

## Acute pulmonary embolism as the first manifestation in a COVID-like severe acute respiratory syndrome.



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### ABSTRACT

In the era of new coronavirus infection pulmonary embolism (PE) is a corollary manifestation that may aggravate the patient's clinical status. In this setting of patients various coagulation abnormalities such as raised D-dimers and prolonged APTT have been reported previously in up to 65% and 45% of adults SARS patients respectively and multiple previously necropsy series of SARS patients showed that vascular thromboses were not uncommonly seen in lung specimens. During this period emergency rooms work is note of worthy in differentiation COVID from non-COVID patients due to separate admission procedure in the hospital. Accordingly, among the non-COVID population there exist a high percentage of patients with a typical radiologic pattern of COVID-19 but without a positive reverse transcription polymerase chain reaction (RT-PCR) resulting in naso-faringeal swab. The above findings raise the suspicion of an occulted COVID-19 or a like-COVID-19 clinical presentation. In the last instance there is a need to pay more attention just to avoid further contamination. In this report we describe a case with high risk PE, as a first manifestation of a like-COVID-19 pneumonia. In the above case the patient in question, after careful CT angiography evaluation, has a clear COVID-19 pneumonia radiological findings in spite of three RT-PCR swab negative for true COVID-19.

**KEY WORDS:** like-COVID-19, coronavirus pneumonia, pulmonary thromboembolism, CT pulmonary angiography.

## INTRODUCTION

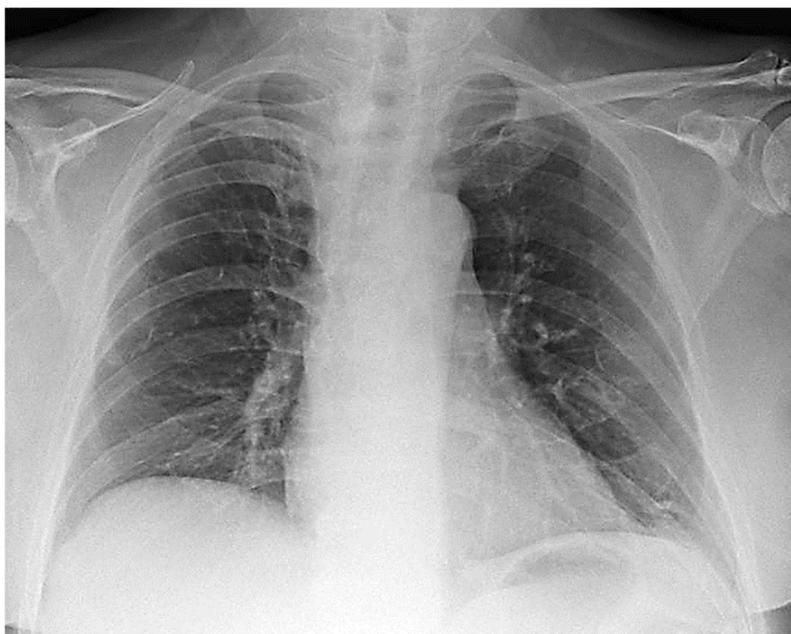
Coronavirus 2019 (COVID-19) is a highly contagious disease appeared firstly in China during winter 2019 [1]. This pathological condition may be associated with a hypercoagulable state and augmented risk for venous and/or pulmonary embolism (PE). The coexistence of the above two conditions creates diagnostic and therapeutic challenges for emergency medicine doctors in patients already at risk due to multiple co-pathologies [2]. In this setting patients with various coagulation abnormalities such as raised D-dimers and prolonged APTT had been previously reported in up to 65% and 45% of adults SARS patients respectively [3,4] and multiple previously necropsy series of SARS patients showed that vascular thromboses were not uncommon in their lung specimens. Moreover, the aforementioned pattern does not previously described in patients with a like-COVID-19 diagnosis. A like-COVID-19 condition was defined as a negative RT-PCR sample for true COVID-19 and a clear COVID-19 pneumonia radiological features. This case illustrates a high risk PE (PESI score=157) [5], with hypercoagulable characteristics, as a first manifestation in a like-COVID-19 respiratory distress syndrome patient, therefore is very important for emergency clinicians to take into consideration in their differential diagnosis.

