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A CASE OF PULMONARY THROMOEMBOLISM OCCURRED IMMEDIATELY AFTER THE FIRST DOSE OF CHADOX1 NCOV- 19 VACCINATION.

Medicine

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ABSTRACT

In the recent studies, COVID-19 vaccines, especially Covishield has been associated with the reports of Vaccine-Induced pulmonary thromboembolism. pulmonary thromboembolism is a complication that can occur after the first dose of the vaccine causing the thrombosis in veins at specific sites like lungs, Brain and Deep Veins and Arteries. It presents commonly as the Pulmonary Embolism (PE), within 7-10 days of vaccination. Patients taking vaccinations under the age of 45 presents at the high risk. Mortality rate in such post vaccination thrombosis is considered to be 50% in some cases. Thus, it is far more important to understand and identify the early signs and symptoms for early diagnosis, proper treatment and interventions. In the following case presented. A 29-year-old male patient was presented with the complaints of High Fever, Cough and Extreme Breathlessness after receiving the first dose of ChADOx1 nCoV-19 Vaccination against the Corona Virus Disease 2019 (COVID-19). He had history of Exertional Dyspnoea for 2-3 weeks. He was diagnosed to have Pulmonary Embolism with severe PAH. 2D ECHO was done which showed Severe Pulmonary Hypertension Likely Pulmonary Thromboembolism, Good biventricular systolic function, Mild TR. CT Chest with Pulmonary Angiography was done which showed Eccentric filling defect seen in bilateral arteries at hila with extension in lower lobe segment branches- likely thrombus. CT Scan of Thorax (Plain & Contrast) was also done which showed bilateral small patchy ground glass haze with superimposed Reticular thickening mainly in Subpleural region. He was immediately thrombolysed with Intrapulmonary TNK after doing Check angiography. He was then managed with Oxygen support, NIV support, Inj. Fondaparinux, Anti biotics, Anti-coagulant, diuretics, Pulmonary vasodilators, Anti-hypertensive, and other supportive drugs. He responded well to the given treatment and was gradually weaned off NIV and oxygen support. Serial D-dimer, CBC, Chest X ray monitoring was done. Repeat CT chest was done in view of fresh lesions on Chest X ray which showed cavitatory lesion in Right mid zone with moderate Pleural effusion. Chest Physician consultation was taken and advice followed accordingly. He was discharged after 19 days, later he was then taken up for follow up every 2 weeks.

KEYWORDS

Pulmonary Embolism, Thrombosis, ChAdOx1 nCoV-19 Vaccine, COVID-19, vaccine induced pulmonary thromboembolism.

INTRODUCTION

SARS-COV-2, the pandemic causing virus that is known to cause the Corona Virus Disease 19 (COVID-19). This disease is known to cause the high mortality and pneumonitis that spread rampantly across the globe. During the COVID-19 Pandemic, it is estimated that 33.4 million affected cases and 447 thousand deaths have been occurred [1]. Scientists and researchers worked enormously to develop the safest and most effective vaccines against COVID-19. In India two vaccines were allowed for Emergency use for Vaccination [2]. The First ChAdOx1 CoV-19 Vaccine or Covishield which was developed by Oxford-AstraZeneca and was manufactured by Serum Institute of India [3]. Second, Covaxin which was developed by Bharat Biotech Limited. Vaccine-Induced Immune thrombosis events are the most common adverse effect of ChAdOX1 nCoV– 19 Vaccine [4].

These events are very rare disorder that takes place followed by the day one or two of the vaccination. It is suspected that many patients develop the symptoms like severe headaches, blurred vision, vomiting, altered sensorium, breathlessness and swelling. Looking at the official reports, In the march 2021, many concerns were raised for the possible thrombosis after the ChAdOx1 nCov-19 Vaccine [5]. One of the first official report was given on March 10, 2021, by European Medicines Agency, which presented two severe cases of thrombosis and one death from the same [6]. Other report was published by Denmark, which reported the death of patient by post ChAdOX1 nCOV-19 Vaccine immunisation due to thrombosis. Thus, the administration of ChAdOX nCov-19 Vaccine was put on hold [7]. The most common cases were the Cerebral Venous Sinus Thrombosis (CVST) [8]. In contrast, the incidence risk of the such adverse effect is 15 cases per million people in each year [9]. As this numbers suggest that the benefits of ChAdOx1 nCoV-19 Vaccine have more benefits as compared to that of risks. The most prone population is of female, children and then males [10]. In this case study we report a rare case of 29-year-old male patient developing Pulmonary Embolism after receiving the first dose of ChAdOx-1 nCoV-19 Vaccination.

