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Case Report

Pulmonary Tumor Thrombotic Microangiopathy: Case Report and Literature Review

Chien-Kuang Chen*

Department of Emergency Medicine, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rapidly progressive pulmonary disease complicated by malignancy. It manifests clinically as respiratory distress with pulmonary hypertension, progressive right sided heart failure, and sudden death.

We describe a case of PTTM associated with metastatic gastric carcinoma. This case demonstrates the diagnostic difficulties in such a rare and rapidly fatal oncological complication. More awareness among clinicians may help make a right diagnosis in the short time available. We also review the literatures to demonstrate the clinical characteristics that might provide clues towards an antemortem diagnosis, and may provide the key in treating PTTM.

Key words: *pulmonary tumor thrombotic microangiopathy (PTTM), pulmonary embolism (PE), gastric adenocarcinoma, dyspnea*

Introduction

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare complication of cancer. Clinically, it is characterised by dyspnea and severe pulmonary hypertension, which almost invariably progresses to right heart failure and cardiopulmonary arrest within days. Traditional radiological findings for pulmonary embolism (PE) on computed tomography (CT) are often nonspecific.

We report a case of a woman of gastric cancer, who visited our emergency department with exertional dyspnea. Although PE was quickly suspected, traditional image study could not find the filling defects. We arrange pulmonary perfusion scan to make the antemortem diagnosis. However, she rapidly deteriorated and died 3 days later. This case report highlights the diagnostic challenges involved in making a timely diagnosis of PTTM, and reviews the possible management options in this rare illness.

Case Report

This 42-year-old woman got gastric cancer, T3N1M0, stage IIIa, signet ring cell carcinoma, status post subtotal gastrectomy with BII reconstruction about 2 years before, and local regional lymph nodes (LN) recurrence under chemotherapy at the next year. Since then she received regular clinic follow-up under a stationary condition. The last follow-up clinic was about 3 months before. She suffered from exertional dyspnea and visited oncology clinic 1 week ago, and thoracic CT was performed. Local recurrence was reported due to thickening of the mucosae of the residual stomach, and stationary in lung condition (no evidence of lung metastasis).

She visited our emergency department due to progressive dyspnea. She was tachycardic (130 bpm), tachypnic (23 beat/min). Her saturation of peripheral oxygen (SpO_2) in room air is 96%. Clinical examination was non-contributory. Arterial blood gas

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*Corresponding author: Chien-Kuang Chen, MD, Department of Emergency Medicine, Linkou Chang Gung Memorial Hospital, No. 5, Fuxing St., Guishan Dist., Taoyuan 333, Taiwan. E-mail: cck2957@gmail.com

analysis showed compensated respiratory alkalosis (pH: 7.462, partial carbon dioxide pressure of arterial blood [PCO_2]: 29.8, partial oxygen pressure of arterial blood [PaO_2]: 75.1, HCO_3: 20.8, saturation [SAT] 95.9 with FiO_2: 21%). The lab data showed red blood cell (RBC): 3.49 million/UL, white blood cell (WBC): 8,900/μL, hemoglobin: 9.0 g/dL, platelets: 87,000/μL, D-dimer: 2,919.35 ng/mL, blood urea nitrogen (BUN): 11 mg/dL, creatinine: 0.7 mg/dL, Na: 135 mEq/L, K: 3.8 mEq/L. Electrocardiography showed sinus tachycardia with the right ventricular strain pattern. Chest radiograph (posterior-anterior [PA] view) was unremarkable.

Transthoracic echocardiography (TTE) showed severe pulmonary hypertension (Fig. 1). Computed tomographic angiography (CTA) was performed under the suspicion of PE. This demonstrated adequate opacification of the pulmonary arterial tree with no evidence of filling defect. There were enlarged LN in the mediastinum and left aortopulmonary (AP) window and bilateral hila and intrapulmonary LN; metastatic LN were suspected (Fig. 2).

However, she developed progressive respiratory distress but with normal blood pressure and stable peripheral oxygen SAT on 2–4 L/min oxygen. Pulmonary perfusion scan was arranged under the suspicion of nonthrombotic PE. The report showed there were two segmental perfusion defects at right lung, high probability of PE (Fig. 3).

She soon received emperic antiotics (levofloxacin), steroid (dexamethasone) and anticoagulant (enoxaparin) therapy, but suddenly deteriorated within 3 days and went into cardio-pulmonary arrest. Despite resuscitation attempt she passed away.

