Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

CASE REPORT

BILATERAL PULMONARY THROMBOEMBOLISM AFTER MODERNA VACCINATION IN A HEALTHY CANDIDATE

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Abstract

Vaccination against severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), the causative agent of corona virus Disease 2019 (COVID-19) is a critical strategy to overcome the COVID-19 pandemic. Multiple SARS-CoV-2 vaccines have been developed in a rapid timeframe to combat the pandemic. As with any other medication, there have been adverse effects associated with the use of vaccines ranging from mild symptoms to life threatening side effects that have led to mortality. One of the more serious adverse effects associated with a number of vaccines such as those produced by AstraZeneca/Oxford and Pfizer BioN-tech is a phenomenon known as vaccine-induced immune thrombotic thrombocytopenia leading to thrombosis and embolism. Our case report highlights bilateral pulmonary embolism, one week after the second dose of the COVID-19 mRNA vaccine (Moderna) in a healthy newly married young women.

Keywords: *Pulmonary Thromboembolism, COVID-19, Moderna vaccination*

Received: 28-02-2022 *Accepted: 06-04-2022*
DOI: https://doi.org/10.3329/bjm.v33i2.59296

Citation: *Mamun SMAA, S Sharkar S, Shaheed S. Bilateral Pulmonary Thromboembolism After Moderna Vaccination in a Healthy Candidate. Bangladesh J Medicine 2022; 33: 213-219.*

Introduction:

The COVID-19 pandemic has claimed nearly six million lives and disrupted societies and economies globally.[1] Vaccines against SARS-CoV-2 were developed in record time and across a variety of vaccine platforms, including adenovirus vectors, protein subunit, and newer mRNA-based platforms.[2] Recently, reports of rare venous thromboembolism (VTE) and thrombocytopenia events were described for two adenovirus-based vaccines, the AstraZeneca ChAdOx1 nCoV-19 vaccine and the Janssen Ad.26.COV2.S vaccine leading to further regulatory and safety review.[3]

While these events are fortunately rare, VTE is a potentially life-threatening adverse event whose prompt recognition is critical. COVID-19 can lead to severe and sometimes life-threatening thrombosis by creating a hypercoagulative state in the body.[4] In a systematic review by Kaur et. al., trial results of eleven vaccines were reviewed with the aim of

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determining the frequency and severity of adverse effects. Of the vaccines reviewed, three vaccines including five cases receiving Comirnaty (BNT162b1), three receiving AstraZeneca (AZD1222), and one individual receiving Covaxin (BBV152) had shown serious adverse reaction.[5] One of the rare but serious side effects of COVID-19 vaccines is a phenomenon known as vaccine-induced immune thrombotic thrombocytopenia (VITT) which can lead to thrombosis and embolism in different regions of the body. This condition has been reported in regard with a number of vaccines currently in use such as AstraZeneca/Oxford vaccine as well the J&J vaccine.[6]

Here, we describe a case of acute PE that occurred 15 days after the second dose of the Moderna mRNA-1273 SARS-CoV-2 vaccine.

Case Report:

A 21 year-old married women, with no significant prior medical history was admitted through emergency department of Evercare hospitals Dhaka, with complain of passage of blood with sputum for 3 days & left sided chest pain for same duration. She is married for one year, with regular period. Symptoms had first appeared 03 days before the admission The patient had received her second dose of Moderna COVID-19 vaccine, 7 days before the onset of her symptoms.

There was no history of recent immobility or surgery, and she was exercising daily before presenting. She denied of taking any oral contraceptive pills, any personal or family history of VTE, PE, or known hypercoagulable state. In the emergency department, the patient's vital signs were normal with a temperature of 36.8 degrees Celsius, pulse rate of 76, blood pressure of 125/80mmHg, respiratory rate of 20, and oxygen saturation of 94% on room air. Inspiratory crackles were heard at the left lung base; Physical examination was otherwise unremarkable including no jugular venous distension and no extremity edema. Laboratory analysis is described in Table I. Briefly; the patient had a normal chemistry panel and a normal complete blood count with negative RT-PCR for covid-19.However, he had elevated C-reactive protein and D-dimer levels.

