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Case Report

COVID-19 Moderna Vaccine and Bilateral Pulmonary Embolism: Case Report

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Abstract

The pandemic of Coronavirus Disease 2019 (COVID-19) has created many problems in the entire world whether the disease itself, whether fighting back with limited treatment options and prevention tools. Owing to the escalating daily death rates from COVID-19, the development of a vaccine against this new disease was quite fast that the first authorized vaccine got approval less than a year after the onset of the pandemic. Data report different side effects of new COVID-19 vaccines including venous and arterial thrombotic events, vaccine-induced prothrombotic immune thrombocytopenia, vaccine-induced thrombosis with thrombocytopenia, and immune thrombocytopenia. Our case report highlights bilateral pulmonary embolism, six days after the first dose of the COVID-19 mRNA vaccine (Moderna) in a healthy gentleman.

Keywords: COVID-19 vaccine; Moderna; mRNA vaccine; Pulmonary embolism; Vaccine side effect; Venous thrombotic event

Case Presentation

A 71-year-old African American gentleman presented initially with a fall and having a generalized weakness six days after taking the first dose of the COVID-19 Moderna vaccine. The patient was on the phone when he fell and hit his head. In the emergency department, the initial complaint of the patient was headache and generalized weakness. The patient stated from 24 hours after taking the first shot of the COVID-19 vaccine he was not feeling good and was dealing with a generalized weakness for the last couple of days. The patient denied loss of consciousness, lightheadedness, dizziness, chest pain, shortness of breath, palpitation, and diaphoresis before or at the time of falling. No recent surgery, trauma, immobilization, straight long-distance trip, and history of cancer was mentioned by the patient. Mast medical history was notable for hyperlipidemia. The patient was not on any medications at home either prescribed or over-the-counter drugs. Social history was unremarkable for tobacco, illicit drug, and alcohol use. Family history was negative for cancers and hypercoagulable states.

On physical exam, the patient was completely alert and oriented (Glasgow Coma Scale 15) with no focal deficits on the neurologic exam, but generally was weak; the heart exam was remarkable for a grade 2/6 systolic flow murmur at the left sternal border; other examination findings were normal.

Initial workup including labs was significant for the mild increase of serial cardiac troponin-T enzyme, slight elevation of D.dimer, and abnormal lipid panel. Complete Blood count (CBC) with the focus on platelet number was within the normal range during admission. Hypercoagulable state profile showed normal findings.

Head CT scan without contrast as a standard post-fall workup revealed small foci (7 x 9 mm) of intraparenchymal hemorrhage within the right frontal subcortical white matter in head Computed Tomography (CT) scan without contrast (Figure 1A). Electrocardiogram was normal except for occasional premature atrial and junctional complexes, no ischemic changes were detected. 2D-Echocardiogram revealed normal left ventricle ejection fraction (LVEF: 55-60%), moderate Right Ventricle (RV) enlargement, moderate Tricuspid Regurgitation (TR) with elevated right ventricle systolic pressure (RVSP: 45mmHg). Lower extremity venous duplex ultrasound documented no Deep Vein Thrombosis (DVT) in lower extremities.

Given the clinical presentation, mild elevation in D.dimer level, and findings in 2D-Echocardiogram, the patient underwent a chest CT angiogram with Pulmonary Embolism (PE) protocol and was diagnosed with bilateral PE most proximally in lobar branches, along with right-sided cardiomegaly, and flattening of the interventricular septum highly suspicious for right heart strain (Figure 2).

