A Suspected Case of COVID-19 with High Altitude-associated Massive Pulmonary Embolism and Right Ventricular Clots

Ammad Akram[1], Mehwish Gilani[2] and Khurshid Muhammad[3]

[1]*Department of Internal Medicine, Armed Forces Bone Marrow Transplant Centre, Rawalpindi, Pakistan*
[2]*Department of Pathology, Armed Forces Bone Marrow Transplant Centre, Rawalpindi, Pakistan*
[3]*Department of Internal Medicine, Armed Forces Institute of Rehabilitation Medicine, Rawalpindi, Pakistan*

ABSTRACT

Pulmonary Embolism (PE) is an elusive entity that has long baffled physicians. At times, it can present as a diagnostic and therapeutic challenge. The aim of this report is to emphasise that high altitude is one of the risk factors for PE. Physicians must keep a high index of suspicion for PE, especially in patients being evacuated from high altitudes with respiratory symptoms. A case of massive PE with right ventricular clots initially suspected to be high altitude-associated pulmonary edema (HAPE) and then novel coronavirus disease 2019 (COVID-19) pneumonia was managed. Computed tomography (CT) pulmonary angiography could not be done initially. The case was managed in intensive care settings. The patient had to be treated with thrombolytic therapy owing to hemodynamic compromise. Significant clinical improvement was noted after thrombolysis. A high index of suspicion is required for the diagnosis and management of PE. If standard imaging techniques cannot be used due to clinical constraints, ancillary techniques must be effectively employed during management.

Key Words: *Pulmonary embolism, Thrombolysis, High altitude, COVID-19.*

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INTRODUCTION

Pulmonary embolism (PE) remains a great master of disguise and can present with multivariate symptomatology.[1] For military physicians, PE should be one of the top differentials, especially in young soldiers being evacuated from high altitudes with respiratory symptoms.[2] PE can easily be missed, especially in the current pandemic where one tends to tilt more towards diagnosing COVID-19 in every patient who has recent-onset shortness of breath. Here, we report a case of a young soldier who was evacuated from high altitude with a history of loss of appetite, shortness of breath, and chest pain on suspicion of high altitude-associated pulmonary oedema (HAPE) and later shifted to our setup on suspicion of COVID-19.

CASE REPORT

A 26-year male, with no known comorbids, serving at a height of 19,000 ft above sea level for about 20 days, was evacuated to the hospital, with a 2-week history of loss of appetite, a 1-week history of shortness of breath, and intermittent pleuritic chest pain.

Correspondence to: Dr. Ammad Akram, Department of Internal Medicine, Armed Forces Bone Marrow Transplant Center, Rawalpindi, Pakistan
E-mail: ammadakramch@gmail.com

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He was in his usual state of health and well-acclimatised to his new working environment when he developed a loss of appetite and slight nausea eight days after arrival. He was given symptomatic treatment by his regimental medical officer but there was no relief. Later on, he started feeling short of breath even while taking a short trip to the washroom. This was accompanied by intermittent central chest pain which was pleuritic in nature and did not respond to non-steroidal anti-inflammatory drugs (NSAIDs). On suspecting HAPE, he was immediately evacuated to the base hospital and then to a tertiary care hospital. The high resolution computed tomography (HRCT) chest showed multifocal patches of ground glass haze with intralobular septal thickening and patches of consolidation in the peripheral sub-pleural distribution in multiple lobe segments. His initial novel severe acute respiratory syndrome *coronavirus* 2 (nSARS-CoV-2) real time polymerase chain reaction (PCR) was negative. Suspecting possible COVID-19 based on history and HRCT findings, the patient was shifted to Pakistan Emirates Military Hospital (PEMH), ITC 3 (probable COVID ITC). On reception, he was found to be anxious with a pulse of 102/min (regular), blood pressure (BP) of 120/80 mmHg, respiratory rate of 20 breaths/minute, temperature 98.6˚F and maintaining oxygen saturation (SaO_2) of 93% on 2L supplemental oxygen *via* nasal prongs while he would desaturate to 89% at room air. His systemic examination was unremarkable. His laboratory investigations revealed haemoglobin (Hb) of 17.9 g/dl (Normal: 12-15 g/dL), total leucocyte count (TLC) 18.26 × 10^9/L (Normal: 4-10 × 10^9