CASE STUDY

A 29-year-old patient was bought to casualty in critical state, He was immediately shifted and admitted to ICU. His presenting complaints were Fever and Cough post Vaccination on 08-07-2021. He had severe breathlessness in the last 15 days and constipation in the past 2 days. He also had the history of Blood Transfusion on 11-08-2021, with type "B" and Rh "+Ve" Blood Group. His vitals when admitted were Pulse (P): 149 / min, Blood Pressure (BP): 132/82 mmHg, SPO2: 77%, Respiration Rate (RR): 28/ min and Random Blood Sugar (RBS): 133 mg/dL. He was immediately shifted on Non-Invasive Ventilation NIV for Breathing support. His SPO2 levels now rose up to 98%. He was stabilised with the Inj. Pantoprazole 40 mg IV (OD), Inj. Ceftriaxone 1 gm IV (BD), T. Clopidogrel 75 mg (OD), T. Aspirin 150 mg (OD), T. Rivaroxaban 15 mg (BD). He was taken up for bedside 2D Echo, showed Severe Pulmonary Hypertension (Figure 1) Likely Pulmonary Thromboembolism (Figure 2), Good Biventricular systolic function, Mild TR. For ruling out the possibility of Pulmonary Embolism, He was advised for CT Pulmonary Angiography (CTPA), which revealed Eccentric filling defect seen in bilateral

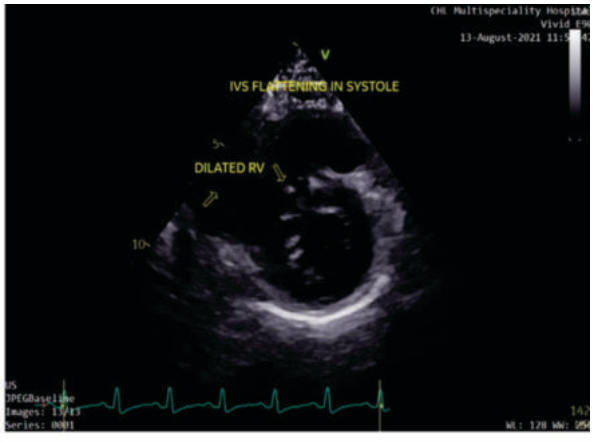

Figure 1. Showing the Pulmonary Hypertension in the 2D Echo. In the Image, IVS Flattening in systole and Dilated RV Can be seen.

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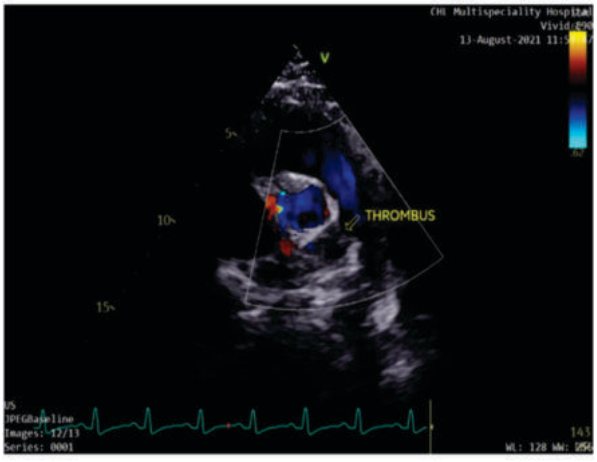

Figure 2. Showing the Signs of Pulmonary Embolism in the 2D Echo. In the Image, the Arrow shows the thrombus.

arteries at hila with extension in lower lobe segment branches – likely thrombus. Thus, with due consent, Intrapulmonary Thrombolysis was started with the Inj. Tenecteplase 40mg IV Slow bolus. For the complaints of Cough, he was prescribed the combination of Ambroxol (30mg/5ml) + Levosalbutamol (1mg/5ml) + Guaifenesin (50mg/5ml). All the basic tests were done along with D-Dimer (6530 mcg/mL), NT-Pro-BNP (1666.1 pg/ml) and Se CPKMB (6.0 U/L).