Discussion

PTTM is a rare pathological entity first described by von Herbay et al. in 1990.[1] It is a complication of cancer characterised by widespread microscopic tumor emboli (usually non-occlusive) in the pulmonary arterioles. Among 2,215 consecutive autopsy cases of carcinoma, 30 patients (1.4%) were diagnosed with definitive PTTM. The common symptom was progressive dyspnea. The median survival time after the initiation of oxygen supplementation was nine days. The most frequent primary site was the stomach (60%), and the most frequent histological type was adenocarcinoma (93.3%). No specific features at clinical presentation or imaging (with CT, nuclear medicine) reliably diagnosed PPTM. Perfusion scanning mostly showed multiple small perfusion defects. Plasma levels of D-dimer or fibrin degradation products are usually elevated, and could raise the suspicion of microvascular thrombosis, once larger PE are excluded.[2]

Echocardiography may show pulmonary hypertension and right heart strain.[3-5] This picture of rapidly progressive dyspnea often prompts the team managing the patient to organize a thoracic CTA. Although pulmonary angiogram still remains the gold standard for PE, it is seldom performed due to its invasive procedure. However, a normal CTA report cannot totally excluded PE. Pulmonary perfusion scan still plays a role to evaluate for PE, especially in nonthrombotic PE.[6,7]

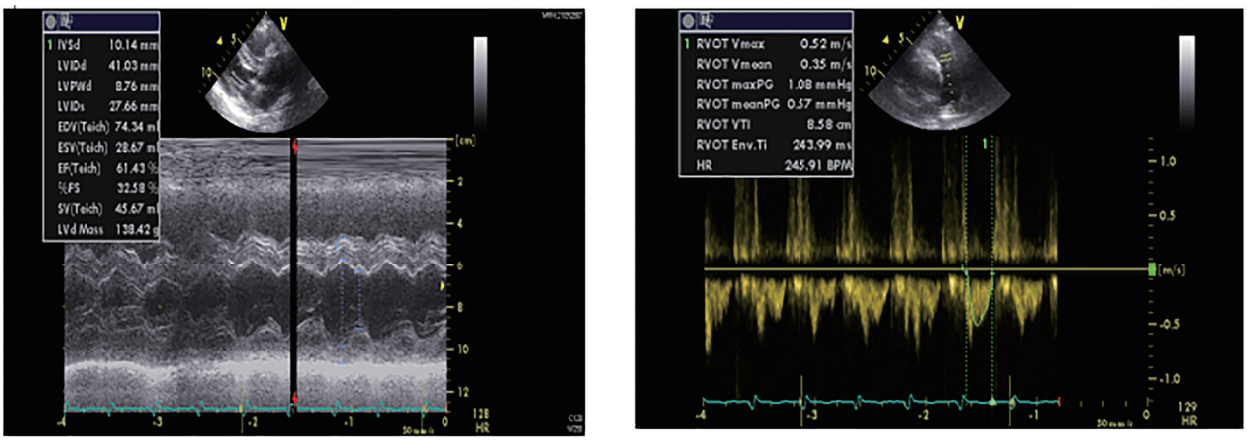

Fig. 1. Transthoracic echocardiography (TTE). (1) Adequate left ventricular systolic function, dilated right atrium and right ventricle. (2) Moderate to severe tricuspid valve regurgitation, mild mitral valve regurgitation and pulmonary valve regurgitation. (3) Severe pulmonary hypertension (rule out [r/o] pulmonary embolism).

