

Pulmonary Tumor Thrombotic Microangiopathy Suspected to be COVID-19 Vaccine-Related Myocarditis: A Case Report

Review began 03/04/2024
Review ended 03/18/2024
Published 03/24/2024

© Copyright 2024

Kageyama et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Soichiro Kageyama¹, Takeki Ohashi¹, Akinori Kojima¹

¹. Cardiovascular Surgery, Nagoya Tokushukai General Hospital, Kasugai, JPN

Corresponding author: Soichiro Kageyama, soi.kageyama@gmail.com

Abstract

Pulmonary tumor thrombotic microangiopathy (PTTM) is a very rare condition that can lead to acute severe pulmonary hypertension and circulatory failure. It is caused by tumor cell microvascular obstruction and is usually difficult to diagnose; in fact, it is often diagnosed after death. We report the case of a patient who experienced a sudden cardiac arrest and developed severe pulmonary hypertension two days after receiving the coronavirus disease (COVID-19) vaccine. The patient was initially diagnosed with vaccine-associated myocarditis, and venoarterial extracorporeal membrane oxygenation (VA-ECMO) implantation with median sternotomy was performed. The patient survived for more than two weeks. PTTM was later diagnosed during a pathological autopsy.

Categories: Cardiac/Thoracic/Vascular Surgery, Cardiology, Emergency Medicine

Keywords: coronavirus vaccine-associated myocarditis, venoarterial extracorporeal membrane oxygenation, circulatory failure, pulmonary hypertension, pulmonary tumor thrombotic microangiopathy

Introduction

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare condition caused by tumor cell microvascular obstruction and can result in acute severe pulmonary hypertension and circulatory failure. Most cases of microscopic tumor embolisms are difficult to diagnose using imaging studies and are not recognized until the patient has died [1]. We present the case of a patient who experienced a sudden cardiac arrest and developed severe pulmonary hypertension two days after receiving a COVID-19 vaccine. The patient was initially diagnosed with coronavirus disease (COVID-19) vaccine-associated myocarditis, and extracorporeal circulation therapy was administered. An extremely rare primary cholangiocarcinoma was diagnosed during pathological autopsy.

This case report relied on existing patient information without intervention for research purposes, and the requirement for obtaining written patient consent was waived.

Case Presentation

A 61-year-old female with no relevant medical history presented to a hospital with sudden dyspnea. She had received a COVID-19 vaccine (Pfizer-BioNTech COVID-19 vaccine: BNT162b2 mRNA) two days before the onset. Transthoracic echocardiography (TTE) revealed right ventricle (RV) dilatation, left ventricle (LV) collapse, and pulmonary hypertension. Pulmonary artery embolism was initially suspected. However, contrast-enhanced CT showed no obvious contrast deficit in the pulmonary artery. Her hemodynamics deteriorated during the examination, leading to cardiac arrest. The patient was treated with venoarterial extracorporeal membrane oxygenation (VA-ECMO) via the femoral artery and vein, and her heartbeat resumed. She was transferred to our hospital for further treatment.

Blood tests at our hospital revealed an elevated inflammatory response and liver and renal dysfunction. TTE revealed LV collapse and a low ejection fraction (LVEF) of 38%. Contrast-enhanced CT revealed a pulmonary ground-glass opacity but no pulmonary artery thrombi (Figure 1).

How to cite this article

Kageyama S, Ohashi T, Kojima A (March 24, 2024) Pulmonary Tumor Thrombotic Microangiopathy Suspected to be COVID-19 Vaccine-Related Myocarditis: A Case Report. *Cureus* 16(3): e56803. DOI 10.7759/cureus.56803