He remained much breathless on day 2, For which HRCT Thorax (Plain and Contrast) was done, which showed bilateral small patchy ground glass haze with superimposed reticular thickening mainly in subpleural region. He was started on anticoagulants focusing on factor Xa inhibitors, for which Inj. Fondaparinux 7.5mg/0.6 ml was started in (BD). Antibiotics like Inj. Ceftriaxone and Sulbactam, Inj. Levofloxacin 500 mg was started. He was still kept on NIV Support.

On day 3, NIV support was continued with serial SPO2 Monitoring. Pulmonary Vasodilator T. Digoxin 0.125 mg (OD) was started, along with T. Ambrisentan 5 mg was started for Pulmonary Hypertension and T. Tadalafil was started to PDE-5 inhibition. His SPO2 levels were between 65% - 72% off NIV and 98% on NIV. His body temperature elevated to 98.1° F, for which Antipyretics were started. T. Furosemide 40 Mg with Spironolactone 50 Mg was started to reduce the breathlessness. Inj. Methylprednisolone 40 mg IV was started on same day. Since, He had fever, we suspected of COVID-19 disease, Nasopharyngeal and Oropharyngeal Swab Sample was sent for RTPCR of COVD-19, which resulted Negative for COVID-19 disease. For the possibility of Viral Etiology, T. Oseltamivir 150 mg was started. CRP (116.8 mg/L), CBC (Refer Table 1) and LFT (Refer Table 2) were sent.

On Day 4, Serial CRP (118.3 mg/L) level was done. Same treatment was continued. There was improvement in his SPO2 Levels by 75% off NIV and 98% on NIV. The Anticoagulant therapy was continued, along with the same treatment.

On Day 5, Serial CBC (Table 1), RFT (Table 3), Serum Electrolytes (Table 4), LFT (Table 2), Chest X-ray (Figure 3) was done. T. Vitamin B Complex was started for nutritional support along with parenteral fluids. Inj. Meropenem 1 gm was started for overcoming the severe infection in lungs. His SPO2 Levels were increased to 82% off NIV and 98% on NIV support. Anticoagulant therapy was stopped.

On Day 6, Serum Electrolytes (Table 4), D-Dimer (8400 mcg/mL), CRP (71.4 mg/L) and NT-Pro-BNP (1379.8 pg/ml) levels were monitored. Same treatment was continued as no new complaints were presented by patient. His SPO2 Levels were increased to 85% off NIV Support and 98% on NIV Support.

On Day 7, Chest Xray (Figure 3), CBC (Table 1) and Homocysteine Levels (25 µmol/L) were monitored. Hemoglobin (Hb) level dropped to 8.8 gm/dL. The same treatment was continued. No new complaints were presented by patient

Table 1 . CBC Reports of the patient on every alternative day.

CBC	DAY 1	DAY 3	DAY 5	DAY 7	DAY 9	DAY 11	DAY 13
Hemoglobin	12.7 gm/dl	11.4 gm/dl	9.0 gm/dl	8.8 gm/dl	10.0 gm/dl	10.5 gm/dl	9.8 gm/dl
Total Leucocyte Counts	12200 cu.mm	19000 cu.mm	14500 cu.mm	13200 cu.mm	13800 cu.mm	13800 cu.mm	10900 cu.mm
DIFFERENTIAL COUNTS							
Lymphocytes	15 %	09 %	09 %	12 %	06 %	12 %	06 %
Neutrophils	82 %	88 %	85 %	83 %	91 %	83 %	90 %
Monocytes	02%	01%	04%	04%	02%	03%	02%
Eosinophils	01%	02%	02%	01%	01%	02%	02%
Band Cells	00%	00%	00%	00%	00%	00%	00%
RBC INDICES							
RBC Count	3.13 mil/cu.mm	2.80 mil/cu.mm	2.36 mil/cu.mm	2.43 mil/cu.mm	2.72 mil/cu.mm	3.00 mil/cu.mm	2.86 mil/cu.mm
MCHC	37.0%	37.1%	36.0%	35.2%	35.3%	36.0%	34.7%
MCV	110 fl	110 fl	106 fl	103 fl	104 fl	98 fl	99 fl
MCH	40.7 pg/cell	40.6 pg/cell	38.2 pg/cell	36.3 pg/cell	36.7 pg/cell	35.2 pg/cell	34.5 pg/cell
RDW-CV	16.2%	15.0%	16.5%	17.4%	17.3%	18.7%	18.8%
PLATELET INDICES							
Platelet Count	2.19 lacs/cu.mm	3.51 lacs/cu. Mm	4.24 lacs/cu.mm	5.84 lacs/cu.mm	6.45 lacs/cu.mm	7.67 lacs/cu.mm	6.33 lacs/cu.mm
PCV	34.5%	30.6%	25%	25.1%	28.4%	29.3%	28.3%

