Letter to the Editor

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Pulmonary Embolism and Inferior Vena Cava Thrombosis in a Young Male Patient after mRNA-1273 (Moderna) Immunization: A Case Report

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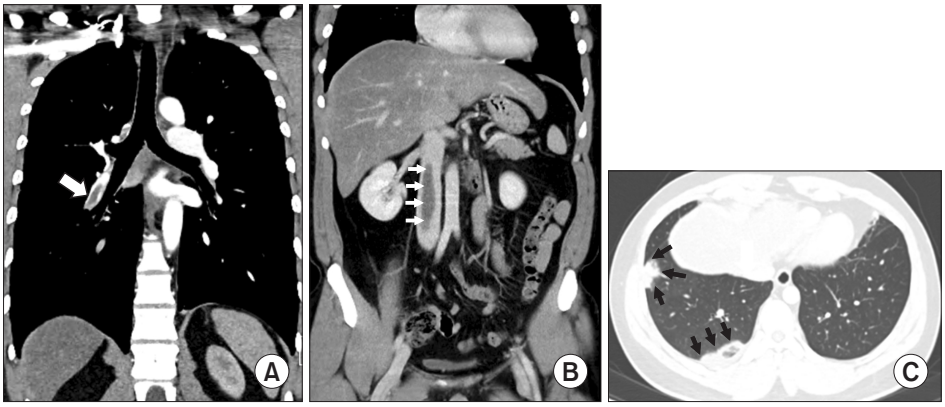
The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is currently in progress, with more than 330 million confirmed cases and 5.5 million deaths[1]. Since the U.S. Food and Drug Administration first approved the emergency use of the BNT162b2 (Pfizer-BioNTech) vaccine in December 2020, more than 60% of the world's population has received at least the first dose of COVID-19 vaccines[2]. Thrombosis with thrombocytopenia syndrome (TTS) is a rare adverse event reported after immunization with adenovirus vector-based vaccines[3]. Additionally, cases of venous thromboembolism (VTE) have been reported after BNT162b2 mRNA vaccination[4]. ere, we present a case of pulmonary embolism (PE) and inferior vena cava (IVC) thrombosis in a young male patient after the second dose of mRNA-1273 (Moderna, Cambridge, MA, USA) vaccination.

A 27-year-old man with no significant medical history presented to the outpatient department with chief complaints of cough, hemoptysis, and epigastric pain. These symptoms began 10 days after he received the second dose of mRNA-1273 vaccine. The patient had no history of recent trauma, surgery, or immobility. He denied any past or family history of VTE or coagulation disorder. The patient's initial vital signs were stable, with a temperature of 36.4°C, pulse rate of 94/min, blood pressure of 110/70 mm Hg, respiratory rate of 18/min, and oxygen saturation of 97% on room air. Laboratory studies showed high levels of inflammatory markers with white blood cell count, C-reactive protein level, and fibrinogen level of $11.46\times10^3/\mu L$, 22.8 mg/dL, 640 mg/dL, respectively. The platelet count was normal range with $354\times10^3/\mu L$ and D-dimer level was slightly elevated to 1.5 μg/mL, and computed tomography (CT) angiography showed pulmonary emboli involving the right lower lobe pulmonary arteries and pulmonary infarcts in the right lower lobe. Moreover, a huge free-floating thrombosis was observed in the IVC and right common iliac vein (Figure 1).

Following the diagnosis of PE with deep vein thrombosis (DVT), treatment with intravenous unfractionated heparin was initiated. In addition, etiologic workup including coagulation and thrombophilia tests was performed, and the results were presented in Supplementary Table S1. The results of etiologic tests including the anti-heparin platelet factor 4 (PF4) IgG test were all negative. After 1 week of heparin treatment, follow-up CT showed no improvement in the thrombosis. The patient underwent IVC filter insertion and aspiration thrombectomy (Supplementary Figure S1), heparin was changed to apixaban for anticoagulation, and the patient was dis-

Figure 1. Pulmonary embolism with deep vein thrombosis after mRNA-1273 vaccination. Computed tomography (CT) angiography showed contrast filling defects (arrow) in the right lower lobe pulmonary arteries (A), a massive free-floating thrombosis (arrows) in inferior vena cava (B). Axial chest CT scan shows pulmonary infarcts (black arrows) in right lower lobe (C).



charged in a stable state and followed up.