## CASE PRESENTATION

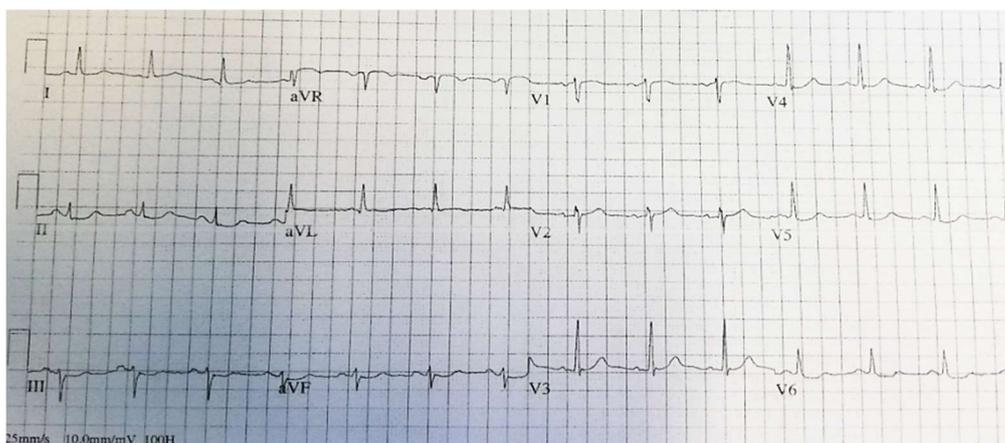
A 64 year-old man with a history of Linfoctic leukemia underwent a bone transplant 2 years ago. During this period the patient had bone rejection transplant twice. After 9 months however, there was no additional clear transplant rejection. The patient now is being monitored and he is in therapy in his transplant Center. Actually, he is currently following instructions from his doctor.

He was admitted to the emergency room (ER) complaining of chest pain and dyspnea. Dyspnea had already started 3 days prior to his arrival. One day earlier this patient was still taking advices from his family doctor via teleconference as is usually the case during this pandemic emergency period related to COVID-19. Because the patient had no other criteria obliging him to contact the emergency room such as cough or fever, he remained at home to avoid being infected via hospital contact. Due to the persistence of dyspnea he went at the nearest ER hospital. On admission he had a temperature of 36.9°C. Based on the current epidemiology guidelines an RT-PCR test was performed as a reference and resulted negative for

COVID-19. At the ER physical examination showed light bilateral basal crepitation. From laboratory investigations, while he was in the emergency room the patient, showed a normal white cell count 6.500 g/L, Hb 14.5 g/dl, PLT 104000g/L (normal values 140000-400000), creatinine clearance 62 ml/min/1.73mq, total bilirubin 0.92 mg/dl, ALT 141 U/L (normal values <41), GGT 783 U/L (normal values 8-61), LDH 558 (normal values 135-225U/L), CRP 8.4mg/L (normal values < 5.0), D-dimer 3750 ug/L (cut-off exclusion VTE<500), Troponin T hs 66ng/L (normal values 99° percentile 15ng/L). His chest radiography did not show any particular parenchymal alterations. Only a PICC via the succlavia vein and the superior vena cava is observed (fig. 1). On the other hand electrocardiogram did not show any troubles of rhythm. Nonetheless, atypical alterations of left ventricular repolarization were present (fig. 2).