Table 2. Liver Function Test Reports of the Patient

LFT	DAY 1	DAY 3
SGOT	35.6 U/L	61.3 U/L
SGPT	38.6 U/L	68.9 U/L
Se. Bilirubin (Total)	2.88 mg/dl	1.1 mg/dl
Se. Bilirubin (Direct)	1.40 mg/dl	0.40 mg/dl
Se. bilirubin (Indirect)	1.48 mg/dl	0.70 mg/dl
Se. Protein (Total)	7.0 gm/dl	4.99 gm/dl
Se. Albumin	4.0 gm/dl	2.38 gm/dl
Se. Globulin	3.0 gm/dl	2.61 gm/dl
Se. Alkaline Phosphatase	54.0 U/L	38.0 U/L

His SPO2 Levels were increased to 87% off NIV support and 98% on NIV Support.

On Day 8, Inj. Ferrium Supplement 1K was given in Stat for low Hb Count. No new complaints were presented by patient. His SPO2 levels were monitored, where his SPO2 levels off NIV were 90% and Off NIV Were 98%. Antihypertensives was started today, as his Blood Pressure remained Persistently 147/83 – 132/69 mmHg.

Table 3. Renal Function Test Reports of the Patient

RFT	DAY 1	DAY 3
Creatine	0.80 mg/dl	0.53 mg/dl
Urea	17.3 mg/dl	28.4 mg/dl

On Day 9, Serial CBC (Table 1) and Chest Xray (Figure 3) Monitoring was done. No new complaints were presented today. His SPO2 Levels were increased to 91% off NIV and 98% on NIV Support. His BP levels were in control, as his average BP through out the day was 125/ 65 mmHg.

On Day 10, His SPO2 Levels were on 93%, He was weaned off from NIV Support and shifted to Oxygen support on 6 L/min. His average BP Throughout the day was 138/73 mmHg. He remained stable throughout the observation period during Switching to the Oxygen support.

On Day 11, Serial Chest Xray (Figure 3), CBC (Table 1) and RFT (Table 3) was done. His SPO2 level increased to 95% on 6L/min. His average BP throughout the day was 129/69 mmHg. Check HRCT Thorax was done, which showed cavitatory lesion in Right mid zone with moderate Pleural effusion. Chest Physician Consultation was done, which advised for T. Faropenem 300 mg Extended Release was started along with Inj. Piperacillin and Tazobactam was started for the same etiology presented in HRCT.

Table 4. Serum Electrolytes (Na+/K+) Test Reports of the Patient

Serum Electrolytes	DAY 1	DAY 3	DAY 5	DAY 7
Sodium (Na+)	139.3 mEq/L	143.7 mEq/L	137.3 mEq/L	5.2 mEq/L
Potassium (K+)	3.7 mEq/L	3.3 mEq/L	4.6 mEq/L	5.2 mEq/L

On Day 12, RFT (Table 3) and Serum Electrolytes (Table 4) was done. His SPO2 Levels were 98% on 6L/min. We started tapering off the Oxygen level concentration 8 hourly with one concentration less. Since his Hb Level and Electrolyte levels were near

