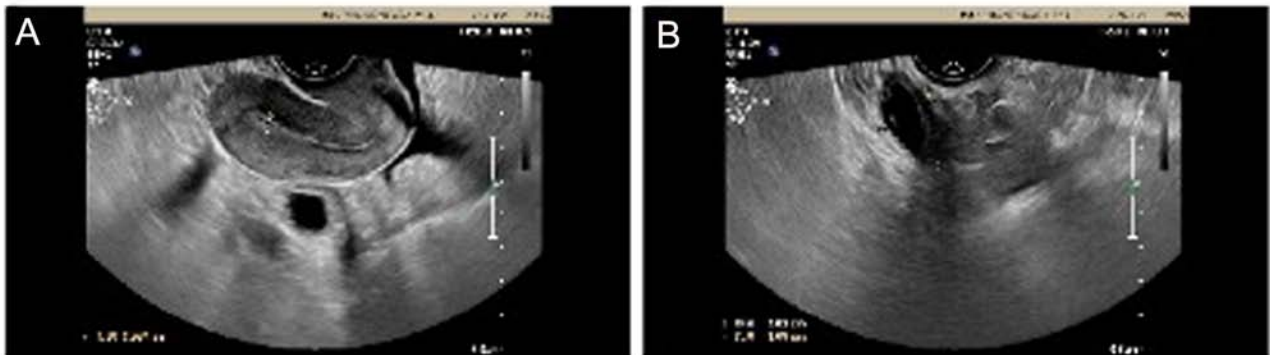


Figure 2. Normal ultrasonography of the pelvis after abortion. (A) No obvious echo found in the uterine cavity. (B) No obvious echo found in the ovary.

Subsequently, 4 months later (May 2022), the patient was referred to the Affiliated Hospital of Qingdao University (Qingdao, China) due to an episode of chest pain and slight fever again. On examination, the patient had a body weight of 48.5 kg, a respiratory rate of 19 breaths per min, a pulse rate of 77 beats/min and a blood pressure of 88/55 mm/Hg. The routine blood test showed the white blood cell count was $4.86 \times 10^9/l$, platelet count was $346 \times 10^9/l$ and the hemoglobin level was 100 g/l. Liver function test showed that the glutamic-pyruvic transaminase level was 7.2 U/l (normal range, 7-40 U/l) and the glutamic oxaloacetic transaminase level was 13.5 U/l (normal range, 13-35 U/l). The coagulation function tests showed that the prothrombin time was 12.3 sec (normal range, 10-14 sec) and the activated partial thromboplastin time was 35.2 sec (normal range, 22-38 sec). The D-dimer value was 420 ng/ml (normal range, <500 ng/ml). The levels of tumor biomarkers, including carcinoembryonic antigen, α -fetoprotein, squamous cell carcinoma antigen, neuron-specific enolase, carbohydrate antigen (CA)125, CA19-9, CA15-3 and CA72-4, were also in the normal ranges. Serum tuberculosis antibody test result was negative. The contrast-enhanced chest CT scan revealed complete occlusion of the right pulmonary artery (Fig. 1A). The scan further displayed multiple nodular fuzzy shadows with necrosis in the bilateral lungs (Fig. 1B). However,

echocardiography displayed poor blood flow filling at the initial segment of the pulmonary artery, pulmonary hypertension (up to 28 mmHg), along with slight tricuspid regurgitation. Bilateral ultrasound examination of the vasculature of the two legs revealed no evidence of deep-vein thrombosis.

To seek the cause of PE, the medical history of the patient was requested. The patient had experienced one drug-induced abortion in July 2021. Ultrasonography of the pelvis after the abortion was normal (Fig. 2). The serum β -hCG decreased from 11,937.00 to 6,410 mIU/l at 1 week after abortion. Later, the patient did not undergo further examination for β -hCG. No intermittent bleeding or complications occurred after the abortion. The last menstrual period of the patient was May 2022. The patient had a long-term use of oral contraceptives and no other relevant medical history. Additional tests were conducted in the Affiliated Hospital of Qingdao University. However, the serum β -hCG level was significantly elevated (>10,000 mIU/l). Ultrasound examination of the pelvis did not reveal an ectopic pregnancy (Fig. 3). Positron emission tomography with 2-(fluorine-18)-fluoro-2-deoxy-D-glucose/computed tomography (FDG-PET/CT), with a sensitivity of 71.4% and specificity of 90% in differentiating between tumor and thromboembolism (4), was performed and revealed the abnormal hypermetabolic lesion (maximum