Although the patient was diagnosed with bilateral PE due to Concurrent Intracranial Hemorrhage (ICH), the patient was not cleared for thrombolytic or anticoagulation therapy. The patient was

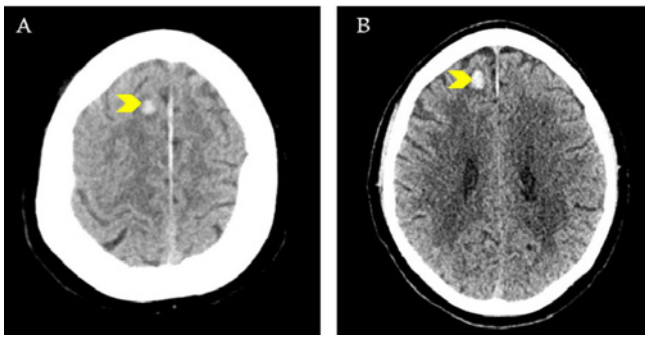

Figure 1: Head CT scan without contrast. A, Initial scan shows small foci (7 x 9 mm) of intraparenchymal hemorrhage within the right frontal subcortical white matter. B, Follow-up scan one day after the first scan shows a slight increase in the size of the right frontal intraparenchymal hemorrhage (9 x 11 mm) [Yellow arrows].

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Table 1: Authorized COVID-19 vaccines' characteristics [8-10].

Characteristics of Vaccines	COVID-19 Vaccines Brand name			
	Comirnaty (BioNTech/ Pfizer)	*Moderna*	*AstraZeneca (Vaxzevria)*	*Johnson & Johnson's (Janssen)*
Validation date	21-Dec-20	6-Jan-21	29-Jan-21	11-Mar-21
Recommended age	≥16yrs	≥18yrs	≥18yrs	≥18yrs
Vaccine substance	mRNA based encoding SARS-CoV-2 spike protein (BNT162b2)	mRNA based encoding SARS-CoV-2 spike protein (nucleoside modified)	Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein (ChAdOx1-S [recombinant])	Adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein (Ad26.COV2-S [recombinant])
Dose(s)	2 separate doses Given 3 weeks apart	2 separate doses Given 28 days apart	2 separate doses Given 4-12 weeks apart	Single-dose
Elderly recommendation	No dose adjustment in age ≥65yrs			

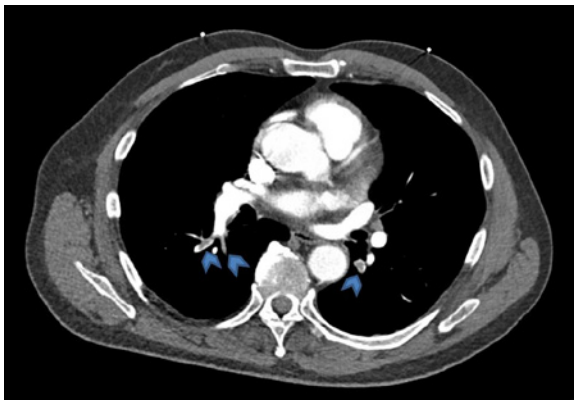

Figure 2: Chest CT angiogram demonstrates bilateral pulmonary emboli in lobar branches [Blue arrows].

under close monitoring for the size of ICH by frequent neuro checks and serial head CT scans without contrast.

The follow-up head CT scan 24 hours apart showed the increased size of the right frontal ICH (9 x 11 mm); the patient's clinical status was stable with no change in mental state and neurologic exam (Figure 1B). Prophylactic Inferior Vena Cava (IVC) filter was considered for the prevention of further PE from pelvic veins as a possible source of the clot(s). However, based on the literature, using prophylactic IVC filters remain controversial or not recommended to be used in any patient group [1,2], but ideally, we suggest weighing the risk-benefit ratio for prophylactic IVC filter is individual-based and is different for every patient.

After establishing the ICH size in repeated follow-up head CT scans, treatment with anticoagulation started, and the patient was put on low-molecular-weight heparin (LMWH) with therapeutic dose [1mg/kg Subcutaneous every 12 hours] along with close monitoring for new bleeding signs and symptoms. After one week of monitoring, when the patient was stable either clinically or paraclinical wise, he was discharged home on Enoxaparin therapeutic dose with an outpatient follow-up recommendation and supplementary workup.