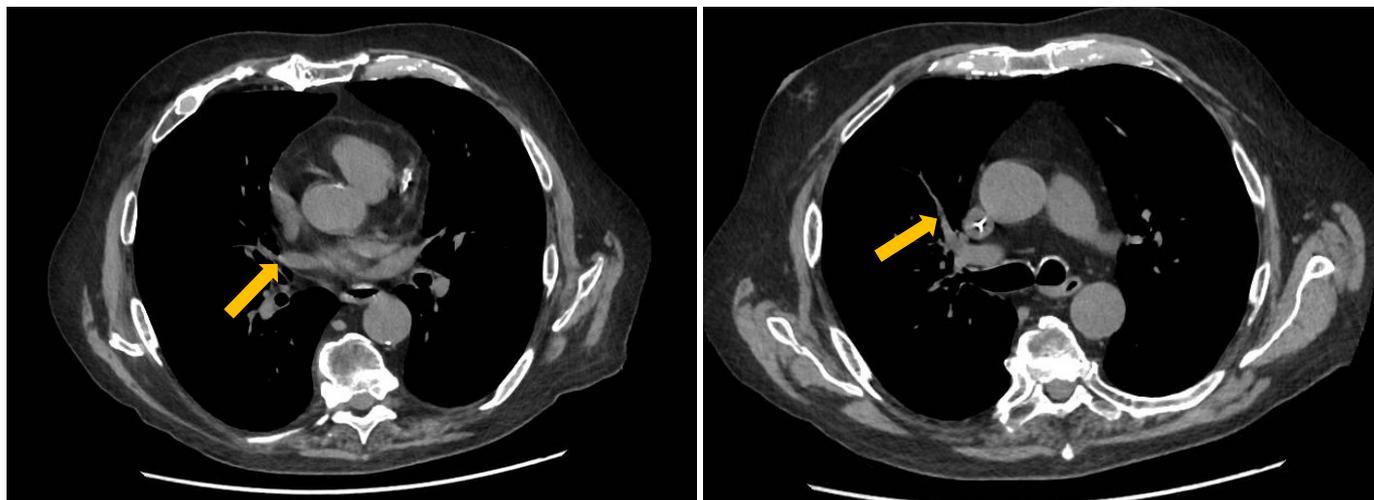


**Figure 1.** Chest radiography in posterior-anterior view.



**Figure 2.** EKG in admission did not showed any rhythm disturbances, associated with atypical alterations of left ventricular ripolarization in the lateral leads.

To exclude a PE disease a chest HR Computed Tomography was obtained. The latter detected the presence of a blood clot in the right main pulmonary artery with an extension into the segmental artery of the right lower lobe, suggestive of thromboembolism (fig. 3). Moreover, a venous CUS inspection excludes deep vein thrombosis.



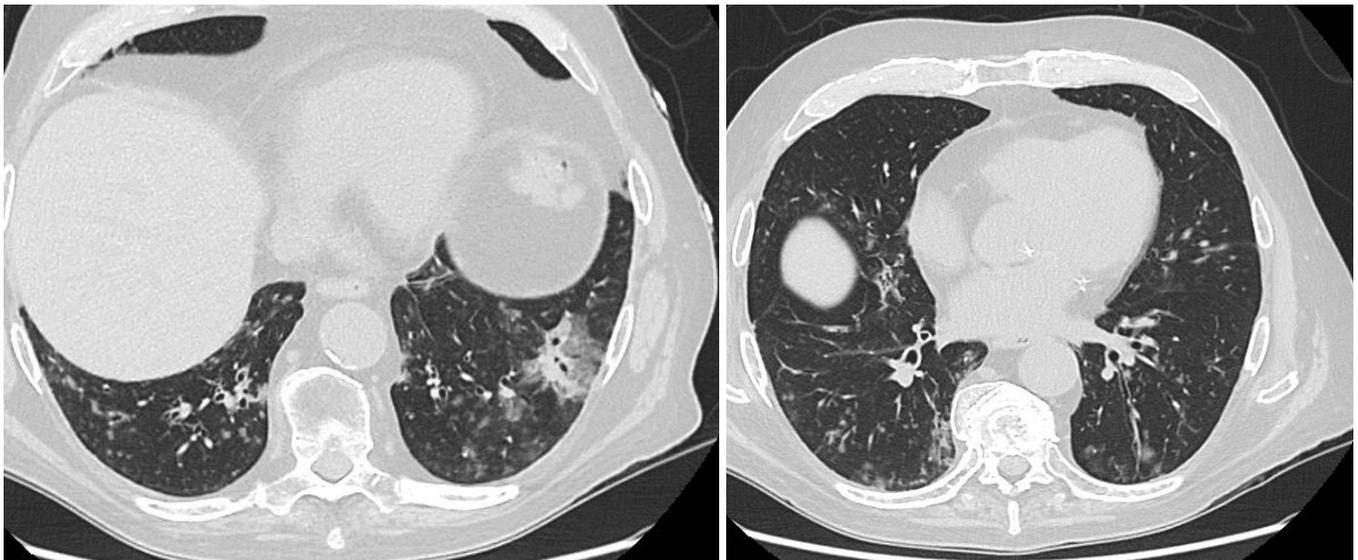
**Figure 3.** Slices from HRComputed Tomography:

Pulmonary embolism was observed in the above right pulmonary angiogram (arrows).

The patient was transferred to Intensive Cardiology Unit for monitoring and treatment. At focused echocardiography the left ventricular ejection fraction was 50%, without any regional contractile defects. The right ventricle had a little global hypokinesis. No pericardial effusion was noted. Blood pressure was 105/70mmHg.