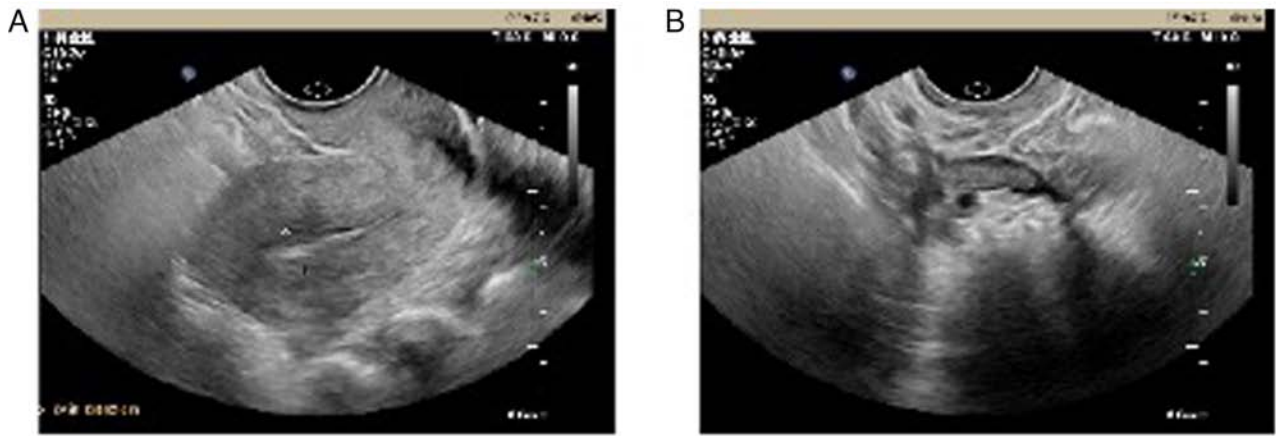


Figure 3. Normal ultrasonography of the pelvis of a 21-year-old woman with pulmonary embolism caused by choriocarcinoma. (A) No obvious echo found in the uterine cavity. (B) No obvious echo found in the ovary.

