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Case Report

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Pulmonary Embolism in COVID-19 and the Unanswered Questions

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has ravaged the global society as we know it. As almost a dozen pharmaceutical agents go into randomized controlled clinical trials, multiple studies have surfaced trying to associate a hypercoagulable state to coronavirus disease 2019 (COVID-19) patients. We report two COVID-19 cases who presented with occlusive pulmonary embolism (PE) strongly supporting a hypercoagulable state incurred by SARS-CoV-2. This is significant as it is one of the early reports of such an initial presentation of COVID-19 in the USA. Through our report, we invite the medical community to share a perspective about long-term management guidelines for SARS-CoV-2 associated venous thromboembolism (VTE) and prompt future research.

Keywords: SARS-CoV-2; COVID-19; Pulmonary embolism; Venous thromboembolism

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has ravaged the global society as we know it. The medical community is in a desperate need to understand the pathophysiology of coronavirus disease 2019 (COVID-19) (caused by SARS-CoV-2) and explore possible therapeutic strategies in the wake of widespread mortality. At the time of writing this article, globally, 305,395 people have succumbed to this disease with 4,508,435 total infections. As almost a dozen pharmaceutical agents go into randomized controlled clinical trials, multiple studies have surfaced trying to associate a hypercoagulable state to COVID-19 patients [1]. We reference these studies and present two novel COVID-19 cases who presented with pulmonary embolism (PE).

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Case Report

The summary of cases with pertinent patient characteristics, histories, findings and supporting data are presented in Table 1. Until now, there have been only sporadic cases of occlusive PE in COVID-19 patients, coming from China, Italy and the USA. Both our patients presented with dyspnea preceded by a mild flu-like illness and were found to have pulmonary emboli with significant clot burden at initial presentation. There were no significant predisposing risk factors, other than a hypercoagulable state due to COVID-19. The history of prostate carcinoma in patient 2 is unlikely to be contributory as he was in remission, suggested by a normal prostate-specific antigen (PSA). Both patients were treated with heparin products. Patient 1 remains hospitalized with moderate illness (day 4). Patient 2 required 3 days of inpatient stay and was discharged on newer oral anticoagulants (NOACs) with a recommended duration of 3 months. Hypercoagulable workup including factor V Leiden mutation, protein C, protein S, antithrombin III levels, and anti-phospholipid antibody tests was ordered upon outpatient follow-up, which remains pending.

Discussion

Initial studies from Greece and France endorse that COVID-19 patients might be at a higher risk of developing venous thromboembolism (VTE), which has been attributed to a hypercoagulable state [1]. The exact putative mechanism of this observation still remains elusive, but the role of antiphospholipid antibodies (APLAs) has been implicated [2]. Interesting autopsy findings from China suggest hyaline thrombi in some microvessels of the alveolar septum on immunohistochemical staining [3]. Our European and Chinese colleagues recommend an early initiation of anticoagulation therapy in selected patients [1, 4]. This has shown to improve prognosis of this group of COVID-19 patients [5]. In summary, all these studies point towards a similar direction, decoding the labyrinth, i.e. pathophysiology of COVID-19 and how anticoagulation

Table 1. Pertinent Patient Characteristics, Histories, Laboratory Findings, and Imaging Results