Table I
Laboratory Studies

Test	Value	Reference
Hemoglobin	9.4 gm/dl	11.5-16.5
WBC Count	5.99 10^9/L	4-11
Platelet	150 10^9/L	15-400
CRP	46.51 mg/L	<0.33
Procalcitonin	0.11ng/ml	<.05
D-Dimer	6648 ugm/L	<500
Creatinine	.78mg/dl	.5-1.2
Uric acid	4.2mg/dl	2.5-6
Albumin	2.8g/dl	3.5-5
Na	140m mol/L	135-145
K+	3.5m mol/l	3.5-5
HCO3	20 mol/l	24-32
Adjusted Ca	8.9 mg/dl	8.5-10.5
SGPT	47 U/L	
Alkaline PO4	214 U/L	
Ferritin	84 ng/ml	15-150
Iron	46 ug/dl	50-170
TIBC	329 ug/dl	250-400
RT-PCR for Covid-19	Negative	Negative

Table-II
Coagulation Studies

Test	Value	Reference
PT	15.1 Seconds	9.8-12.1
INR	1.29	.9-1.1
APTT	36 Seconds	35-37
Antiphospholipid IgM	7.37 U/ml	0-10
ANA	<0.50	>1.5 Positive
C-ANCA(ANTI-PR3)	3.68 U/ml	<5
P-ANCA(ANTI-MPO)	3.72 U/ml	<5
Protein C activity	102%	70-150%
Protein S activity	137%	65-160%
Homocysteine	12.4 nmol/L	7.1-15.8

As a first step, broad spectrum antibiotics with supplemental O_2 was provided for the patient via nasal cannula and an ECG was obtained which proved unremarkable. Her Chest X-ray shows left sided inhomogeneous opacity which is peripherally located (Fig.-1). So considering Covid in this pandemic time a HRCT CHEST was done which reveals consolidation in lingular segment of left lung and left lower lobe. Due to suspicion of filling defect in pulmonary artery,the radiologist was contacted for CTPA in same sitting immediately.

Surprisingly her CTPA revealed thrombus in the left lower lobe pulmonary artery causing about 75-80 % luminal narrowing (Fig 2) and thrombus in right lower lobe pulmonary artery causing about 50 % luminal narrowing (Fig 3 & 4) with consolidation in left lung with reversed Halo sign.

An echocardiography was also performed which showed normal findings. In search of DVT lower limb doppler studies have done which reveals no abnormality.

Following the diagnosis of PE, a 1 mg/kg subcutaneous injection of enoxaparin was immediately administered, and labs were drawn approximately three hours later. A coagulation evaluation and thrombophilia workup were initiated. The patient's prothrombin time (PT) and international normalized ratio (INR)were within normal limit. She demonstrated normal protein C and protein S activity. Antinuclear antibodies were negative and serum homocysteine levels were normal and her antiphospholipid IgM antibodies were also negative.

