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A Lesson from Rare Cause of Pulmonary Embolism

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Introduction

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Pulmonary embolism(PE) may be a life-threatening condition, which needs immediate medical intervention. Early detection plays an important role in improving the survival rate. However, Pulmonary embolism is a difficult diagnosis that may be missed because of non-specific clinical presentation. According to guidelines on the diagnosis and management of acute pulmonary embolism, Pulmonary embolism should be diagnosed by the combination of the clinical presentation, radiological detection and blood test like D-dimer. Generally, anticoagulant therapy is the mainstay of treatment in most cases of pulmonary embolism. The massive or submassive pulmonary embolism causing hemodynamic instability is the indication for thrombolysis or embolectomy.[1] Most commonly, pulmonary embolism is caused by venous thromboembolism, however, other diseases can also mimic the clinical presentation of pulmonary thromboembolism, such as metastatic tumors, septic emboli, and foreign bodies occasionally. Choriocarcinoma is a malignant, trophoblastic tumor, which is characterized by early hematogenous spreading to the lungs. Bagshawe and Brooks were first to document pulmonary embolism attributable to choriocarcinoma.[2] Because the clinical presentation of pulmonary metastatic choriocarcinoma can mimic pulmonary thromboembolism, it makes the differential diagnosis between the two entities very challenging. In this report, we are introducing a case of pulmonary embolism caused by pulmonary metastatic choricarcinoma in a 24-year-old reproductive woman.

Case Summary

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A 24 year-old female patient was admitted due to extreme dyspnea and frequent coughing. She had experienced three spontaneous abortions, the last one occuring one year before. She had never documented irregularities in her menstrual period. During the past four years, she spent over 10

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hours playing card games every day. Six months ago, she experienced an episode of sudden dyspnea for the first time. Several days later, she sought treatment at local hospital when her symptoms became unbearable. She was diagnosed as acute pneumonia based on chest X-ray, in which several small, scattered nodular shadows appeared in both lungs(Figure 1A). Treatment was initiated with the antibiotics and her condition seemed to be improved over the course of administration.

On 15th May 2012, she was referred to our hospital because of urgent orthopnea. She was afebrile with a heart rate of 132 beats perminute (bpm), respiratory rate 32 bpm, blood pressure 96/52 mmHg. Her arterial blood gas with 3L/min mask oxygen inhalation showed PO_2 50mmHg, PCO_2 26.3 mmHg and SpO_2 89%. The emergency contrast-enhanced CT scan showed several scattered nodular shadow in both lungs(Figure 1B) and pulmonary embolism occluded left pulmonary artery (Figure 1C). Meanwhile, the echocardiography supported the diagnosis of pulmonary embolism and illustrated severe pulmonary hypertension up to 105mmHg along with mild tricuspid regurgitation. Blood BNP result and CK-MB result were 5683 pg/ml(0.5–30 pg/ml) and 44u/l(0-23 U/L) respectively. D-dimer test showed 270ug/l(<500ug/l). The day after her admission, pulmonary angiography was performed via the right femoral vein, which found complete occlusion of the left pulmonary artery (Figure 1B). The filling defects were also observed in several parts of the deep vein of right crus and was thought to be caused by deep venous thrombosis. Within the angiography procedure, we failed to dissolve the emboli by direct injection of 400,000iu urokinase. Consequently, in order to prevent progressive pulmonary thrombus, a venous filter was placed in inferior vena cava. After discussion with consulting physicians, a consensus was reached to perform pulmonary embolectomy. During the procedure under cardiopulmonary bypass, the white and reddish soft emboli was observed completely obstructing the opening of the left pulmonary artery and part of the right pulmonary artery (Figure 2).We completely

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removed the emboli. Prior to decannulation, the pulmonary artery pressure ranged from 90-110mmHg and surpassed the systemic pressure. The hemodynamic situation was so desperately unstable that a 5mm hole in atrial septum was made to mitigate the condition. The patient was then transferred to ICU for the intense monitoring and treatment.

Despite all our efforts, the patient ultimately died of heart failure due to severe pulmonary hypertension and acute renal failure. To our great surprise, the intraoperative pathologic evaluation showed that the pulmonary emboli consisted of the intimately related syncytiotrophoblasts and cytotrophoblasts without formation of definite placental type villi(Figure 3A).In conjunct with the positive human chorionic gonadotropin (Figure 3B) and cytokeratin immunostaining (Figure 3C) in the tumor cells, the diagnosis of choriocarcinoma was confirmed .