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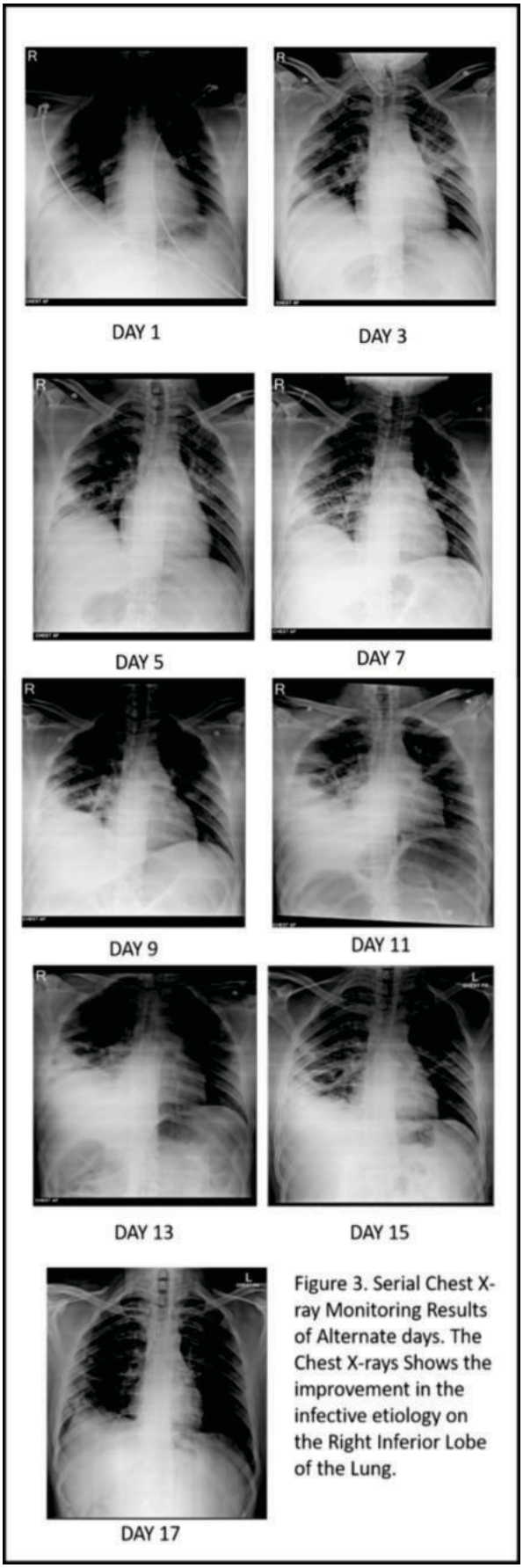

Figure 3. Serial Chest X-ray Monitoring Results of Alternate days. The Chest X-rays Shows the improvement in the infective etiology on the Right Inferior Lobe of the Lung.

normal, Multivitamin supplement containing contains Iron, Folic acid, Methyl-cobalamin, and Zinc was started along with Antiarrhythmic Drug Diltiazem 90 mg was started.

Table 5. Other Functional Test Reports of the Patient

OFT	DAY 1	DAY 3	DAY 5
CRP	116.8 mg/dl	118.3 mg/dl	71.4 mg/dl
CPKMB	6.0 U/L	---	---
D-Dimer	6530.0	8400.0	---
NT-Pro-BNP	1666.1 pg/ml	1379.8 pg/ml	---

On Day 13, He was discharged from Cardiac ICU and Admitted to IPD with Oxygen Support. He had risen temperature to 99° F, for which Antipyretics were started. His Average BP was 129/ 73 mmHg. His

SPO2 Level was 95% on 4 L/min. He remained stable and no signs of breathless was seen. He could now walk and talk without getting breathless. Serial CBC (Table 1) and Chest Xray (Figure 3) was done.
On day 14, He was serially monitored for SPO2 Levels, along with tapering off the Oxygen Concentration to 2L/min. He remained stable and no new complaints were presented.

On day 15, Spirometry Exercises were started to enhance the breathing. Chest Physiotherapy was started. Same treatment was started. Oxygen was completely weaned off. Patient did not present any new complaints. His SPO2 Levels were 98%. His average Blood Pressure was 128/69 mmHg.

On Day 16, Patient was all stable, breathing exercises were continued along with serial SPO2 Monitoring with the average SPO2 of 97% through out the day with BP of 132/75 mmHg. He was kept under observation for any discomfort or any kind of complaints.

On Day 17, He was all normal and presented no complaints. His Blood Pressure was 124/ 67 mmHg and SPO2 levels were 96%.

On day 18, CBC (Table 1), Chest Xray (Figure 3) and CRP (18.1) was done. His SPO2 levels was 98% and Blood Pressure was 116/69 mmHg. He remained stable throughout the day.

On day 19, Patient's vitals were SPO2: 98%, BP: 124/63 mmHg, HR: 79/min and RR: 19 /min. He was discharged after the final check and completion of all medicines. He responded well to the given treatment. He remained stable throughout the stay period and was discharged. He was asked for follow-up after 15 days of discharge. He was discharged with Tablet form of Cefuroxime 500 mg, Atorvastatin 20 mg and Clopidogrel 75 mg, T. Faropenem 500 mg, T. Ambrisentan 5 mg and T. Tadalafil, T. Rivaroxaban 20mg, T. Diltiazem CD 90 mg, T. Metoprolol Tartrate 25mg, T. Methylprednisolone 8 mg, T. Furosemide 40 mg and Spironolactone 50 mg, T. Digoxin 0.125 mg, Expectorant, Antaacid and Nutritional support was started.