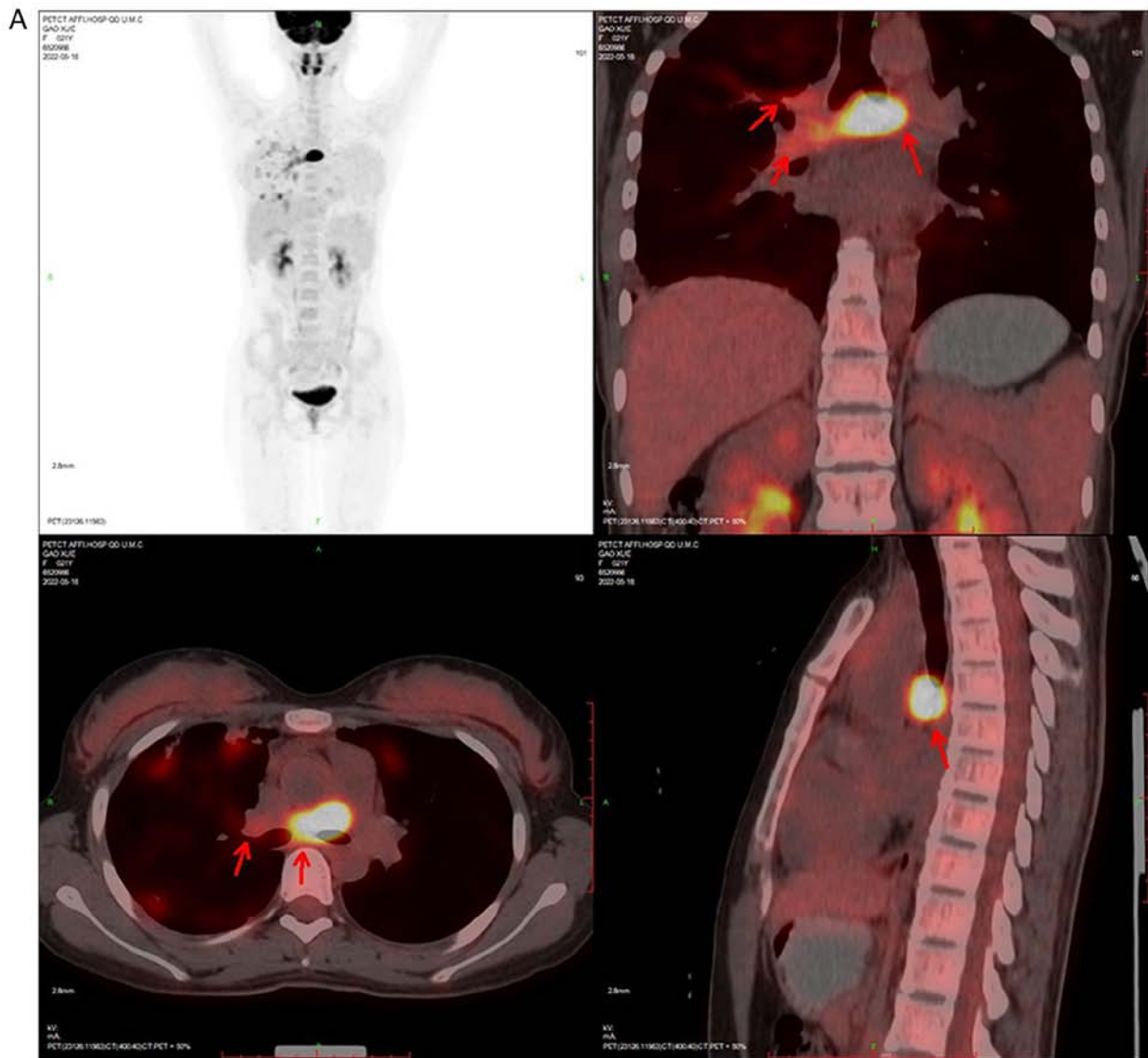


Figure 4. Continued.

standardized uptake value, 27.5) overlying the right pulmonary artery (Fig. 4A). Bilateral peripheral lungs opacities with

mild hypermetabolic lesions were suggestive of a pulmonary infarction caused by tumor embolism (Fig. 4B). No other