COVID-19 associated coagulopathy may be an immunothrombosis phenomenon in which the release of proinflammatory cytokines caused by SARS-CoV-2 infection induces the production, activation, and aggregation of platelets[5]. In March 2021, a new clinical syndrome, TTS, was reported among patients who received recombinant adenoviral vector vaccines, including ChAdOx1, nCoV-19, and AD26.COV2.S. Similar to heparin-induced thrombocytopenia, adenoviral vaccines appear to stimulate the development of autoantibodies against PF4 which activate platelets and cause thrombosis in the absence of heparin exposure[6].

Although thromboembolic events rarely occur after mRNA vaccination, cases of cerebral venous thrombosis have been reported recently after BNT162b2 vaccination[7]. In addition, several cases of PE and/or DVT after mRNA-1273 vaccination have been reported. Andraska et al. reported three cases of PE or DVT after mRNA-1273 vaccination, but all these patients had risk factors for thrombosis, such as taking oral contraceptives, history of breast cancer, and old age[8]. Wiest et al.[9] reported a case of PE with DVT after mRNA-1273 immunization, and this patient also had a history of renal cell carcinoma. The clinical characteristics of previously reported cases of thrombosis after mRNA-1273 vaccination are presented in Supplementary Table S2.

In this report, we present a case of VTE that developed after mRNA-1273 immunization in a 27-year-old male patient with no risk factors and no history of VTE or SARS-CoV-2 infection. The incidence of PE or DVT in young men is extremely rare. The annual incidence of PE with or without DVT is only 7/100,000 person-years in men aged 25–29 years[10]. Although it is possible that PE occurred accidentally in patient of this case, acute onset of abdominal pain and hemoptysis after mRNA vaccination may suggest the vaccine-related thrombosis. Theoretically, mRNA-1273 vaccine developed a lipid-nanoparticle encapsulated mRNA encoding spike protein of SARS-CoV-2, a phenomenon such as COVID-19 associated thrombosis may also occur after mRNA-1273 vaccination. However, the mechanism of thrombosis after SARS-CoV-2 mRNA vaccination has not been elucidated.

To the best of our knowledge, this is the first reported case of PE with DVT following mRNA-1273 vaccination in a young male patient with no risk factors. By confirming negative result of anti-PF[4] antibody, it is the first report suggesting that thrombosis after mRNA vaccination is caused by different mechanism from TTS. Moreover, vaccination to terminate the COVID-19 pandemic needs to be continued, it is important to monitor and report these patients to better understand vaccine-associated side effects. In addition, further research is needed to elucidate the mechanism of mRNA vaccine-related thrombosis.

Authors' Contributions

Conceptualization: Kim T. Methodology: Kim T. Formal analysis: Ahn EY, Choi H, Sim YS, Shin TR. Data curation: Ahn EY, Choi H, Sim YS, Shin TR. Software: Ahn EY. Validation: Kim T. Investigation: Ahn EY. Writing - original draft preparation: Ahn EY. Writing - review and editing: Kim T. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Material

Supplementary material can be found in the journal homepage (http://www.e-trd.org).

Supplementary Table S1. Patient's results of coagulation and thrombophilia studies.

Supplementary Table S2. Clinical characteristics of previously reported cases of thrombosis after mRNA-1273 vaccination.

Supplementary Figure S1. Inferior vena cava (IVC) filter insertion and aspiration thrombectomy. Before aspiration thrombectomy, IVC filter (arrow) was implanted at the supra renal level via right jugular vein and right femoral vein approach (A). Venography shows an extensive thrombus (arrows) in the IVC (B). Thrombus aspirated in IVC is shown (C).

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