Pulmonary Embolism in COVID-19 Pneumonia: An Overlapping Diagnosis or a Misdiagnosis?

Eleonora Secco, Maria Cristina Pasqualetto, Fausto Rigo
Department of Cardiology, Ospedale Civile di Dolo, AULSS 3 Serenissima, Venice, Italy

Abstract

Coronavirus pneumonia (COVID-19) is a novel infectious disease with a high mortality rate due to severe acute respiratory syndrome. A 57-year-old woman was admitted to the emergency department (ED) with fever, cough, atypical chest pain, and dyspnea. She remained in the ED for about 48 h while waiting for the result of the COVID-19 oropharyngeal swab. Once she tested positive, she was hospitalized in the pneumological department with a diagnosis of pneumonia based on a chest X-ray and biochemical tests. Although azithromycin and hydroxychloroquine were promptly administered, she had a worsening of dyspnea even with a high-flow oxygen mask. D-dimer was increased, and a computed tomography scan with pulmonary and leg angiogram was positive for bilateral pulmonary embolism, deep-venous thrombosis, and multiple consolidated opacities in the lung parenchyma. This case highlights the fact that, in a pandemic situation, there is a potentially fatal risk of overlooking an alternative diagnosis in a COVID-19 patient who is generally considered as suffering only from pneumonia.

Keywords: COVID-19, D-dimer, pneumonia, pulmonary embolism

Introduction

Coronavirus pneumonia (COVID-19) is a novel infectious disease with high mortality due to severe acute respiratory syndrome (SARS), and recent observations suggest that a hypercoagulative status induced by an inflammatory response could be a potential risk factor for pulmonary embolism.

Case Report

We present the case of a 57-year-old Caucasian woman who was admitted to the emergency department (ED) with fever, dyspnea, cough, and atypical chest pain on the left hemithorax following a week at home in isolation for fever during the COVID-19 outbreak. She had a history of varicose vein surgery 2 years previously, had autoimmune hypothyroidism in substitutive hormonal therapy, and was mildly overweight (body mass index 27.6); no cardiovascular risk factors such as smoking, diabetes, arterial hypertension, dyslipidemia, or family history were declared. An oropharyngeal swab for COVID-19 was performed in the ED. The patient was placed in isolation room while waiting for the result and remained there for about 48 h. While she was in the ED, her blood pressure (BP) was 120/80 mmHg with mild sinus tachycardia (heart rate [HR] 95–113 bpm), her body temperature was 35.4°C, respiratory rate was 28 breaths/min, peripheral oxygen saturation was 92%, and a blood gas analysis (BGA) confirmed blood saturation of 91% without supplemental oxygen, with PaO₂ of 60.7 mmHg, PaCO₂ of 26.3 mmHg, and lactate of 3.3 mmol/L. A high-flow oxygen mask with reservoir was applied (10 L/min), and saturation was progressively raised to 98%. Blood chemistry tests showed increased inflammatory parameters with neutrophilic leukocytosis (white blood cell count 15.59 × 10⁹/L), neutrophil count 12.13 × 10⁹/L, and elevated C-reactive protein (174.7 mg/L). In addition, troponin I (280.8 ng/mL), brain natriuretic peptide (312.9 pg/mL), liver enzymes (aspartate aminotransferase 217 IU/L and alanine aminotransferase 326 IU/L), lactate dehydrogenase (479 IU/L), and ferritin (1335.2 ug/L) were increased. Procalcitonin was negative (0.3 ng/ml). A chest X-ray showed bilateral basal infiltrate opacities, and these findings were confirmed by a lung ultrasound.
which identified basal bilateral B lines and rare subpleural consolidations. Electrocardiogram (EKG) showed mild sinus tachycardia with HR of 113 bpm in the presence of negative T waves in the inferior and V1–V3 leads, S wave in DI, and RSr’ in V1 as incomplete right branch block [Figure 1]. Diagnosis of COVID-19 pneumonia was made considering the positive results of the oropharyngeal swab and imaging exams; the patient was transferred to the pneumology ward, where medical therapy with hydroxychloroquine and azithromycin was administered. Prophylactic anticoagulation was not prescribed because the woman was considered low risk (Padua prediction score for risk venous thromboembolism = 2). However, a few hours later, she suffered a sudden worsening of dyspnea and chest pain. BP mildly decreased to 100/70 mmHg. BGA with high-flow oxygen supplement revealed the following: PO$_2$ 87 mmHg, PCO$_2$ 28 mmHg, saturation 96%, and lactate 1.33 mmol/L. A new EKG was performed which confirmed the same findings of the previous EKG with initial signs of right ventricle overload. A very abnormal pathological value of D-dimer was found (>128,000 ng/mL), and a focus echocardiography revealed a right ventricle dilatation with increased systolic pulmonary artery pressure of around 40 mmHg [Figures 2 and 3]. Due to the suspicion of pulmonary embolism, an urgent computed tomography scan with pulmonary angiography (CTPA) extended to the legs was performed. The CTPA was positive for bilateral filling defects of the principal pulmonary arteries [Figures 4 and 5], with multiple bilateral consolidation particularly in the inferior lobes and a deep thrombosis of the left popliteal vein. Prompt intravenous unfractionated heparin was administered, and the woman was immediately transferred to the intensive cardiology department where she underwent thrombolytic treatment, resulting in rapid clinical improvement. The patient was discharged 8 days later in good health and with two negative oropharyngeal swabs.

**Discussion**

From the beginning of the COVID-19 pandemic, the association between pulmonary embolism and pneumonia has been extensively described. The current gold standard for the etiological diagnosis of SARS-coronavirus-2 infection is real-time reverse transcription-polymerase chain reaction on respiratory tract specimens, with 95% sensitivity.[1,2] Considering the high level of accuracy of this test, the medical approach is often entirely focused on interstitial pneumonia and respiratory management, leading to the potential risk of a missed or overlapping diagnosis, with associated prognostic implications. On the other hand, clinicians may consider the
role of COVID-19 infection in an abnormal activation of the coagulation system with thrombotic complications.\textsuperscript{[3,4]} Although the exact cause remains unclear, it is well documented in the literature that any kind of pneumonia results in a more pronounced relative risk of pulmonary embolism,\textsuperscript{[5]} and two important retrospective cohort studies have already highlighted that patients with pneumonia have a 2–3-fold increased risk of acute venous thrombosis.\textsuperscript{[6,7]} Current case reports\textsuperscript{[8,9]} have also described this phenomenon and have reinforced the association. However, we consider it important not to forget other possible diagnostic hypotheses in the context of respiratory failure, especially regarding COVID-19-positive patients. Clinicians should make a diagnosis of pneumonia only after correct evaluation of other possible causes of respiratory distress. This is vital because misdiagnosis could not only be potentially life-threatening for patients but also have medicolegal implications for clinicians. Finally, we suggest the prompt provision of prophylactic anticoagulant measures with low-molecular-weight heparin also in low-risk patients with COVID-19 infection to avoid pulmonary thromboembolism. This consideration is based on recently published evidence\textsuperscript{[10]} but also on day-to-day clinical practice in a COVID hospital.

\textbf{Declaration of patient consent}

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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\textbf{Conflicts of interest}

There are no conflicts of interest.

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