MEGA JOURNAL OF CASE REPORTS

Case Presentation

Compiled Date: November 25, 2022

Pulmonary Tumor Thrombotic Microangiopathy: A Case Report

Fangfang Niu, Yao Wang, Baicheng Zhang, Jingjing Xu, Changsong Wang, Qi Chen, Qing Yang, Wenjing Mu, Zipeng Zhuo, Yingnan Ju* and Haitao Liu*

Department of Critical Care Medicine, Harbin Medical University Cancer Hospital, China

***Corresponding authors**: Yingnan Ju, Departments of Critical Care Medicine, Harbin Medical University Cancer Hospital, Harbin Medical University, Harbin, Heilongjiang, 150081, China, Tel: 13804560454; E-mail: juyingnan2010@126.com

Haitao Liu, Departments of Critical Care Medicine, Harbin Medical University Cancer Hospital, Harbin Medical University, Harbin, Heilongjiang, 150081, China, Tel: 13613622338; E-mail: dr633@foxmail.com

Abstract

Background: Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare disease characterized by progressive pulmonary hypertension and hypoxemia in patients with a history of malignancy.

Case report: We reported a case of a 57-year-old woman with breast cancer who presented with fatigue for 4 weeks and expiratory dyspnea 3 days earlier, which worsened during the last day. First, she was highly suspected of having a pulmonary embolism due to the classic findings of increased pulmonary arterial pressure, right heart enlargement, left ventricular compression, and elevated D-dimer levels.

However, despite the immediate initiation of anticoagulation therapy, her general condition continued to deteriorate. Further improvement of pulmonary angiography, in view of no thrombus found in the pulmonary artery, left supraclavicular hypoechoic mass, considered the possibility of tumor metastasis. At the same time, tumor markers increased, and we clinically diagnosed her with pulmonary neoplasm thrombotic microangiopathy.Despite respiratory support, inotropic agents, and prostaglandins, she died of respiratory and circulatory failure 21 hours after admission.

Conclusion: The patient had a history of malignant breast cancer, and we should strengthen our understanding that PTTM can occur even in patients with early or completely cured malignant tumors. Despite the challenges of early and definitive diagnosis of PTTM, there is a need for optimal diagnostic and therapeutic strategies.

Keywords: Pulmonary hypertension; Pulmonary embolism; Lung neoplasm; Thrombotic microangiopathy; Case report

Abbreviations: PTTM: Pulmonary Tumor Thrombotic Microangiopathy; ICU: Intensive Care Unit; CEA: Carcinoma Embryonic Antigen; CT: Computed tomography; CTA: Computed Tomography Angiography;

VEGF: Vascular Endothelial Growth Factor; TF: Tissue Factor; PDGF: Platelet-Derived Growth Factor; COPD: Chronic Obstructive Pulmonary Disease; OPN: Osteopontin; CTEPH: Chronic Thromboembolic Pulmonary Hypertension

Background

PTTM is a rare disease discovered by Herbay et al. in 1990. It is characterized by progressive pulmonary hypertension and hypoxemia in patients with a history of malignancy **[1].** The first manifestation may be similar to pulmonary embolism, and it is difficult to distinguish PTTM from pulmonary embolism. However, the prognosis for PTTM is worse, with patients surviving only days or weeks. One of the purposes of this report is to provide a reference and help for the early diagnosis of PTTM in other patients by comprehensively analyzing the symptoms, clinical signs, examination results, laboratory results, imaging features and pulmonary hypertension of the patients.

Case Presentation

A 57-year-old female patient was admitted to the ICU because of fatigue for 4 weeks, dyspnea for 3 days and aggravation for 1 day. She suffered from left breast cancer, and underwent radical surgery for left breast cancer four years ago. The pathological diagnosis was invasive ductal carcinoma. The patients were treated with an ECF-P (cyclophosphamide + fluorouracil + doxorubicin) regimen for 4 cycles after the operation and received radiotherapy and targeted therapy 3 months after the operation. Four days before entering our hospital, a hypoechoic mass on the left supraclavicular was found in the other hospital, and the possibility of tumor metastasis was considered **(Figure 1).**