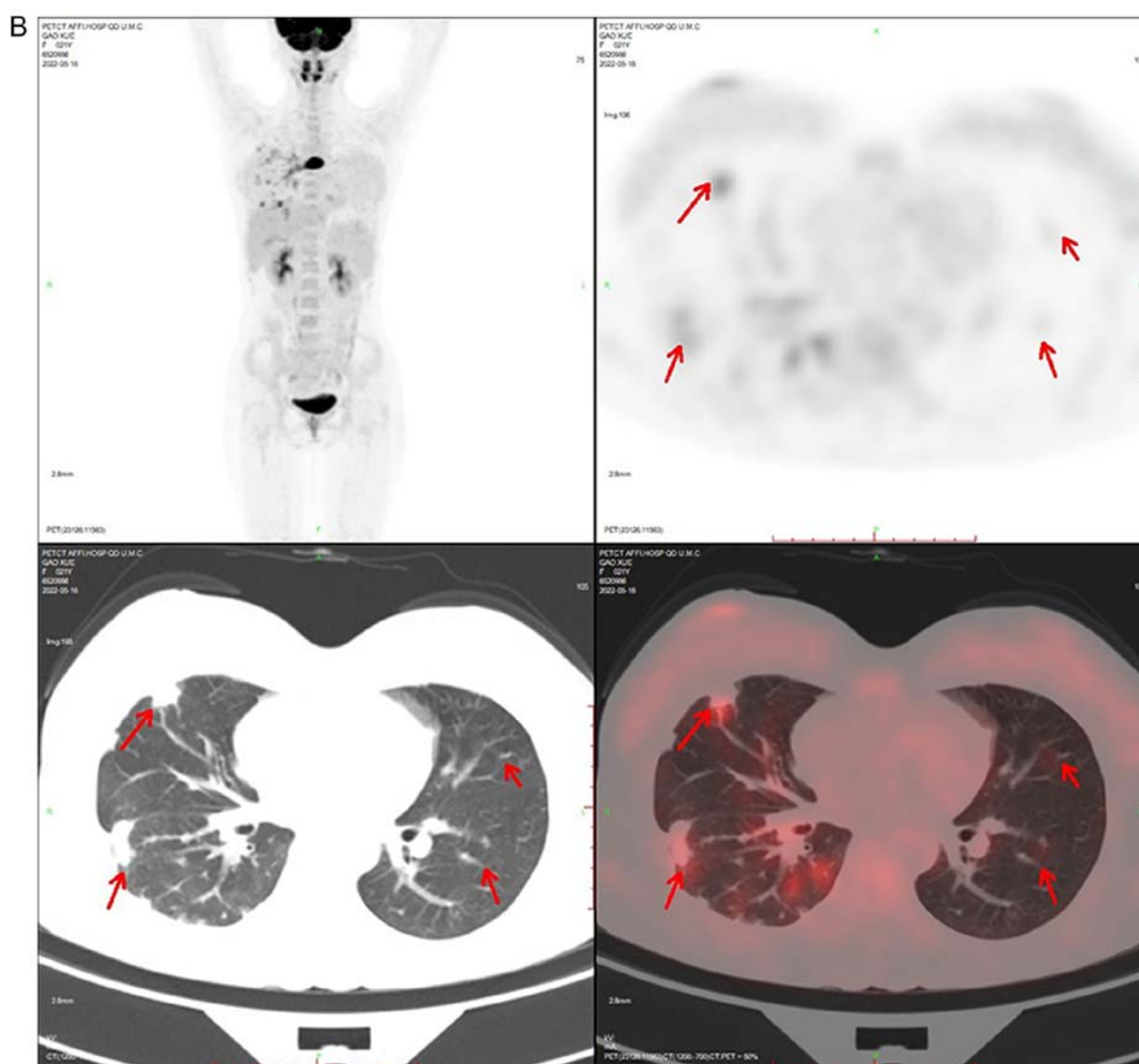


Figure 4. FDG-PET/CT images of a 21-year-old woman with choriocarcinoma presenting as a pulmonary embolism. (A) FDG-PET/CT images shows the region of hypermetabolic focus in the right pulmonary artery ($SUV_{max}=27.5$; indicated with an arrow). (B) FDG-PET/CT images shows low accumulation of FDG in the nodules ($SUV_{max}=7.2$; indicated with an arrow). SUV_{max} , maximum standardized uptake value; FDG-PET/CT, positron emission tomography with 2-(fluorine-18)-fluoro-2-deoxy-D-glucose/computed tomography.

focal FDG-avid lesion was observed in the brain, abdomen or pelvic cavity. According to the guidelines of European Society for Medical Oncology (5) and the criteria formulated by the International Federation of Gynecology and Obstetrics (6), the diagnosis of a primary pulmonary artery with choriocarcinoma was established. Subsequently, the patient was initiated on chemotherapy (EMACO regimen) and responded well to the treatment. The period of chemotherapy with EMACO was from May 2022 to March 2023. After the 12 cycles of chemotherapy, serum β -hCG decreased to <0.10 mIU/l (Fig. 5) and the occlusion in the right pulmonary artery disappeared on contrast-enhanced chest CT (Fig. 6). The patient is currently alive and has achieved complete remission during follow-up.