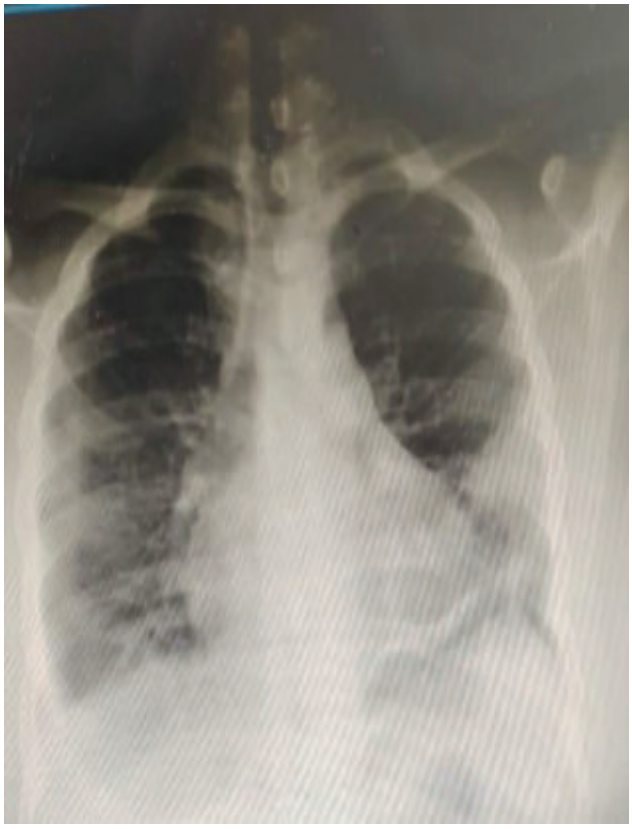

Fig.-1: *Chest X-ray*

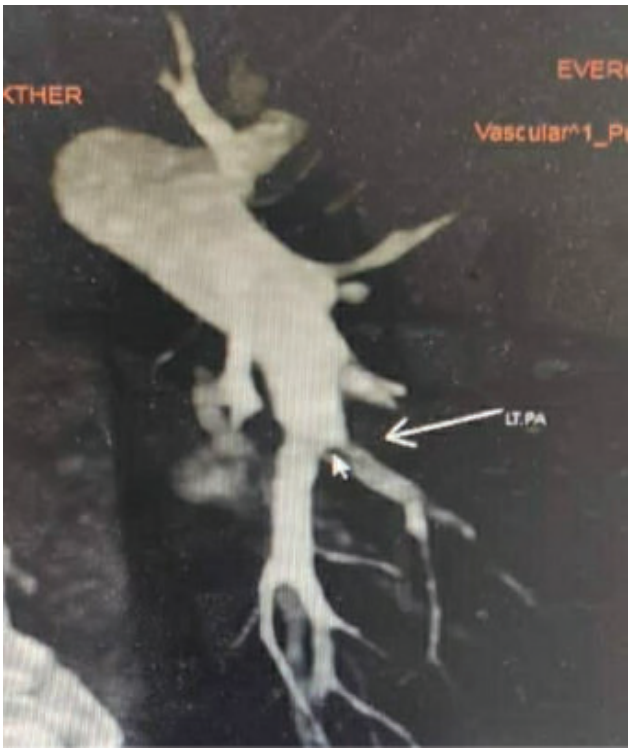

Fig.-2: *Filling Defect in LPA in CTP A(Arrow)*

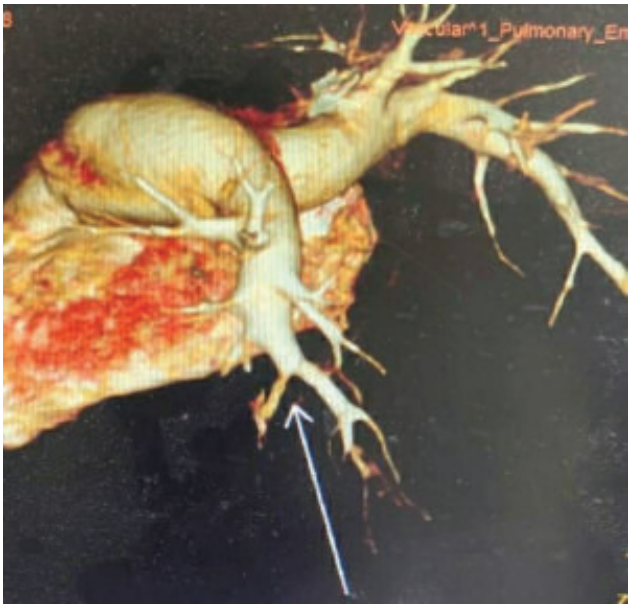

Fig.-3: *Thrombus in RPA (Arrow)*

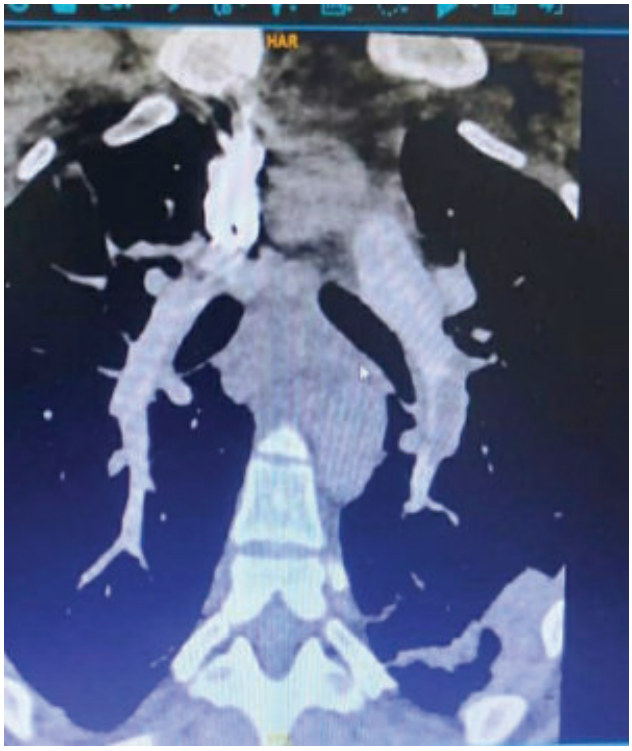

Fig.-4: *Bilateral Thrombus in CTPA*

Vital signs were also closely observed for the duration of the admission. The patient remained stable and was eventually discharged from the hospital 03 days after the admission. A prescription of 10mg Rivaroxaban twice daily for one week was provided to the patient. The medicine was maintained at 10mg once daily after that and prescribed for the next three months.

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.[7] The SARS-CoV-2 virus is one of the fatal human corona viruses that has caused more than 1 million death in the first 6 months of the pandemic[8]. 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.[8]

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) [10]. 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.[11]

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.[12] 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 [13];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.[13]

There is significant interest in the topic of VTE after COVID-19 immunization based on reports of a rare syndrome of VTE and thrombocytopenia in patients who received the adenovirus-platform AstraZeneca ChAdOx1 and Janssen Ad.26.COV2.S vaccines [13].Scully et al. described 23 patients who received the AstraZeneca ChAdOx1 nCoV-19 vaccine in the United Kingdom and developed thrombosis and thrombocytopenia. Furthermore,22 of 23 patients with this syndrome, which the authors entitled vaccine-induced immune thrombocytopenia (VITT), were found to have circulating platelet factor 4 (PF4) antibodies[13]. All of the patients in these two reports who were tested for PF4 antibodies had positive ELISA results. Similarly, a cohort of patients who developed VTE after the JanssenAd.26.COV2.S vaccine in the United States had a syndrome of cerebral venous thrombosis (CVT) and thrombocytopenia in 12/15 cases, though PF4 antibody levels were not reported.[13]