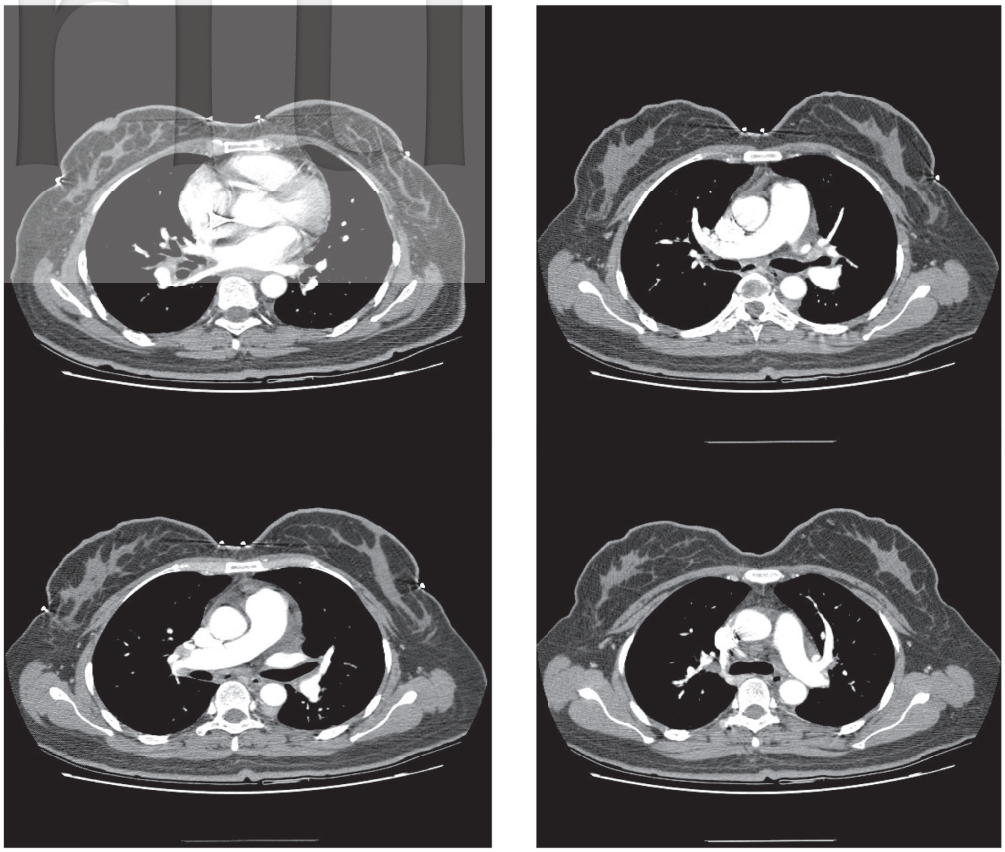

Fig. 2. Computed tomographic angiography (CTA) of pulmonary artery for survey of pulmonary embolism shows: (1) No definite filling defect in the bilateral pulmonary arteries. (2) Enlarged lymph nodes in the mediastinum and left aortic-pulmonary window and bilateral hila and intrapulmonary lymph nodes suggestive metastatic lymph nodes. (3) No definite space-taking lesion in the bilateral lung. (4) No pleural effusion in the bilateral chest. (5) Status post port-A catheter insertion via right subclavian vein. (6) No defintie filling defect in the deep vein of bilateral thigh and lower inferior vena cava. Impression: no evidence of pulmonary embolism. Metatastic lymph nodes in the mediastinum as above mentioned.

A perfusion scan might be a more useful tool for the diagnosis of PTTM. It was reported that a perfusion scan typically shows numerous symmetric and peripheral defects (termed the "segmental contour pattern")[8] in pulmonary tumor embolism, including PTTM, whereas pulmonary thromboembolism usually shows one or more, larger and more centrally located, perfusion defects.

A high probability pulmonary perfusion scan is defined as showing two or more unmatched segmental perfusion defects according to the modified Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria.[9] Although the classic perfusion scan is multiple small, peripherally based, bilateral subsegmental defects, a high-probability perfusion should persuade the clinician pursuing further management.[7]

In short, this patient exhibit acute worsening respiratory insufficiency accompanied by severe pulmonary hypertension and elevated D-dimer. Her pulmonary CTA is normal. Nonthrombotic PE should be suspected. Pulmonary perfusion scan shows peripheral segmental defects. PTTM as an antemortem timely diagnosis is reasonable, especially in this patent with gastric cancer.[10-12]

No treatment was recommended due to the patients' rapid deterioration and clinical condition upon diagnosis, but if detected early enough, chemotherapy is believed to reduce the burden of tumor cells in PTTM,[13,14] and thereby lessen the stimulus for intimal proliferation. Whilst no definite treatment had been established, it is perceived chemotherapy may prolong the survival period. The first was in 2007 when a patient with video-assisted thorocoscope (VATS) biopsy-proven PTTM from gastric adenocarcinoma