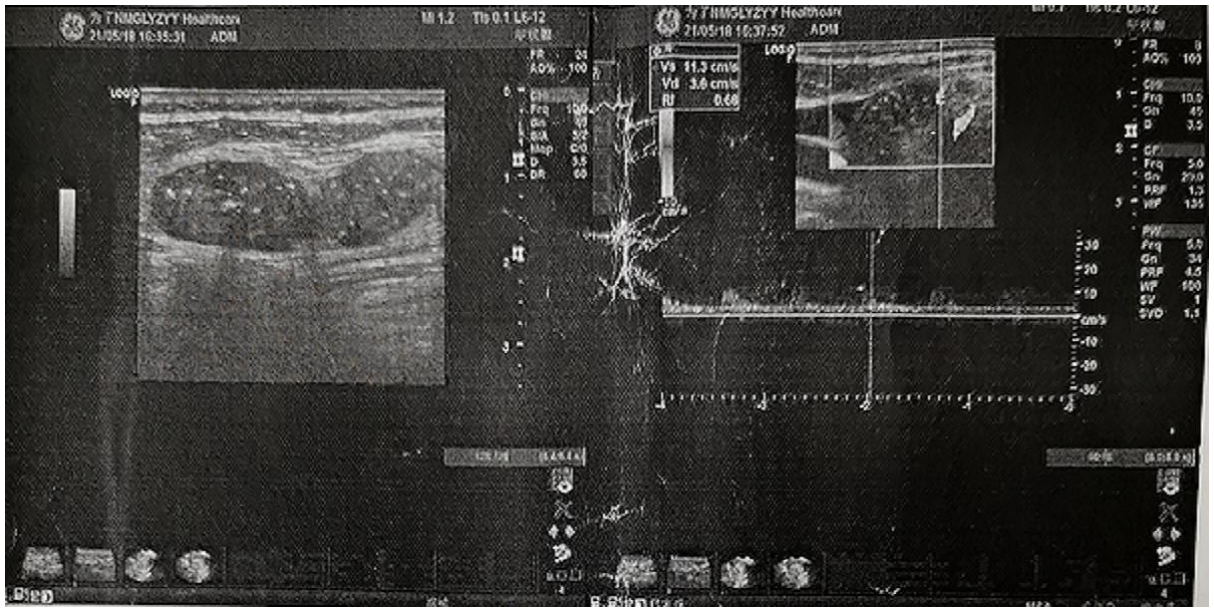

Figure 1: Left supraclavicular hypoechoic mass, considering tumor metastasis.

The patient was transferred to our hospital complaining of fatigue, wheezing, no precordial discomfort, and chest pain. Heart rate: 86/min, blood oxygen saturation: 72%, respiratory rate: 32/min, blood pressure: 102/77 mmHg, physical examination: bilateral thorax symmetry, auscultation bilateral lung breath sound thick, bilateral

lower lung can be heard and a small amount of scattered dry and wet rales, no positive abdominal signs, no edema in both lower limbs.Blood gas analysis showed pH: 7.51, PCO2: 18 mmHg, PO2: 41 mmHg, and FIO2: 41%. After entering the ICU, the patients were given ventilator-assisted breathing, mode: a/C, FIO2: 100%, and pressor drugs to maintain blood pressure. D-dimer: 9.17 mg/L (reference range 0-0.55), fibrinogen content determination: 0.85 g/L (reference range 2-4).

Three days ago, ultrasound examination showed increased pulmonary artery pressure and an enlarged right atrium **(Figure 2).** In our hospital, emergency bedside ultrasound showed no thrombi in either lower extremity. The right atrium and ventricle were enlarged, the left ventricle was compressed, the size and shape of the left atrium were normal, and the diameter of the pulmonary artery was obviously widened. The electrocardiogram showed normal sinus rhythm and T wave inversion **(Figure 3).** At this time, we highly suspected the possibility of pulmonary embolism, so we began to administer anticoagulation therapy.However, the patient's oxygen saturation and oxygen index were not significantly improved, and the patient's oxygen saturation was always 75%-85%. For further diagnosis, pulmonary angiography was performed, and no pulmonary embolism was found **(Figure 4)**. Upon further improvement of the examination, for patients with parenchymal organs and intra-abdominal vascular ultrasound examination, no abnormalities were found.