Discussion

Pulmonary embolism is a significant cause of mortality and morbidity worldwide. Primarily, pulmonary embolism originates from deep venous thrombus. However, other causes have been detected occasionally, including metastatic tumors. Metastatic tumors resulting in pulmonary embolism mostly come from breast cancer, stomach cancer, and lung cancer, whereas choriocarcinoma is rarely found.[3] As is well-known, gestational choriocarcinoma is a highly malignant epithelial tumor arising from the trophoblast of any type of gestational event , about half following a hydatidiform mole; others occurring after abortion (25%), normal pregnancy (23%), or ectopic pregnancy (2%). Bagshawe and Brooks were first to document pulmonary embolism and pulmonary hypertension attributable to choriocarcinoma . [2] Only a few relevent reports have been published. [4,5]

Pulmonary embolism derived from choriocarcinoma retains its own unique characteristics.[4] First and foremost, this condition can be completely treated by chemotherapy, even in advanced stages. The

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complete recovery rate of choriocarcinoma is reported to be over 80% with appropriate chemotherapy.[6] Secondly, presentation of remarkably high serum and urinary human chorionic gonadotropin(HCG) level, which is a reliable marker for choriocarcinoma.[7] In this case, we failed to test serum and urinary hCG levels, as we assumed this patient suffered from pulmonary thromboembolism based on her history of sedentary behavior and related test results.

The correct diagnosis of choriocarcinoma is frequently detectable by symptoms of metastatic diseases. When the pulmonary metastatic lesions are presenting prior to the primary tumors, the patients with choriocarcinoma are prone to be misdiagnosed as having pulmonary diseases.[6] In our case, X–Ray showing atypical radiologic findings in both lungs misled to the diagnosis of infection at the beginning, in which metastases were difficult to be distinguished from other nonmalignant lesions.[8] Although CT and MR scans are valuable in the diagnosis of pulmonary embolism , it is difficult to obtain noninvasive proof of presumed pulmonary embolism of gestational trophoblastic disease. To reduce the misdiagnosis, there is evidence illustrating the great usefulness of positron emission tomography (PET) for differentiating tumor embolism from thromboembolism.[9] The PET imaging was shown to be very sensitive in identifying malignant tissues including choriocarcinoma by their high uptake of fluorodeoxyglucose. PET may provide the only noninvasive procedure to differentiate between tumor and blood clot. The other potiential way to diagnosis of tumor embolisation is to make cytologic evaluation of pulmonary artery catheter-derived blood specimens, which represents currently the most promising new diagnostic technique.[10]

D-dimer, a specific fibrin derivate, is very important in distinguishing between thrombotic PE and non-thrombotic PE. The D-dimer assays are sensitive but nonspecific markers, so positive D-dimer results are not useful to ‘rule in’ the diagnosis. The evidenced-based study indicated that pulmonary

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thromboembolism can almost be excluded safely in patients with a low or moderate clinical probability when the D-dimer value is under a cutoff value of 500 micrograms/L.[1,11]Therefore, when D-dimer is negative, it is extremely reasonable to figure out the other pathogeneses contributing to the pulmonary embolism.

Teaching Points

The clinical presentation of patients with non-thrombotic pulmonary embolism is nonspecific and similar to that of patients with pulmonary thromboembolism. Non-thrombotic causes of pulmonary embolism should be considered in selected patients according to the whole clinical context of the specific patients, including the possibility of choriocacinoma especially in child bearing woman. A negative D-dimer result in a highly sensitive assay could safely exclude pulmonary thromboembolism in patients with non-high clinical probability. High-level HCG is a reliable tumor marker for choriocarcinoma. If possible and needed, positron emission tomography (PET) is recommended for differentiating tumor embolism from thromboembolism. Pulmonary wedge aspiration cytology is currently the most promising new diagnostic technique. Due to the rarity and high efficacy of chemotherapy for choriocarcinoma and related pulmonary embolism, this case report's primary aim is to alert the physicians about the possibility of pulmonary embolism caused by choriocarcinoma among women of child-bearing age. Chemotherapy should be initiated as soon as the diagnosis was made or highly suspected. Choriocarcinoma should be considered in the differential diagnosis of fertile women presenting with symptoms of pulmonary embolism or pulmonary hypertension

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Illustrations

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Figure-1 (A)The chest film indicated several small, scattered nodular shadows appeared in both lungs. The contrast-enhanced CT scan showed (B)several scattered nodular shadow in both lungs and (C) the left pulmonary artery was occluded, The pulmonary angiography (D) illustrated complete occlusion of the left pulmonary artery.

Figure-2 The multiple fragments of white and reddish soft tissue was removed from pulmonary artery.

