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CASE REPORT



Isolated pulmonary embolism following COVID vaccination: 2 case reports and a review of post-acute pulmonary embolism complications and follow-up

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ABSTRACT

Acute pulmonary embolism (PE) is a frequent cause of hypoxemic respiratory failure and presentation to the emergency department. The incidence is on the increase since the COVID-19 outbreak. While COVID infection represents a prothrombotic state, the introduction of COVID vaccines to a lesser extent increased the risk of unprovoked venous thrombus formation and risk of pulmonary embolism. PE is mostly associated with deep vein thrombosis (DVT) and only a few cases of isolated or De novo PE exist in literature. We report two cases of isolated PE associated with COVID-19 vaccinations. We aimed to highlight the need to suspect isolated PE in patients presenting with hypoxemic respiratory failure days to several weeks following COVID-19 vaccination and emphasize the importance of post-discharge follow-up for evaluating chronic thromboembolic pulmonary hypertension (CTEPH).

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Isolated pulmonary embolism; deep vein thrombosis; COVID-19 vaccine; chronic thromboembolic pulmonary hypertension

1. Introduction

Pulmonary embolism is frequently associated with deep vein thrombosis (DVT) and less so in isolation [1,2]. COVID-19 infection is associated with an increased risk of venous and arterial thrombosis [3,4]. The incidence of pulmonary embolism is on the rise since the outbreak of the COVID-19 pandemic.

COVID infection is a hypercoagulable disease and is associated with an increased risk of thromboembolism. Infection may lead to endothelial dysfunction, hypoxia-related increased blood viscosity, and dysregulation of hypoxia-inducible transcription factor-dependent signaling pathway important in thrombus formation [5].

Vigorous efforts by scientists and biopharmaceutical companies to find a cure and reduce the spread of the virus led to the rapid development of several vaccines like the mRNA BNT-162B2 (Pfizer), mRNA-Moderna, and Ad26.COV2.S (Johnson & Johnson) vaccines, which were granted emergency use authorization (EUA) by the food and drug administration (FDA) in the USA, and the AstraZeneca ChAd0x1 nCoV-19 coronavirus vaccine authorized for use by the medicines and healthcare products and regulatory agency (MHRA) in the UK.

Since the rollout of the COVID vaccine, there have been reports of unprovoked venous thromboembolism such as cerebral venous sinus, portal, and lower

extremity vein thrombosis, and only a few cases of isolated pulmonary embolism exist in the literature [6–11].

Currently, more than 5 billion people are vaccinated worldwide [12].

With the increasing number of suspected COVID vaccine-associated thrombosis, we report two cases of unprovoked PE post-COVID-19 vaccination and highlight the importance of post PE follow-up for early detection and management of chronic thromboembolic pulmonary hypertension.

2. Case 1

A 61-year-old man with a past medical history of hypertension, type 2 diabetes mellitus, and hypercholesterolemia attended the emergency department following a syncopal episode. Five days prior, the patient endorsed worsening exertional shortness of breath, lethargy, and a day history of bilateral calf pain. Of note, these symptoms began 8 days post 2nd dose of the ChAd0x1 nCoV-19 vaccine. He is active and independent with no family history of thromboembolic disorders, is a non-smoker, and consumes less than 14 units of alcohol/week. Physical examination noted an alert and responsive patient with hypoxia and oxygen saturation of 89% on room air. His respiratory rate was 19 breaths per minute,

afebrile, tachycardia with a heart rate of 114 beats per minute, and blood pressure of 165/95 mmHg. Further examination noted clear lung fields and an absence of lower extremity swelling or tenderness. Other systemic examination findings were unremarkable. Oxygen saturation maintained >94% with 6 L of supplemental oxygen using a nasal cannula.

Pertinent laboratory investigations were raised D-dimer of 2,156 (0–230 ng/ml), Troponin I 8.6 (2–11 ng/L), and elevated CRP and LDH. COVID PCR was negative. His platelet count was normal – 216 ($150\text{--}450 \times 10^9/\text{L}$).

Electrocardiogram (ECG) was significant for sinus tachycardia and mild lateral ST depression (Figure S1).

CT angiogram chest showed multiple filling defects in the segmental and subsegmental branches of both lobes in keeping with extensive pulmonary embolism (Figure S2).

Echocardiogram was significant for right heart strain, raised pulmonary pressure PASP40–45 mmHg, and mild tricuspid regurgitation.

Doppler studies of the lower extremities were negative for DVT.