/L), platelets 145 $\times 10^9$/L (Normal: 150-400 $\times 10^9$/L), urea 9.4 mmol/L (Normal: 2.1-7.1 mmol/L), creatinine 145 umol/L (Normal: 61-115 umol/L), D-Dimers >200 <400 (Normal: <200 ug/ml), Trop I 1st set, 0.2 ng/ml (Normal: 0.02-0.06 ng/ml) and 2nd set, 0.25 ng/ml after 4 hours, and NT-Pro BNP was 1000 pg/ml (Normal: <125 pg/ml). His serum ferritin was 520 ng/ml (Normal: 20-250 ng/ml), Lactate dehydrogenase (LDH), 400 U/L (Normal: 208-378 U/L) and C-Reactive protein (CRP) was 100 mg/L (Normal: <10 mg/L) while his Pro-Calcitonin levels, liver functions tests, electrolytes, prothrombin time (PT), and activated partial thrombinplastin clotting time (APTT) were within normal limits. His arterial blood gases revealed P_aO_2 70 mmHg, P_aCO_2 30 mmHg with a pH of 7.4. His electrocardiography (ECG) revealed sinus tachycardia and inverted T waves in II, III, AVF, V_1 to V_6. Echo revealed 2 flopping but adherent clots in the right ventricle measuring 2 × 2 cm and 1.5 × 1.5 cm, with dilated right ventricle and atrium and an ejection fraction (EF) of 60% (Figure 1). Doppler ultrasonography of both lower limbs did not reveal any evidence of deep venous thrombosis (DVT). Before anticoagulation, his blood samples were sent for antinuclear antibody (ANA), antiphospholipid antibodies, extractable nuclear antigen (ENA), RA factor, Factor V Leiden, protein C and S and homocysteine levels, which were found to be normal. CT pulmonary angiography (CTPA) was deferred keeping in view renal derangement. He was started on intravenous unfractionated heparin (UFH), 5,000 units bolus followed by an infusion of 1,333 units per hour with a plan of monitoring APTT and international normalised ratio (INR). Broad-spectrum antibiotics with Gram--positive, negative coverage and supportive care were also started. After 10 hours of initiation of treatment, the patient deteriorated. His BP dropped to 80/50 mmHg and did not respond to 500 ml fluid bolus. He was now maintaining SaO_2 of 91% on 6 L oxygen through a non-rebreathing mask. An immediate decision was taken for thrombolysis after ruling out all contraindications. Streptokinase was chosen as the agent of choice due to its easy availability and the treating team's experience with the drug. A dose of 250,000 units of streptokinase were infused over 30 minutes followed by an infusion of 100,000 units per hour with a plan to continue this for at least 24 hours or till clinical improvement. During this period, the patient's vital signs, ECG trace, neurological status, and signs of overt bleeding were continuously monitored. Three hours after initiating thrombolytic therapy, the patient started showing clinical improvement. His BP improved to 110/90 mmHg and O_2requirement gradually improved. At the end of 24-hour period, the patient had become considerably stable. BP was 120/70 mmHg and the patient only required 2 L Oxygen to maintain SaO_2 of 97%. ECG showed reduction in rate and T wave inversions. Bedside echocardiography, however, did not show any apparent regression in the size of right ventricular clots. Post-thrombolysis, the patient was started on IV UFH. Over the next 72 hours, his renal profile improved and a CTPA was done which showed large hypodense intraluminal filling defects in the left main pulmonary artery (3.4 × 2.1 cm) extending predominantly into the left inter-lobar artery and its all segmental and sub-segmental branches, an apical subsegmental branch of the left upper lobar artery, right inter-lobar artery, and its segmental and sub-segmental branches with relative sparing of the lateral segmental branch of the right middle lobe (Figure 2). There were also areas of consolidation with accompanying ground glass haze in peripheral sub-pleural distribution, in keeping with the embolic infarcts. Over the following days, his two more sets of nSARS-CoV-2 RT PCRs were negative. His antibodies for COVID-19 (IgM and IgG) were non-reactive. The patient was subsequently shifted to the Armed Forces Institute of Cardiology (AFIC) for further management.