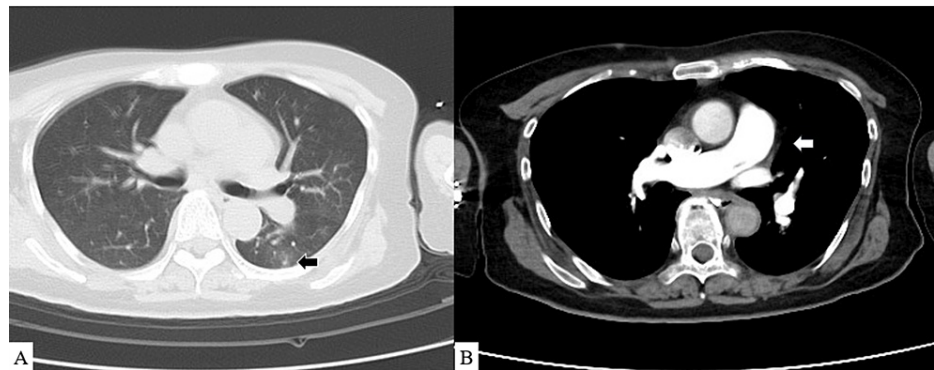


FIGURE 1: CT findings on the first day

(A) Black arrow: pulmonary ground-glass opacity is observed. (B) White arrow: no contrast deficit is observed in the pulmonary artery

CT: computed tomography

COVID-19 vaccine-related myocarditis was suspected given sudden post-vaccine severe cardiac decompensation, and steroid pulse therapy and high-dose gamma globulin treatments were initiated. Nitric oxide therapy for pulmonary hypertension was also initiated, and an Impella® heart pump (Abiomed, Danvers, MA) was placed for LV decompensation and reduced LV afterload. This stabilized the hemodynamics (VA-ECMO flow: 1.8 L/min, Impella® flow: 2.2 L/min, blood pressure: 100/87 mmHg, pulmonary artery pressure: 43/25 mmHg, and central venous pressure: 5 mmHg). A myocardial biopsy was performed as well.

On the seventh day, the flow through the Impella® heart pump dropped and could not be maintained despite the reduction in the ECMO flow. The Impella® heart pump was removed. Transesophageal electrocardiography showed further RV enlargement and LV collapse. This seemed insufficient for blood flow from the right to the left heart system. A myocardial biopsy revealed no significant inflammatory cellular infiltrates or evidence of amyloidosis or sarcoidosis. Chest radiography revealed severe pulmonary congestion. Follow-up CT showed the worsening of the lung field consolidation, and contrast defects of the pulmonary arteries remained absent. Multiple masses in the liver were not observed on a previous CT scan (Figures 2, 3). The cardiac function improved; however, the native pulmonary hypoxia worsened (respirator FiO₂: 100%; ECMO flow: 3.5 L/min; left radial artery PaO₂: 47 mmHg; left radial artery PaCO₂: 49 mmHg). Therefore, we decided to upgrade the VA-ECMO to central ECMO via the ascending aorta and femoral vein for cerebral protection.