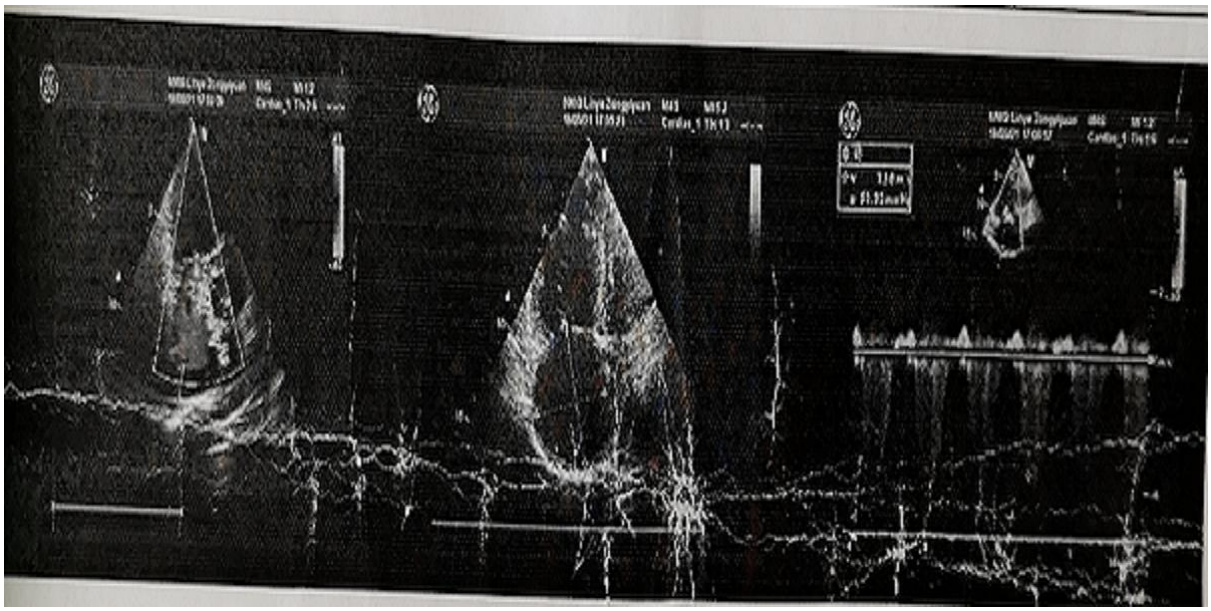

Figure 2:Ultrasound showed increased pulmonary artery pressure and enlargement of the right atrium.

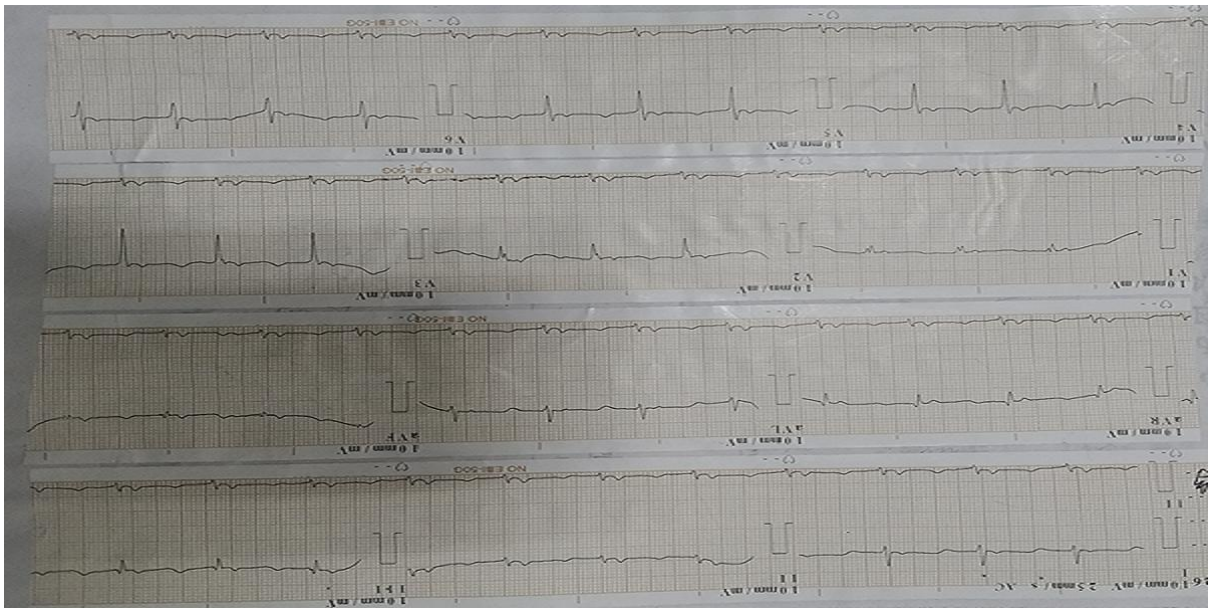

Figure 3: ECG showed normal sinus rhythm with T wave invers.

Figure 4: No pulmonary embolism was found on pulmonary angiography.