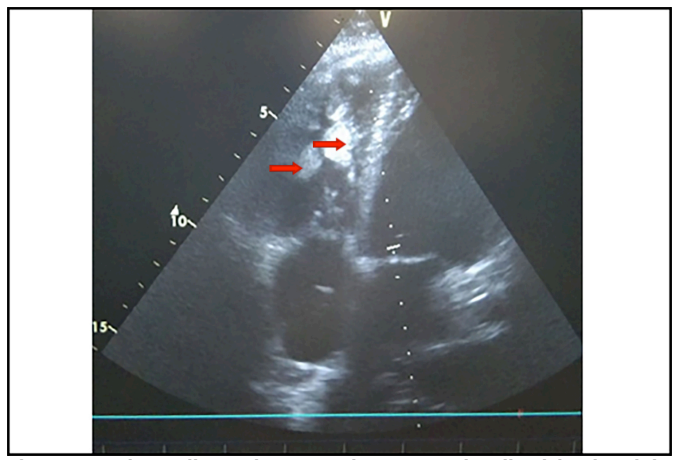

Figure 1: Echocardiography. Two clots were visualised in the right ventricle as indicated (arrows) measuring 2 × 2 cm and 1.5 × 1.5 cm each.

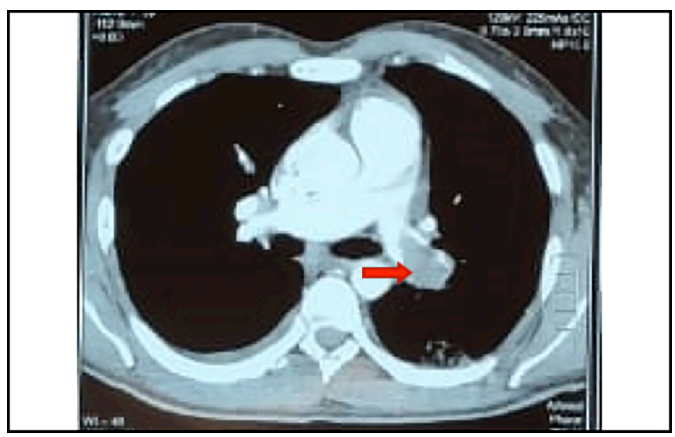

Figure 2: CT pulmonary angiography. A large hypodense intraluminal filling defect can be seen in the left main pulmonary artery (3.4 × 2.1 cm) extending predominantly into the left inter-lobar artery as indicated (arrow).

DISCUSSION

PE is not a rarity at high altitudes. Hendriksen *et al.* concluded in a retrospective study that there is usually a diagnostic delay of more than 7 days in the diagnosis of PE when a patient makes contact with a physician at primary care centres.[3] Bedside echocardiography can serve as an excellent diagnostic tool when combined with other modalities like ECG. Non-availability or clinical constraints to do a timely CTPA must not keep a physician from connecting the dots and reaching a diagnosis. Delaying diagnosis and treatment can cause significant morbidity and mortality. Ironically, about 70% of PEs are misdiagnosed or missed by physicians, only to be discovered at post-

mortem.[4] When clinical suspicion is high, anticoagulation must be initiated without delay. In patients with a low bleeding risk, the only widely accepted indication for full-dose systemic thrombolysis is acute PE causing shock or persistent hypotension, *i.e.*, systolic BP <90 mmHg, need for vasopressors, or a decrease in BP ≥40 mmHg from the baseline for 15 minutes or longer despite resuscitation.[5] Evidence from randomised and retrospective observational studies indicates that systemic thrombolytic therapy leads to early and rapid hemodynamic improvement.[6] The choice of thrombolytic agent must be tailored based on easy availability and experience of treating team with the drug. During thrombolysis, the patient should be monitored for improvement in hemodynamic status, oxygenation, and development of neurological signs or obvious signs of bleeding. Only major bleeding, *e.g.* hemodynamic compromise, altered mental status, a significant reduction in haemoglobin (*e.g.* by 1 to 2 g/dL), and a copious amount of bleed should lead to immediate cessation of thrombolytic agent followed by resuscitation efforts. Following thrombolysis, anticoagulation with IV UFH must be done while monitoring APTT. Once the patient is stable for 24 to 48 hours, a transition should be made to an oral anticoagulant (*e.g.* DOAC or warfarin).

CONCLUSION

A high index of suspicion is required for the diagnosis and management of PE, particularly in patients presenting with respiratory symptoms at high altitudes. If standard imaging techniques cannot be used due to clinical constraints, ancillary techniques must be effectively employed during management.

PATIENT'S CONSENT:

Written informed consent was taken from the patient for publication of his case as a case report.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

AK: Acquisition, analysis, interpretation of data for the work, drafting, and conception or design of the work.

MG: Drafting of the manuscript, revising it critically for important intellectual content, and interpretation of data for the work.

KM: Proofreading.

All authors have approved the final version of the manuscript to be published

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