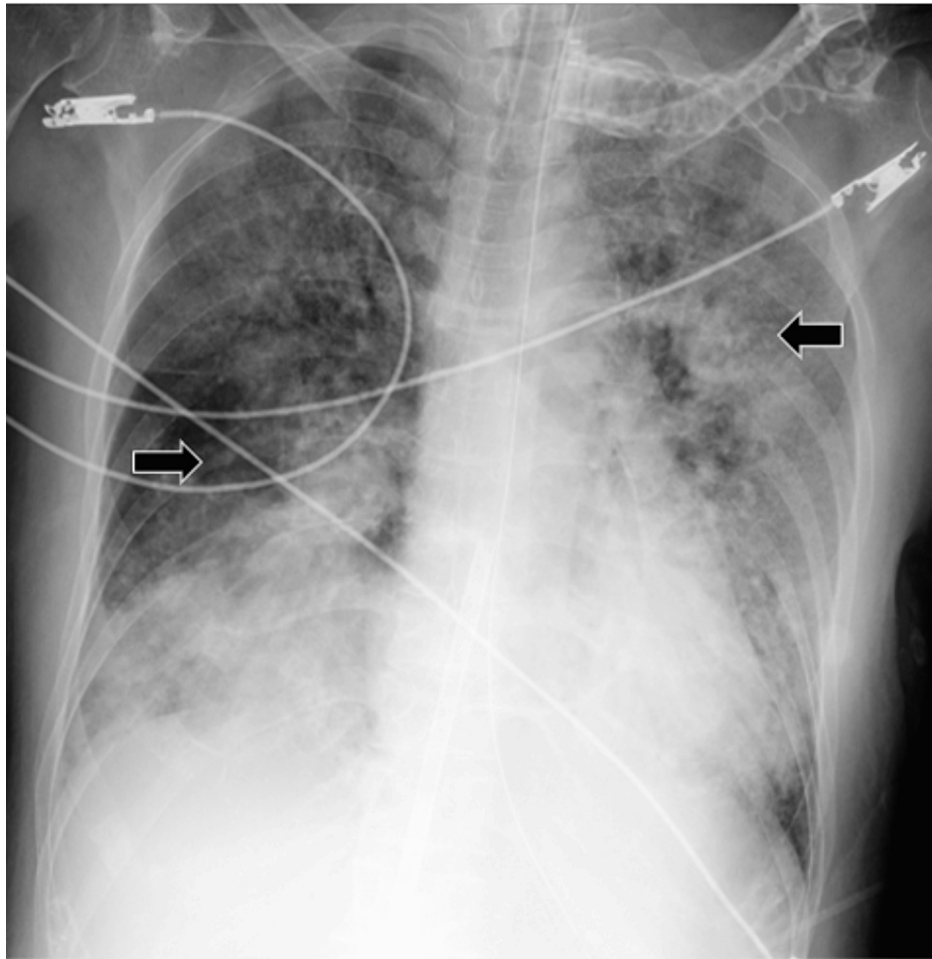


FIGURE 2: Chest radiography findings on the seventh day

Black arrow: chest radiograph reveals severe pulmonary congestion



FIGURE 3: CT findings on the eighth day

(A) Black arrow: severe lung field consolidation is observed. (B) White arrow: no contrast defect of the pulmonary artery is observed. (C) White arrow: multiple masses are observed in the liver

CT: computed tomography

On the eighth day, central ECMO attachment with a median sternotomy was performed. Central ECMO reduced the pulmonary artery pressure (54/32 mmHg to 10/9 mmHg); the cerebral oxygenation also improved (left radial artery PaO₂: 186 mmHg). Part of the lung was dark reddish and had hardened (Figure 4). Furthermore, a lung biopsy performed during surgery revealed tumor embolism in almost all peripheral pulmonary arteries (Figure 5). This suggested that the PTM was due to a malignant tumor with an unknown primary site and metastasis to the liver. After that, multiple organ failure developed gradually, and the patient died on the 15th day of the disease onset. Histological examination of the tumor cells revealed a small cell carcinoma. The pulmonary artery was filled with tumor cells and thrombi, and no primary tumors

were found in the lungs. Multiple 1-2 cm nodules were scattered throughout the liver, and some formed abscesses. The pathological diagnosis was of an intrahepatic cholangiocarcinoma, and the mass in the liver was considered the primary tumor with intrahepatic metastasis. Immunostaining was negative for TTF-1 and positive for CD56; positivity for TTF-1 and CD56 is often observed in primary small-cell lung carcinomas and intrahepatic cholangiocarcinomas, respectively (Figure 5).