Patient tumor marker examination results:CEA:19.5 ng/ml (0-5, CA125:172.5U/ml(0-25), CA153:85.3U/ml(0-25), ultrasound examination showed: left supraclavicular hypoechoic mass, considered metastatic cancer. Based on the patient's clinical signs and examination results, we considered that the patient might suffer from PTTM, and to further confirm the diagnosis, we planned to perform pulmonary artery aspiration cytology, but unfortunately, the family refused to perform this test considering the patient's condition.However, after we talked to the family, we still gave the patient prostaglandin; unfortunately, the patient died on the same day. We suggested performing an autopsy on the patients.However, due to the influence of Chinese traditional culture, the family members refused.

Final diagnosis

Diagnosis of PTTM: The patient had fatigue and dyspnea, and a history of breast cancer. Out-of-hospital ultrasound showed increased pulmonary artery pressure and right atrial enlargement. CT examination showed a small amount of scattered ground-glass opacities in the bilateral lung.Ultrasound examination in our hospital showed increased pulmonary artery pressure, pulmonary artery widening, right atrial ventricular enlargement, and left ventricular compression. Therefore, we suspect pulmonary embolism.However, there was no significant effect of anticoagulant therapy, and no pulmonary thrombus was found on CTA. Combined with the patient's history and clinical signs, the recent increase in tumor markers, ultrasound showed that the left supraclavicular metastatic cancer may be. For the antemortem diagnosis of PTTM, cytological examination must be performed. However, unstable and progressive PTTM is usually not available for lung biopsy. However, we made a clinical diagnosis of PTTM based on the patient's acute progressive clinical course and CTA results.

Discussion and Conclusions

Pathophysiological features

In recent years, the reported frequency of PTTM has increased, but its pathophysiology is not yet fully understood. It has been reported that there are tumor cells, fibrin deposition and fibrocyte intimal hyperplasia in the pulmonary capillary lumen of PTTM patients **[2].** However, most studies indicate that tumor emboli in PTTM patients attach to the pulmonary artery intima, damage the endothelium, activate the coagulation system and induce fibrocyte intima hyperplasia, resulting in pulmonary vascular stenosis and obstruction, leading to pulmonary hypertension, rather than just mechanical obstruction of tumor cells. Toyonaga found alveolar inflammatory cell infiltration and hyaline membrane formation in patients with PTTM, suggesting that ischemia-induced lung injury may also be one of the pathogenic mechanisms of PTTM **[3].** Kubo studied 6 autopsy cases of PTTM and found that pulmonary artery pressure was related to the degree of pulmonary vascular stenosis and the extent of the lesion. It is worth noting that this study suggests that tumor emboli initially block small branches of large blood vessels, which are numerous and form PTTM lesions, and with the accumulation of tumor emboli, PTTM lesions expand to the main trunk of large blood vessels, which can cause a sudden increase in vascular resistance and a rapid increase in pulmonary artery pressure, thus leading to the rapid progression of the disease.Vascular Endothelial Growth Factor (VEGF), Tissue Factor (TF) and Platelet-Derived Growth Factor (PDGF) have been proven to be the most effective growth factors in the treatment of Chronic Obstructive Pulmonary Disease (COPD). PDGF and Osteopontin (OPN) may be related to the morbidity of the disease.

Diagnosis

A diagnostic method for PTTM has not been established. With regard to imaging studies, it has been reported that Ground Glass Opacity (Ggo) can be seen on chest CT in patients, and most PTTM patients have signs of pulmonary hypertension on pulmonary angiography: widening of the main pulmonary artery and enlargement of the right heart, but no signs of pulmonary embolism **[4].** PTTM patients with ventilation perfusion scans may exhibit chronic thromboembolic pulmonary hypertension (Chronic Thromboembolic Pulmonary Hypertension, CTEPH) similar to perfusion defects and peripheral and subsegmental performance **[5].** Because the results of the examination can also be negative, the diagnostic value is limited. Pulmonary angiography is expected to

become the gold standard for PTTM. However, it has been reported to have poor sensitivity and specificity for detecting tumor emboli **[6].** In addition, the patient's cardiac color Doppler ultrasound showed pulmonary hypertension, right ventricular hypertrophy, and ventricular septal thickening, but the left heart function was normal. For pathological examination, lung biopsy can be performed by CT guidance, bronchoscopy or surgery and thoracoscopy. Gainza et al. considered PTTM to be only one of the clinical signs of thrombotic microangiopathy in tumors of multiple organs [7]. The tumor may not only metastasize to the lung, so biopsy of other sites can also provide help for the diagnosis of PTTM.