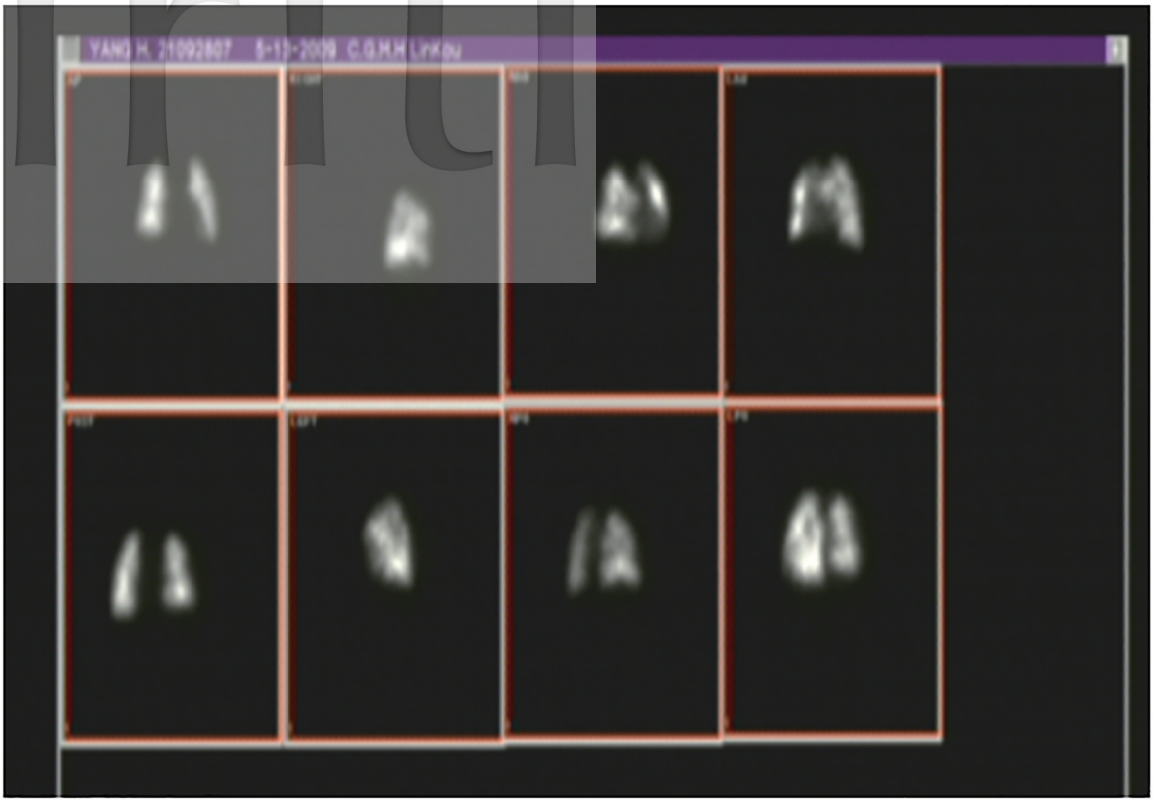

Fig. 3. Report: The Tc-99m macroaggregate albumin (Tc-99m MAA) lung perfusion scan performed after intravenous 5 mCi of Tc-99m MAA revealed mild heterogeneity of radioactivity distribution in the bilateral lung fields. There were two segmental cold areas in lateral and medial segments of middle lobe of right lung. Impression: segmental perfusion defect at right lung, high probability of pulmonary embolism.

was treated with steroid, warfarin, aspirin and chemotherapy.[1] Anti-coagulants and corticosteroids might be ineffective. Further study is needed to assess the therapeutic strategy for PTTM.[15,16]

This case shows the challenges of diagnosing and managing PTTM. This is particularly true for three reasons: the relatively non-specific symptom of dyspnea; the fact that traditional image studies (chest PA film, thoracic CTA) often does not have a specific finding; and the rate of clinical decline leading almost inevitably to death.[4,5,11]

For early antemortem diagnosis of PTTM, serum D-dimer measurements may be effective for screening. We suggest pulmonary perfusion scan if PE is suspected and CTA shows no filling defect. PTTM with exertional dyspnea as the initial presentation for metastatic cancer combined with a rapid deterioration makes diagnosis a significant challenge. Early antemortem diagnosis is, however, only the first step towards successful treatment.[17] Clinicians should be aware of this as a diagnostic entity, aided by the radiographic findings of rapidly progressive pulmonary arterial hypertension.

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