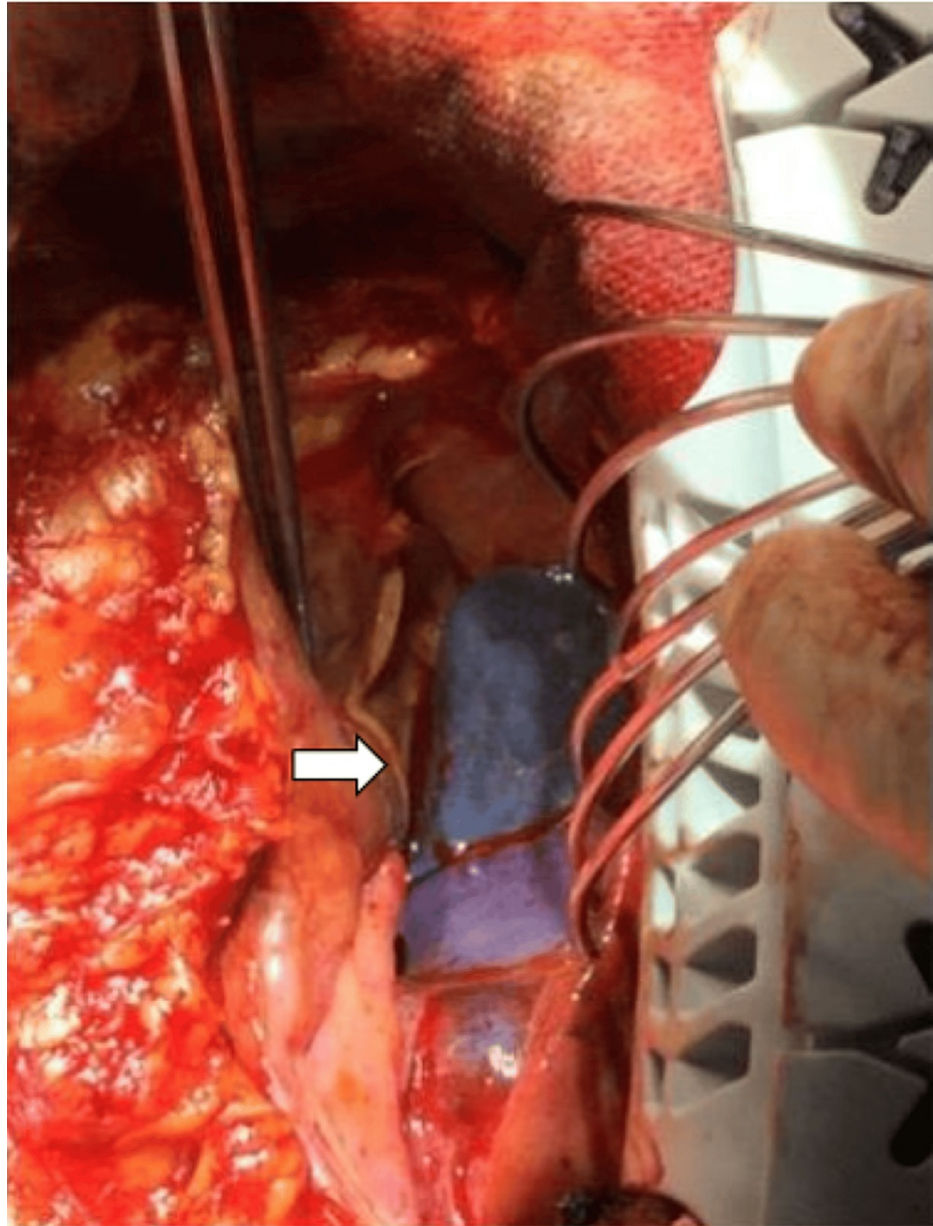


FIGURE 4: Operative findings

White arrow: the right lower lobe of the lung appears dark reddish and hardened

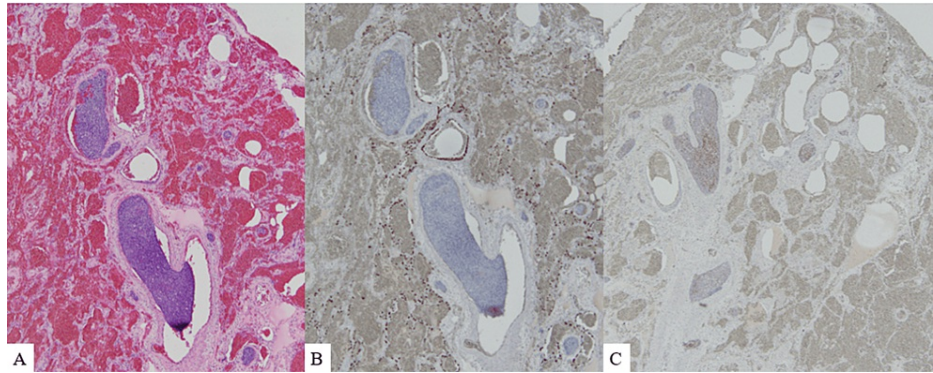


FIGURE 5: Pathological findings

(A) Lung biopsy reveals tumor embolism in the peripheral pulmonary arteries. (B) Immunostaining is negative for TTF-1. (C) Immunostaining is positive for CD56

Discussion

Diagnosing PTTM is generally challenging; 79% of the cases are diagnosed after death [2]. Patients may present with cough (85%), dyspnea (95%), hypoxemia (95%), anemia (84%), and thrombocytopenia (95%). CT predominantly reveals pulmonary ground-glass opacities (82%) and nodular shadows (86%). The average duration from onset to death is 9.5 weeks. Advanced therapies, such as phosphodiesterase inhibitors, endothelin-receptor antagonists, prostacyclin analogs, inhaled nitric oxide, and antineoplastic agents, have been shown to prolong life by several months; however, several challenges remain [3]. Gastric adenocarcinoma (59%) is the most common primary site for PTTM; conversely, cholangiocarcinoma is extremely rare and has been limited to case reports [3,4]. Most small-cell carcinomas occur in the lungs, and primary small-cell carcinomas of the liver are extremely rare [5]. However, the association between PTTM and COVID-19 vaccines remains unclear.