He received a treatment dose of low molecular weight heparin. He was discharged on Apixaban. A 3 months echocardiogram was arranged. The patient was advised to follow up with the venous thromboembolism and cardiology clinics. An MHRA yellow card was completed.

3. Case 2

A 51-year-old man with a past medical history of hypertension presented to the emergency department with acute onset shortness of breath and cough of less than 24 hours duration. He had contacted the emergency medical services, and paramedics noted oxygen saturation of 75% on room air at rest. The patient denied any fever, chest pain, extremity swelling, or extremity pain. He had his 1st dose of the ChAd0x1 nCoV-19 vaccine 4 weeks before the presentation. He was a lifetime non-smoker, lived an active life. There was no family history of blood clots.

Physical examination noted a middle-aged man who was tachypneic at rest with a respiratory rate of 24 breaths per minute, tachycardia to 102 beats per minute, blood pressure of 138/95 mmHg, and was afebrile, temperature 36.3 degree Celsius. Chest findings were positive for bilateral crackle. Heart sounds were normal and there was no raised jugular venous pressure. The rest of the physical examination was unremarkable.

Investigations showed type 1 respiratory failure on arterial blood gas, chest X-ray features in keeping with bilateral pneumonia, raised inflammatory markers CRP 106 (0–6 mg/L), platelet count 294 (150--

$450 \times 10^9/\text{L}$), neutrophils 8.1 ($1.75\text{--}7.5 \times 10^9/\text{L}$), D-dimer-5,538 (0–230 ng/ml). Chest X-ray findings of a bilateral lung infiltrate include consolidation and ground-glass opacities (Figure S3).

CT angiogram chest showing multiple filling defects in the distal right and left main pulmonary arteries consistent with bilateral pulmonary embolism, with consolidations of the right lobe of the lungs (Figure S4).

ECG noted sinus tachycardia with no acute ST-segment changes (Figure S5).

An echocardiogram showed no evidence of right heart strain or regional wall motion abnormalities, normal ejection fraction, mild LV diastolic dysfunction, and no valvular dysfunction.

Bilateral lower extremity dopplers showed no evidence of DVT (Figure S6).

He was treated with low molecular weight heparin and intravenous antibiotics to cover for bacteria pneumonia. He made clinical improvement, was weaned off oxygen, and switched to Apixaban at discharge with a scheduled echocardiogram in 3 months, cardiology and venous thromboembolism clinic follow-up.

4. Discussion

PE may occur in isolation in COVID patients without a co-existing deep vein thrombosis. Studies have shown no clear association between the two in patients with COVID infection [13]. COVID-19 vaccine-associated thrombosis is increasingly being reported in the literature.

The timing of vaccination with the development of thrombosis is nonspecific. Thrombosis can occur as early as the first 7–10 days [8]. Our cases represent late presentation occurring 4 weeks following the initial dose and within 8 days of the 2nd dose of vaccination.

As more cases of PE occur, we aim to highlight an important life-threatening and often misdiagnosed long-term complication of acute PE, which is chronic thromboembolic pulmonary hypertension (CTEPH), and the importance of planned follow-up and early echocardiogram for evaluation and management.

CTEPH is defined in the setting of mismatched perfusion defect on ventilation-perfusion lung scan (V/Q lung scan), as pulmonary artery pressure ≥ 25 mmHg, pulmonary artery wedge pressure ≤ 15 mmHg, in a patient who has been on at least 3 months of anticoagulation [14,15].

Unprovoked PE, young or old age at the time of PE, and echocardiographic findings of right ventricular dysfunction or pulmonary hypertension at the time of acute PE are some of the many risk factors associated with increased risk of CTEPH [3,15].

Post-acute PE follow-up should not simply concentrate on the review of anticoagulation duration or thrombophilia workup, but active evaluation for CTEPH with the use of echocardiogram and V-Q lung scan at least within 3 months of an acute PE[16].

High-risk patients or those with CTEPH must be referred to specialized centers for evaluation and management.

Although sporadic cases of COVID-19 vaccine-associated thrombosis exist, the authors believe that the benefit of vaccination far outweighs the risk of adverse effects in the general population.

5. Conclusion

COVID-19 infection and very occasionally COVID-19 vaccines are potential risk factors for the development of isolated PE. Clinicians should have a high index of suspicion in patients with acute hypoxemic respiratory failure even in the absence of an obvious DVT. Moreover, a well-planned post-discharge follow-up following an acute PE must be in place for the evaluation and early detection of CTEPH, a potentially life-threatening complication of PE. Despite the possible association of this adverse effect, CDC strongly recommends the COVID vaccine as it protects life to a greater extent.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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