	Patient 1	Patient 2
Age	43	64
Gender	Male	Male
CC	Sudden-onset dyspnea × 1 day	Progressively worsening dyspnea × 5 days
History of presenting illness	CC associated with right upper chest pain radiating to the right arm and back preceded by cold symptoms 2 weeks prior	CC preceded by myalgia, dry cough, and low-grade fever (T-max 37.7 °C) 4 weeks prior
Pertinent negatives	Fever, chills, cough, sick contacts, palpitations, diarrhea, immobilization, smoking, use of testosterone therapy	Chills, headache, sick contacts, chest pain, palpitations, paroxysmal nocturnal dyspnea, wheezing, lower extremity edema/ tenderness, diarrhea, immobilization, smoking, use of testosterone therapy
Pertinent histories	Negative for clotting disorders, cancer, or family history of clotting disorders	Hypertension, prostate cancer (status post prostatectomy: in remission since 2003). Negative for clotting disorders in self or family
Physical examination on admission	Tachycardia (HR 122 beats/min), tachypnea (RR 40/min), decreased breath sounds at bilateral bases, mild respiratory distress	Tachypnea (RR 23/min), decreased breath sounds bilaterally
Laboratory data on admission		
While blood cell (4.1 - 11.0 × 10^3/μL)	14.3	6.5
Lymphocytes (25.0-40.0%)	11	32
Absolute neutrophils (2.1 - 8.4 × 10^3/μL)	11.5	3.2
Absolute lymphocytes (1.0 - 4.4 × 10^3/μL)	1.6	2
HGB (13.5 - 17.5 g/dL)	14.3	16.1
PLT (150 - 400 × 10^3/μL)	267	382
Blood urea nitrogen (8 - 24 mg/dL)	12	17
Creatinine (0.55 - 1.30 mg/dL)	0.76	1.03
Glomerular filtration rate (> 60 mL/min/1.73 m^2)	> 60	> 60
Alanine aminotransferase (12 - 78 U/L)	36	49
Aspartate aminotransferase (13 - 41 U/L)	21	56
Albumin (3.5 - 4.8 g/dL)	3.7	2.8
Alkaline phosphatase (45 - 117 U/L)	117	64
Lactic acid	1.9	-
Brain natriuretic peptide (< 100 pg/mL)	-	34
Troponin (ng/mL)	< 0.01	< 0.01
C-reactive protein (< 3 mg/L)	82.4	95.2
Ferritin (12 - 300 ng/mL)	365.1	640.9
Procalcitonin (0.10 - 0.49 ng/mL)	< 0.05	0.17
Prothrombin time (11 - 13.5 s)	9.8	11
International normalized ratio (< 1.1)	0.9	1
Partial thromboplastin time (60 - 70 s)	26	< 21
D-dimer (< 250 ng/mL)	1,720	16,610
Lactate dehydrogenase (140 - 280 U/L)	290	464
PSA level (0 - 0.40 ng/mL)	-	< 0.01

Table 1. Pertinent Patient Characteristics, Histories, Laboratory Findings, and Imaging Results - *(continued)*

	Patient 1	Patient 2
COVID-19 RT-PCR	Positive	Positive
Blood cultures	No growth of pathogenic bacteria	No growth of pathogenic bacteria
Imaging		
Chest X-ray	Low lung volumes with patchy opacities in the medial left lung base and right upper lobe suggestive of atelectasis or pneumonia	Focal infiltrates in bilateral upper lobes and right lower lobe indicative of infection. No pulmonary edema.
CT pulmonary angiogram	Acute bilateral PE with predominant clot burden in the right lower lung. Bibasilar consolidation greater in posterior right lower lobe, suggestive of developing pulmonary infection.	Mild to moderate occlusive/partially occlusive pulmonary emboli in the right lower lobe and left lingula. Moderate subpleural/peribronchial ground-glass infiltrates in bilateral lungs with mild interlobular septal thickening. Mild mediastinal lymphadenopathy.
Venous Doppler bilateral lower extremities	Negative for deep vein thrombosis	Negative for deep vein thrombosis
Treatment	Hydroxychloroquine, ceftriaxone, azithromycin, IV heparin (day 1), subcutaneous LMWH (day 2 onwards)	Ceftriaxone, azithromycin, IV heparin (day 1), subcutaneous LMWH (day 2 onwards)
Discharge	Pending	Novel oral anticoagulant
Follow-up	Pending	Hypercoagulable workup pending

CC: chief complaint; HR: heart rate; RR: respiratory rate; HGB: hemoglobin; PLT: platelet; PSA: prostate-specific antigen; COVID-19: coronavirus disease 2019; RT-PCR: reverse-transcriptase polymerase chain reaction; CT: computerized tomography; IV: intravenous; LMWH: low-molecular-weight heparin.

therapy might fit in the algorithm. Future randomized controlled studies might help clear this association. In the meantime, low-molecular-weight heparin (LMWH) is being widely used in patients who fit this picture [4, 5]. This brings us to our questions to the medical community: 1) Are NOACs appropriate for these patients? 2) Should we consider these PEs as provoked or unprovoked? 3) What should be the duration of therapy?

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None to declare.

Conflict of Interest

None to declare.

Informed Consent

Verbal consent for publication of the clinical details was obtained from both patients and all patient identifiable information is anonymized in the manuscript.

Author Contributions

AB and NJ contributed to literature review and manuscript preparation; VS contributed to case information and reviewed manuscript. All authors have read the uploaded manuscript and consented to submission.

Data Availability

The authors declare that data supporting the findings of this study are available within the article. Any further inquiries regarding supporting data availability of this study can be directed to the submitting author.

Abbreviations

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: coronavirus disease 2019; PE: pulmonary embolism; VTE: venous thromboembolism; APLAs: antiphospholipid antibodies; LMWH: low-molecular-weight heparin; NOAC: newer oral anticoagulant; RT-PCR: reverse-transcriptase polymerase chain reaction; PSA: prostate-specific an-

tigen; HR: heart rate; RR: respiratory rate; HGB: hemoglobin; PLT: platelet; CT: computerized tomography; IV: intravenous

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