Discussion

Choriocarcinoma is an aggressive and highly malignant tumor that can be classified into two subtypes: Gestational or non-gestational (7), ~50% of cases follow a complete

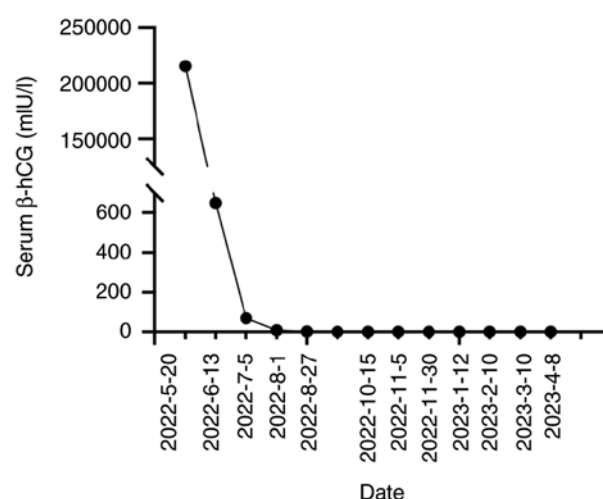


Figure 5. Dynamic changes of serum β -hCG during the course of a pulmonary embolism with choriocarcinoma. The period of chemotherapy with EMACO was from May 2022 to March 2023. β -hCG, human chorionic gonadotropin β -subunit.

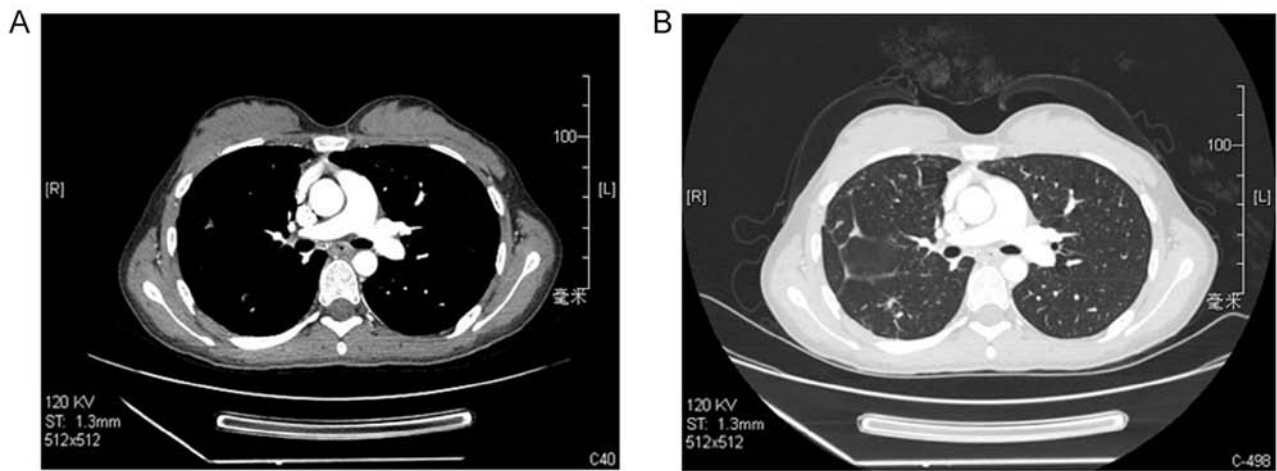


Figure 6. Contrast-enhanced chest CT images of pulmonary embolism by choriocarcinoma after 12 cycles chemotherapy. (A) Contrast-enhanced chest CT (mediastinal window setting) scan image showing no occlusion within the right pulmonary artery. (B) Chest CT (lung window setting) scan image showing cordlike, nodular fuzzy shadows in the right lung.

hydatidiform mole, 25% arise after abortion and 25% occur after normal or ectopic pregnancies (8). Non-gestational can be found in various organs, often in the lung (9). Pulmonary artery embolism caused by choriocarcinoma is extremely rare and has been described as a rare cause of PE and pulmonary artery hypertension. The present study searched the PubMed database (<https://pubmed.ncbi.nlm.nih.gov>) for articles published from January 1, 1959, to February 28, 2023, using the term 'choriocarcinoma' and 'pulmonary artery'. The exclusion criterion was that the choriocarcinoma had not metastasized to the pulmonary artery. Only 15 cases have previously been documented in English-language medical literature, which have been reviewed in Table I (10-21). The mean age of presentation was 32.06 years (range, 21-51 years), and the sex were all female. The most common symptoms were dyspnea (11/15 or 73.3%) and chest pain (8/15 or 53.3%). Approximately 13 cases had a history of spontaneous abortion and no primary uterine tumor, and the average time for diagnosis of choriocarcinoma after the onset of symptom was 5 months.