Our patient was initially diagnosed with cardiogenic shock due to myocarditis and managed with VA-ECMO and the Impella® blood pump. However, blood flow from the right to left native cardiac system became more inhibited as the disease progressed, and the flow through the Impella® pump could not be maintained. These hemodynamic patterns mimicked those associated with pulmonary artery embolism, and PTTM was suspected. VA-ECMO is useful for hemodynamic patterns, such as those for pulmonary artery embolism; however, the cardiac function is preserved, and the brain and upper body are perfused with deoxygenated blood via the native circulation system in case of coexisting respiratory dysfunction [6]. In such cases, upgrading to central ECMO may be useful; herein, the oxygenated blood is sent to the ascending aorta, and the coronary artery or cerebral vessels remain oxygenated. Conversely, veno-venous ECMO, wherein oxygenated blood is sent to the pulmonary artery, may be ineffective in cases of PTTM with an LV collapse due to an inhibited blood flow from the right to the left cardiac system.

Conclusions

PTTM is extremely rare and can be difficult to diagnose because patients experience rapidly worsening oxygenation and hemodynamics. VA-ECMO or central ECMO may be useful for maintaining circulation and oxygenation; however, these are not radical treatments for PTTM. Our patient died 15 days after the onset of this disease. PTTM should always be considered in cases of acute pulmonary hypertension of an unknown etiology.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Soichiro Kageyama, Takeki Ohashi

Acquisition, analysis, or interpretation of data: Soichiro Kageyama, Akinori Kojima

Drafting of the manuscript: Soichiro Kageyama

Critical review of the manuscript for important intellectual content: Soichiro Kageyama, Takeki Ohashi, Akinori Kojima

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Nagoya Tokushukai General Hospital Medical Ethics Committee issued approval 2023-04-04. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

We would like to thank Editage® (<https://www.editage.jp>) for the English language review.

References

1. Roberts KE, Hamele-Bena D, Saqi A, Stein CA, Cole RP: Pulmonary tumor embolism: a review of the literature. *Am J Med.* 2003, 115:228-52. [10.1016/s0002-9343\(03\)00305-x](https://doi.org/10.1016/s0002-9343(03)00305-x)
2. Uruga H, Fujii T, Kurosaki A, et al.: Pulmonary tumor thrombotic microangiopathy: a clinical analysis of 30 autopsy cases. *Intern Med.* 2013, 52:1317-23. [10.2169/internalmedicine.52.9472](https://doi.org/10.2169/internalmedicine.52.9472)
3. Godbole RH, Saggarr R, Kamangar N: Pulmonary tumor thrombotic microangiopathy: a systematic review. *Pulm Circ.* 2019, 9:4-6. [10.1177/2045894019851000](https://doi.org/10.1177/2045894019851000)
4. Schwartz BP, Tracy P, Hon S, Farber HW, Udelson JE: Pulmonary tumor thrombotic microangiopathy as a cause of pulmonary hypertension. *JACC Case Rep.* 2021, 3:1029-31. [10.1016/j.jaccas.2021.04.013](https://doi.org/10.1016/j.jaccas.2021.04.013)
5. Jo JM, Cho YK, Hyun CL, et al.: Small cell carcinoma of the liver and biliary tract without jaundice. *World J Gastroenterol.* 2013, 19:8146-50. [10.3748/wjg.v19.i44.8146](https://doi.org/10.3748/wjg.v19.i44.8146)
6. Stevens MC, Callaghan FM, Forrest P, Bannon PG, Grieve SM: Flow mixing during peripheral veno-arterial extra corporeal membrane oxygenation - a simulation study. *J Biomech.* 2017, 55:64-70. [10.1016/j.jbiomech.2017.02.009](https://doi.org/10.1016/j.jbiomech.2017.02.009)