Discussion

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a novel Coronavirus that has caused Coronavirus Disease 2019 (COVID-19) pandemic across the world in the years 2019 - 2020 with over 100 countries reporting high infection rates [3].

SARS-CoV-2 is a spherical, enveloped, single-strand, positive-sense RNA virus, encoding different types of proteins including 16 non-structural proteins (NSP's 1-16), 8 accessory proteins (ORF 3a,6,7a,7b,8,9b,9c and 10), and 4 structural proteins known as S (Spike), E (Envelop), M (Membrane), and N (Nucleocapsid) proteins. The virus is attaching to the host cell membrane Angiotensin Converting Enzyme 2 (ACE2) receptors by spike glycoprotein [3,4].

The SARS-CoV-2 virus is one of the fatal human coronaviruses that has caused more than 1 million death in the first 6 months of the pandemic [5,6]. Given the increasing daily mortality rate from COVID-19 disease, the process of producing vaccine against SARS-CoV-2 was so rapid that the first authorized vaccine entered into the market on December 21, 2020, less than a year from the onset of the pandemic, and more than 600 million doses of COVID-19 vaccines have been administered globally in a short period after vaccines' production [7,8].

Between December 2020 to March 2021, the European Medical Agency approved four vaccines for the prevention of symptomatic COVID-19 disease, including Comirnaty (BioNTech/Pfizer), Moderna, AstraZeneca (Vaxzevria), and Johnson & Johnson's (Janssen). Table 1 summarizes the characteristics of these 4 types of authorized COVID-19 vaccines [7,9,10].

Based on Hodgson et al. study, various factors should be considered in vaccine efficacy definition; the most important one is the ability of the vaccine to protect against severe disease and mortality [11]. However, besides vaccine efficacy, vaccine safety is another important factor that needs to be considered in the vaccine production process. Data reveal that the greatest concern to both physicians and the general population are fears of the vaccines' safety, and one of the important causes for vaccine hesitancy is an aversion to the potential side effects of the new vaccines [12,13]. Currently, some studies reported different side effects of the newly licensed vaccines against SARS-CoV-2, such as Venous Thrombotic Events (VTE), Arterial Thrombotic Events (ATE), Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT)/Vaccine-Induced Thrombosis with Thrombocytopenia (VITT), and Immune Thrombocytopenia (ITP) [14-18].

Vaccine-induced VTE and ATE could present in different forms including Cerebral Venous Thrombosis (CVT), Cerebral Sinus Vein Thrombosis (CSVT), Pulmonary Embolism (PE), lower limb DVT, splenic venous thrombosis, stroke, acute myocardial infarction, and limb/ intestinal/ retinal arteries thrombotic events [14,15].

The exact pathophysiological mechanism(s) of the reported side effects of new vaccines against SARS-CoV-2 are still unclear. However, one of the known mechanisms for severe VTE is a high level of antibodies to the PF4-polyanion complex [8].

Scully et al. reported that detection of anti-PF4 antibodies, unrelated to the use of heparin, could present with acute atypical thrombosis, primarily involving the cerebral veins and concurrent thrombocytopenia [19]; also Scully's study interestingly highlights that "The risk of thrombocytopenia and the risk of venous thromboembolism after vaccination against SARS-CoV-2 do not appear to be higher than the background risks in the general population" and the symptoms developed more than 5 days after the first vaccine dose, could be an immunologic pattern similar to heparin-induced thrombocytopenia [19].

Also, seems the type of vaccine could influence the incidence of adverse events and the timeframe of the side effect presentation so that in mRNA vaccines (Moderna and Pfizer) the risk of ATE is more than VTE; but about AstraZeneca, VTE reported more than ATE [14].

To our knowledge, although recent data have documented the variety of adverse events of COVID-19 vaccines, current evidence is insufficient to draw definitive and precise conclusions about the effectiveness and safety of these newly licensed vaccines; further analysis including extensive clinical and biological studies are needed in the future to address outcomes of COVID-19 prevention by vaccines.

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