Prompt anti-coagulation therapy in terms of heparin based on weight and renal function was started. After 72 hours the patient's symptoms gradually improved. Five days later while he was in ICU and performed shifting from heparin to anti-vitamin K anticoagulants the patient showed a rapid deterioration of his respiration with PaO<sub>2</sub>= 69mmHg and oxygen saturation of 87% in room air and he was further supported by oxygen administration. On 6th day the patient presents fever 38,5°C with Hb 10.1, little linfocytopenia 0.96 (normal values 1.00-4.00 10<sup>9</sup>/L), thrombocytopenia with PLT 57000 and worsening of renal function with creatinine 1.93 (normal values 0.70-1.20 mg/dl), creatinine clearance 36 ml/min/1.73mq and fibrinogen 236 mg/dl (normal values 150-400) were observed. Another RT-PCR test for COVID-19 was performed and resulted negative.

After consultation with the infectivologist additional investigation for antibodies for parvovirus IgG and IgM, anti-mycoplasma IgM, anti-Chlamydia pneumoniae IgG and IgM and anti-mitochondrial was carried out. All these tests were negative. In order to clarify better the details of the new clinical picture a new chest HR Computed Tomography was requested (figure 4). This revealed peripheral “ground glass” opacifications and crazy paving appearance consistent with COVID-19 pneumonia.



**Figure 4.** Chest CT slices demonstrating peripheral “ground glass” opacification in the inferior pulmonary lobes consistent with COVID-19 pneumonia

Four days later an initial improvement of creatinine clearance and PLT (to 71000) was observed. Pro-BNP value was 1536 ng/L and ferritin level was increased (4035ug/L). The patient was treated with Hydroxychloroquine, antiviral (acyclovir) and corticosteroids (prednisone). After a prolonged period of convalescence this patient, was finally discharged from hospital. Before his discharge another RT-PCR test for COVID-19 was obtained with a negative result.

## DISCUSSION

The novel COVID -19 coronavirus presents with a variety of clinical phenotypes that range from asymptomatic to profound, multiple organ dysfunction syndrome and sometimes leading to death. Among the aforementioned clinical phenotypes one of the most frequent clinical complication is pulmonary embolism (PE) [6]. In this setting various pathophysiological mechanisms have been proposed. A crucial one includes a hypercoagulable condition which is extended from micro- to macro-circulatory thrombosis. Some previously

isolated case reports showed COVID-19 pneumonia was complicated by an acute PE [7,8]. In this case we do not have RT-PCR positive test. This may raise difficulties when diagnosing a true from like-COVID-19 interstitial pneumonia. Moreover, it is also well known from previous studies [9,10] that the RT-PCR test may give false negative results in almost 30% of cases and only chest CT may be helpful for patients suspected of COVID-19 infection. On the other hand, PE has frequently presented in advanced stages of true COVID pneumonia namely and on average at around 12 days from symptom onset [6]. On the contrary, in this specific case PE is the first manifestation of a like-COVID-19 pneumonia. The above condition may be suspected from D-dimers levels increase and a quick chest HR Computed Tomography performed revealed PE. Moreover, PE and lactate dehydrogenase increase, as it was seen at least in one study, were risk factors associated with the development of ARDS and progression from ARDS to death [11]. Therefore, awareness and recognition of this complication at an earlier stage are necessary. In the above context heparin [12] is an indicated and valid anti-coagulant treatment. Additionally, its anti-inflammatory properties have the potential to benefit patients as well. The elevated D-dimer may be an indirect marker either for PE or for a latent increased inflammatory response in this patient. In the theory of the immune-thrombosis relationship where inflammation and thrombin formation are directly correlated as in COVID or like-COVID pneumonia, heparin could decrease the inflammatory response by blocking thrombin formation. Among the proposed mechanisms for COVID-19 induced-thrombosis is included a disease-specific hypercoagulopathy with diffuse microvascular damage due to inflammation substrate.

## CONCLUSIONS

Usually PE is a late complication of true COVID-19 patients due to diffuse microvascular damage and a state of hypercoagulopathy. In the aforementioned described case PE has been shown as a first manifestation of a like-COVID-19 pneumonia pattern which does not have an RT-PCR positive test but has presented some of the coagulopathy characteristics and positive radiologic features on chest HR computed tomography. This clinical pattern may cause difficulties to diagnose a like-COVID-19 or a true COVID-19 pneumonia syndrome and must be taken into consideration in the differential diagnosis.

## Disclosure statement

The authors did not report any potential conflict of interest.

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