DISCUSSION

All over the world, epidemiological data on the events following the trends of thrombosis after the ChAdOx1-nCOV-19 Vaccine. The initial studies have reported the wide age range, gender, type and timing across different countries. It is estimated that Individual below the age of 50 years is at the high risk, with the average age of 40.5 years, approximately ranging from age 23 to 75 years [11]. It was seen that the most thrombolytic events occurred with females, with the case percentage of 67-92% [12]. Any thrombotic event after the ChAdOx-1 nCOV-19 Vaccine would occur between the 4-28 days after the day of administration [13]. The most common site of occurring the Thrombus is Cerebral Venous Sinuses, followed by Splanchnic veins, Deep Veins of Legs, Pulmonary Veins and Cerebral Arteries [14]. In some cases, patients had two or more site involving the thrombus [15]. A Canadian study demonstrated that the Incidence rate of the thrombotic event after the first dose of ChAdOx1 nCoV-19 is about 1 case / 75,000 recipients [16]. In US study, the same rate was increased to 3.6 Cases / Million [17], 8.6 Cases/ Million in European Countries [18]. The Incidence rate were same for the patients taking the second dose of ChAdOx1-nCoV-19 Vaccine [19]. The Mortality Rate for the VITT was between 20% to 50% [20].

Most Symptoms after the adverse effect of ChAdOx1 nCov-19 Vaccine was headache, Blurred Vision, Vomiting, Fever, Altered sensorium, Severe leg and abdomen Pain. It was seen that many cases presenting late to the hospital, after the adverse effect has already started, would just increase the high risk but also the increased morbidity rate for the same patient. Dyspnea, Cough, Persistent Chest Pain could be the possible symptoms for the Pulmonary Embolism in patients. Other factors that increase the mortality rate of the patient

depends on the past medical history of the patient.

As soon as the patient is introduced to the hospital with such symptoms, patient must be advised for the imaging diagnosis, like HRCT, 2D Echo, if neurological factors are involved, MRI must be done immediately. After the imaging diagnosis is done, Patient must me managed with the Antiplatelet or Anticoagulation therapy must be given to patient. The Early management can reduce the risk of the morbidity of the patient.

Though the benefits of the ChAdOx1 nCoV-19 Vaccine are more than that of the adverse effects. The ChAdOx1 nCoV-19 Vaccine was very helpful in preventing the risk of COVID-19 disease by 90%. Furthermore, its low cost of development makes it a perfect vaccine for the public use. In India, most of the vaccination is done with the ChAdOx1 nCOV-19. Thus, the less numbers of the thrombotic events as compared to the sample size of the patients who are benefitted with the same vaccine. The ChAdOx1 nCOV-19 Vaccine is Very Safe to be vaccinated with some adverse effects.

CONCLUSION

This case demonstrates a very rare possibility of Pulmonary Embolism in 29-Year-old Male, 15 days after receiving the first dose of ChAdOx1 nCOV-19 vaccine, with no other possible clarity and explanation for Pulmonary Embolism. At present, In India there are very rare cases reported of thrombosis after millions of doses of COVID-19 Vaccine recipients, caused by the association of ChAdOx1 nCOV-19 vaccine. Thus, this does not explain the cause of Pulmonary Embolism but further data needed to support such association and reference. In the same perspective, COVID vaccination can lead to this very rare, life-threatening thrombosis events and complication. The medical authorities have informed about the high number of benefits as compared to the risks. Awareness of the precautions and the warnings of the thrombosis events must be done, so that early medical treatment must be started for the patients having it. Also, modification of the mechanism of the thrombotic event will help in preventing the high morbidity and mortality.

DECLARATION

The occurrence of Pulmonary Thromboembolism is suspected to be occurr immediately after the first dose of ChAdOx-1 nCoV-19 Vaccine. This may be an adverse effect of the vaccine, but no possible explanation and casaul relation could be proved while dealing with this case. The case paper is presented for the medical or clinical management of the patient and for medical viligance of such symptoms , if presented with such complications. This occurrence of such symptoms were not explained, thus we used “Suspected to occur” and “Immediately”.

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Conflict Of Interest

Authors do have any conflict of Interest as this case study was done after taking the due consent of the patient and his family members.

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