Therapy

Treatment of PTTM: There is no uniform treatment strategy for PTTM. Anticoagulation and thrombolytic therapy are often routinely performed, although in most cases they are ineffective. Some scholars also suggest that the treatment of primary malignant tumors may be effective. In a Japanese case report, imatinib, a PDGFR tyrosine kinase inhibitor, may cause regression of PTTM pulmonary hypertension and pulmonary arterial remodeling **[8].** There was one case of breast cancer with PTTM but without pulmonary hypertension. The diagnosis of PTTM was confirmed, and the patient responded well to treatment with trastuzumab **[9].**

Outcome and prognosis

The prognosis of patients is generally very poor, and patients in critical condition often die within a few days to a few weeks after symptoms appear.

In conclusion, PTTM should be included in the differential diagnosis when a patient with breast cancer exhibits progressive respiratory symptoms with lung infiltration but no lung infection. One of the purposes of this report is to provide a reference and help for the early diagnosis of PTTM in other patients by comprehensively analyzing the symptoms, clinical signs, examination results, laboratory results, imaging features and pulmonary hypertension of the patients.

Acknowledgements

We thank the critical care physicians at Harbin Medical University Cancer Hospital for their medical expertise and useful discussions. These cases have not been published elsewhere.

Conflicts of Interest

The authors of this manuscript declare that there are no conflicts of interest.

Authors' Contributions

NFF, JYN and LHT prepared and created the published work, specifically wrote the initial draft (including substantive translation),and analysed pulmonary tumor thrombotic microangiopathy and provided treatment protocols.WY, ZBC, JJX, WCS, CQ, YQ, MWJ and ZZP have made substantial contributions to the conception and design of the case report, acquisition of data and images, drafting and revision of the article. JYN and LHT revised the text. All authors read and approved the final manuscript.

Consent for Publication

All authors have given consent for publication.

References

1. von Herbay A, Illes A, Waldherr R, Otto HF. Pulmonary tumor thrombotic microangiopathy with pulmonary hypertension. Cancer. 1990;66(3):587-92.
2. Godbole RH, Saggar R, Kamangar N. Pulmonary tumor thrombotic microangiopathy: a systematic review. Pulm Circ. 2019;9(2):2045894019851000.
3. Toyonaga H, Tsuchiya M, Sakaguchi C, Ajimizu H, Nakanishi Y, Nishiyama S, et al. Pulmonary tumor thrombotic microangiopathy caused by a parotid tumor:early antemortem diagnosis and long-term survival. Intern Med. 2017;56(1):67-71.
4. Jie Wang, Xi Li, Huaping Huang. Progress in the study of pulmonary tumor hemorrhagic microangiopathy. Chinese J Lung Dis. (electronic version). 2018;11(1):111-4.
5. Godbole R, Saggar R, Zider A, Betancourt J, Wallace WD, Suh RD, et al. Insights on pulmonary tumor thrombotic microangiopathy:a seven-patient case series. Pulm Circ. 2017;7(4):813-20.
6. Schriner RW, Ryu JH, Edwards WD. Microscopic pulmonary tumor embolism causing subacute cor pulmonale: a difficult antemortem diagnosis. Mayo Clin Proc. 1991;66(2):143-8.
7. Gainza E, Fernandez S, Martinez D, Castro P, Bosch X, Ramirez J, et al. Pulmonary tumor thrombotic micro angio pathy: report of 3 cases and review of the literature. Medicine (Baltimore). 2014;93(24):359-63.
8. Takahashi Y, Uruga H, Fujii T, Kishi K, Hanada S, Takaya H, et al. Antemortem diagnosis of pulmonary tumor thrombotic microangiopathy in a patient with recurrent breast cancer: a case report. BMC Cancer. 2016;16(1):666.
9. Ogawa A, Yamadori I, Matsubara O, Matsubara H. Pulmonary tumor thrombotic microangiopathy with circulatory failure treated with imatinib. Intern Med. 2013;52(17):1927-30.

Citation of this Article

Fangfang N, Yao W, Baicheng Z, Jingjing X, Changsong W, Qi C, Qing Y, Wenjing M, Zipeng Z, Yingnan J and Haitao L. Pulmonary Tumor Thrombotic Microangiopathy: A Case Report. Mega J Case Rep. 2022; 5: 2001-2007.

Copyright

© 2022 Yingnan J and Haitao L. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cite.