Figure-3 (A)Tumor was constituted by only a thin peripheral rim of viable tissue with the central necrosis and hemorrhage. The tumor cells were consisted of an intimate mixture of multinucleated syncytiotrophoblast, mononuleate cytotrophoblast and intermediate trophoblast. There were considerable cytological atypia in the trophoblast with the polymorphic- hyperchromatic nuclei and

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abnormal mitotic figures(hematoxylin-eosin, original magnification,×200). The syncytiotrophoblast was strongly positive for (B)beta-hCG and (C) Cytokeratin immunostaining (original magnification,×200).

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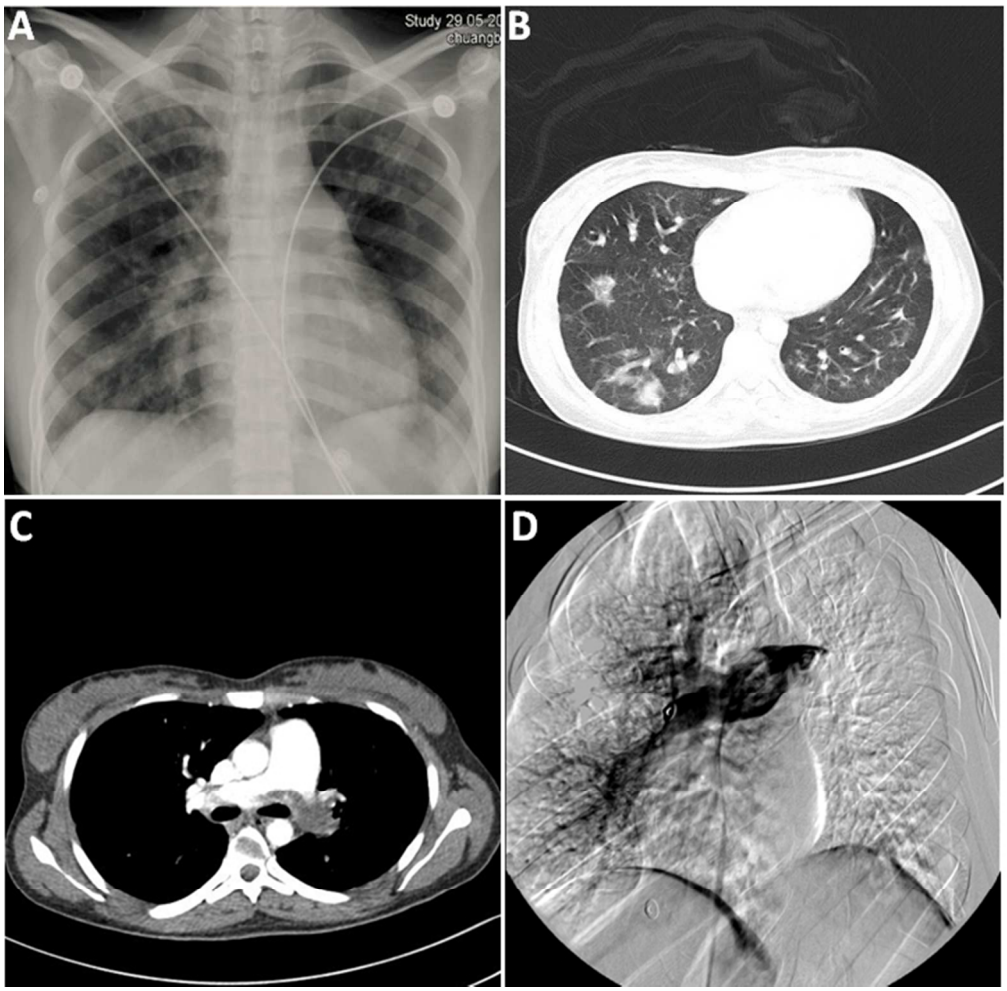

Figure-1 (A)The chest film indicated several small, scattered nodular shadows appeared in both lungs The contrast-enhanced CT scan showed (B)several scattered nodular shadow in both lungs and (C) the left pulmonary artery was occluded, The pulmonary angiography (D) illustrated complete occlusion of the left pulmonary artery.
60x59mm (300 x 300 DPI)