The underlying mechanism of primary choriocarcinoma of the pulmonary artery is still uncertain. Cases of choriocarcinoma arising a number of years after total hysterectomy and bilateral salpingo-oophorectomy are rare (17). Tanimura *et al* (22) revealed that trophoblasts can be found in the pulmonary artery in autopsies of 9/10 patients who died after delivery or abortion. Therefore, it has been hypothesized that primary pulmonary artery with choriocarcinoma in women may be due to malignant transformation of the normal villous trophoblasts that entered the pulmonary artery at the time of delivery or abortion (22). However, others hypothesize that a pulmonary choriocarcinoma without the evidence of pelvic cavity lesions may represent metastases from an undetected gonadal tumor, which might undergo a spontaneous regression, the so called 'burn-out' phenomenon that is a unique and specific feature of choriocarcinoma (23-25).

Due to the lack of distinct symptoms, specific signs or typical radiography, the diagnosis of pulmonary artery choriocarcinoma embolism is difficult in the early stages. In the present case, the patient was initially misdiagnosed with acute pneumonia and given antibiotic treatments. However,

most physicians may pay little attention to the irregular period of menstruation and abortion, and/or has low awareness of linking the choriocarcinoma with respiratory symptoms. As found in the literature review, the average time for the diagnosis of pulmonary artery choriocarcinoma after the onset of symptoms was 5 months. Although choriocarcinoma is rare, it should be considered for any women of child-bearing age who present with dyspnea, chest pain, PE or pulmonary arterial hypertension, and a history of menstruation, pregnancy and abortion should be reviewed in detail (21).

Choriocarcinoma is a malignant epithelial tumor characterized by secretion of β -hCG (26). Accurate and prompt diagnosis of choriocarcinoma depends on correlation with clinical findings and the β -hCG levels. Watanabe *et al* (15) indicated the importance of considering choriocarcinoma and testing the serum β -hCG levels when evaluating women of childbearing age presenting with pulmonary artery hypertension or PE. The serum β -hCG level performed as a diagnostic indicator and was recommended to be tested in fertile women to differentiate the causes of a PE. The degree of tumoral enhancement appears to correlate with β -hCG level. A previous report suggests that finding an elevated serum β -hCG level may have led to an earlier diagnosis (21). In addition, it also plays an important role in the evaluation of its prognosis of treatment outcomes. In the present study, the β -hCG levels notably dropped following chemotherapy in the patient. Thus, testing the β -hCG level is recommended as a parameter of prognosis and follow-up after treatment (26).

FDG-PET/CT has been increasingly performed to diagnose and stage primary malignancies. A previous report has confirmed that PET/CT can be useful to accurately distinguish between benign and malignant tumors, as malignancy shows high FDG accumulation (18). Similarly, PET/CT has been considered to be a sensitive tool for the detection of lung metastasis from choriocarcinoma (27). In the present case, PET/CT was performed to reveal a lesion in the right pulmonary artery, which showed that FDG accumulation to the pulmonary artery was high and no other abnormal FDG uptake was found in the whole body including the pelvic cavity. Although PET/CT can demonstrate sites of metastasis

Table I. Clinical features of primary pulmonary artery with choriocarcinoma cases.