Thrombophilia, antinuclear antibody, and antiphospholipid antibodies were negative in the UK VITT patients though 5/10 patients tested for LA hada positive result that was considered potentially unreliable.[13] Amongst the case series of the VITT/TTS patients, notable similarities include that most of the patients were young(<50 years old), female (61–100%), and many developed either disseminated intravascular coagulation or multiple sites of thrombosis including portal vein and CVT leading to serious illness with mortality in 20–60% of cases.[13,14,15]

We did not test for PF4 antibodies in our patient as we had no clinical suspicion for HIT and VITT/TTS after COVID-19 immunization was not yet described. Unfortunately, stored serum remained from our patient's hospital encounter for us to send for PF4 antibody testing after VITT/TTS was described.

Our patient's D-dimer level was 3840 ng/mL fibrinogen equivalent units (FEU), whereas the median D-dimer level in the VITT patients was 31,301 FEU, or approximately ten times that of our patient.[13,14] This, combined with the fact that our patient had a normal platelet count, significantly reduces the likelihood that VITT/TTS was the mechanism of thrombosis in our patient, though we cannot rule out a mechanism similar to that of the Al-Maqbali et al. report with normal platelets and a positive HIT ELISA.[17] We look forward to the publication of more reports of VTE after SARS-CoV-2 immunizations so that a better assessment of potential mechanisms and comparison of patient characteristics and laboratory data can be performed.

Conclusion:

Determination and close surveillance of possible adverse reactions regarding the use of COVID-19 vaccines is an important and crucial step in humanities fight against the disease.

Although the Moderna vaccine has shown to theoretically decrease the risk of clotting by decreasing risk ofCOVID-19 infection, as more of the world becomes vaccinated, the incidence of side effects could increase, despite preliminary data.In summary, we encourage clinicians to remain vigilant for adverse events after SARSCoV-2 immunization and to report these events to the Vaccine Adverse Event Reporting System (VAERS) in the United States or the equivalent system in other countries.[18]

Conflict of Interest:

The authors stated that there is no conflict of interest in this study.

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