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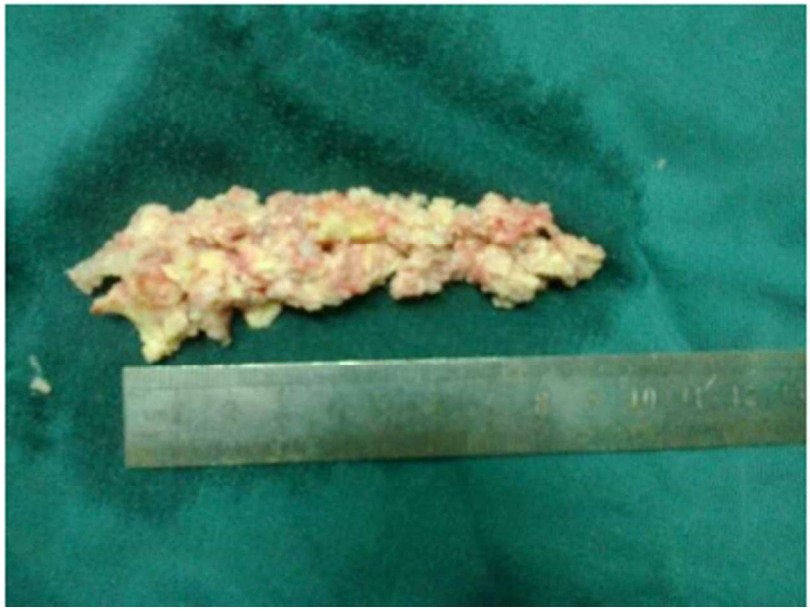

Figure 2 The multiple fragments of white and reddish soft tissue was removed from pulmonary artery 34x25mm (300 x 300 DPI)

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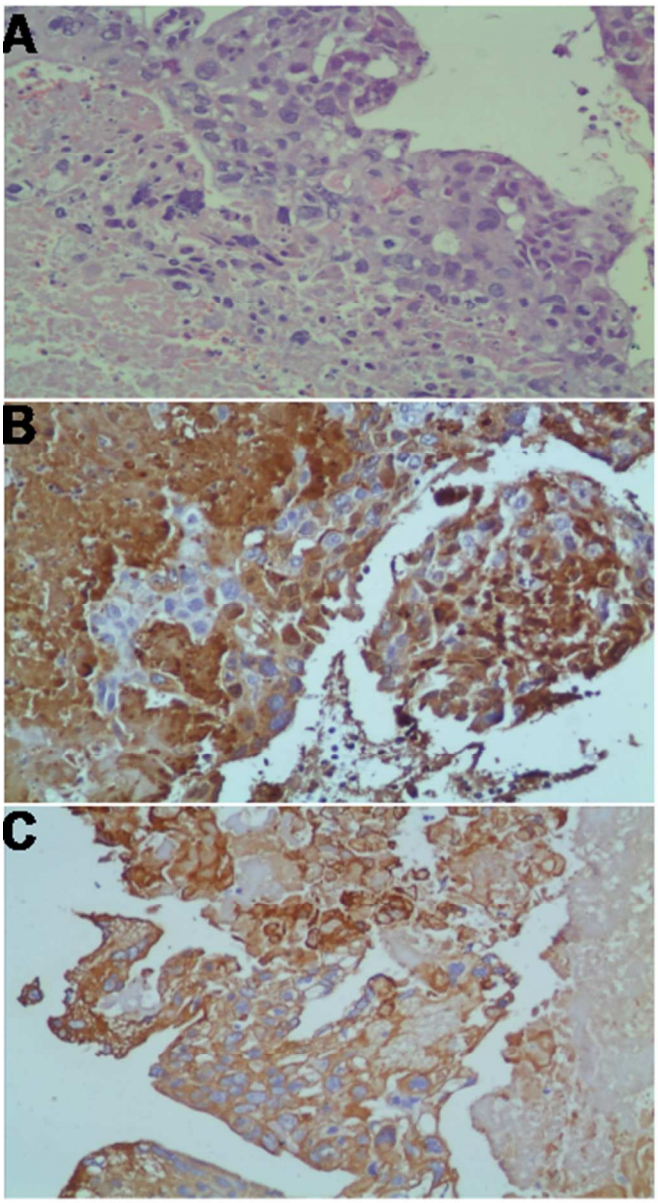

Figure 3 (A)Tumor constitutes only a thin peripheral rim of viable tissue with the central necrosis and hemorrhage. The tumor cell consisted of an intimate mixture of multinucleated syncytiotrophoblast, mononuleate cytotrophoblast and intermediate trophoblast. There were considerable cytological atypia in the trophoblast with the polymorphic- hyperchromatic nuclei and abnormal mitotic figures(hematoxylin-eosin, original magnification,×200). The syncytiotrophoblast is strongly positive for (B)beta-hCG and (C) Cytokeratin immunostaining (original magnification,×200).
33x60mm (300 x 300 DPI)