First author (year)	Sex	Age, years	History	Clinical presentation	Serum HCG, IU/l	Treatment	Survival	(Refs.)
Seckl <i>et al</i> (1991)	F	25	Spontaneous abortion 6 years before	Pleuritic chest pain, exertional dyspnea	103,200	Chemotherapy + anticoagulation	ANED (4 years)	(10)
	F	24	Spontaneous abortion 2 months before	Pleuritic chest pain, hemoptysis, dyspnea	280,000	Chemotherapy + anticoagulation	ANED	
	F	30	Spontaneous abortion 8 months before	Chest pain	132,300	Chemotherapy + anticoagulation	ANED (8 years)	
Yutani <i>et al</i> (1993)	F	47	Therapeutic abortion 3 years before	Chest pain, dyspnea	No	EL	DOD	(11)
Trubenbach <i>et al</i> (1997)	F	33	Abortion 10 months before	Exertional dyspnea, chest pain, cough	129.5	Chemotherapy	DOD	(12)
Savage <i>et al</i> (1998)	F	28	Three live pregnancies, the latest one 3 years before	Cough, shortness of breath, chest pain	339,535	Anticoagulation + chemotherapy	ANED	(13)
Chai <i>et al</i> (2000)	F	23	Spontaneous abortion 10 months before	Progressive dyspnea, cough	>2,000,000	NO	DOD	(14)
Watanabe <i>et al</i> (2002)	F	42	Two previous spontaneous abortions	Exertional dyspnea	>70,000	EL + chemotherapy	ANED	(15)
Brusselle <i>et al</i> (2005)	F	31	Four previous spontaneous abortions	Progressive dyspnea	168,000	EL + chemotherapy	ANED	(16)
Ong <i>et al</i> (2008)	F	51	Abortion 5 years before	Dyspnea, dry cough, hemoptysis	No detail	EL + chemotherapy	NA	(17)
Zaheer <i>et al</i> (2009)	F	51	Two live pregnancies	Dyspnea, chest pain, cough, fever	291,128	Chemotherapy	ANED	(18)
Ma <i>et al</i> (2013)	F	24	Three previous spontaneous abortions, the latest one 1 years latest	Dyspnea	No detail	EL	DOD	(19)
Zhu <i>et al</i> (2016)	F	25	Three spontaneous abortions	Dyspnea, cardiopalms	Undetected	EL	DOD	(20)
Yang and Peng (2017)	F	26	Two abortions, the latest one 3 years before	Cough, expectoration, night sweat	128,575.77	Chemotherapy	DOD	(21)
Present case	F	21	One previous abortion	Chest pain, slight fever	>100,00	Chemotherapy	ANED	

F, female; ANED, alive with no evidence of disease; DOD, dead of disease; NA, not available; EL, embolectomy; NO, no treatment.

with increased metabolic imaging, it did not have a greater diagnostic accuracy compared with the conventional imaging

techniques in gestational trophoblastic neoplasia (28,29). PET-CT may attribute to discriminate ambiguous lesions at

conventional imaging techniques and assess disease recurrence that may not be revealed at routine imaging with elevated β -hCG levels. Thus, the present case emphasizes the important role of PET-CT in differentiating between a tumor and a blood clot.

Choriocarcinoma responds well to chemotherapeutic agents, which implies timely diagnosis and initiation of chemotherapy are crucial to achieve the best possible outcome. It is important to start prompt treatment in order to prolong patient survival, and complete remission can be achieved with appropriate chemotherapy (cure rate >89%) (20). The guidelines of the European Society for Medical Oncology suggest that gestational trophoblastic neoplasia is treated clinically, as a biopsy of the lesion is highly risky in the vascular disease (5). Similar to the present case, the diagnosis of a pulmonary artery with choriocarcinoma is based mainly on high levels of serum β -hCG and the characteristic appearance of PET-CT scans in non-pregnant women. EMACO chemotherapy was initiated immediately and the patient responded positively, with serum β -hCG levels falling to within normal levels. Chung *et al* (30) reported a case where a patient under venoarterial extracorporeal membrane oxygenation (ECMO) accepted chemotherapy successfully and achieved a good outcome. Therefore, chemotherapy compromises an attractive management approach for pulmonary choriocarcinoma embolism.

In conclusion, pulmonary artery embolism by choriocarcinoma is a rare malignant tumor, with a lack of distinct symptoms, specific signs or typical radiography. Early diagnosis is challenging, which leads to substantial delays in the treatment. Choriocarcinoma should be considered for any women of child-bearing age who presents with a massive PE. It can be diagnosed by the combination of elevated serum β -HCG with a characteristic appearance of PET-CT. The present case emphasizes the importance of early diagnosis and promptly appropriate chemotherapy in this disease.

Acknowledgements

Not applicable.

Funding

This study was supported by the Youth Foundation of the Affiliated Hospital of Qingdao University (grant no. QDFYQN202102033).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

QW and PZ were responsible for patient management and interpreted the patient data. WX, PW, DR, CG, XD and YC designed the study, acquired the data and analyzed the data. WX draft the manuscript and critically revised the manuscript. PW and WX confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case presentation and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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