

## Thrombophilia and COVID-19. A Case Report of Young Man 53 Years Old with Acute Cerebral Ischemia

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F. Foieni and M. Ciola contributed to the acquisition of data, clinical follow-up and editing the manuscript. G. Sala and M. Pistoia contributed to acquisition of data and clinical evaluation. A. Agostinelli, B. Valvo and P. Ghiringhelli contributed to editing the manuscript.

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## 1. Abstract

A 57-year-old male was admitted to our Hospital on March 2020 for SARS-Cov2 related interstitial pneumonia. Chest x-ray showed a bilateral interstitial-alveolar pneumonia and Blood gas analysis (BGA) in room air highlighted a severe respiratory failure (pO<sub>2</sub> 46 mmHg, pH 7.41). Due to clinical and biohumoral worsening (stable CRP at 24 mg/dL), tocilizumab (800mg) was performed after acquiring patient's informed consensus. In the evening, after 96 hours of hospitalization, the patient presented a clear hyposthenia / hemiparesis of the right hemisome whit hyperreflexia, confusion and slowed speech.

For suspected ischemic stroke, a basal brain CT scan was performed that excluded ongoing bleeding events. In conjunction with evidence of a significant increase in D-Dimer (from 2599 µg/L to 95090 µg/L - nv <500 µg / L), we decided to start the systemic thrombolysis with Alteplase with a slow and gradual recovery of the motility of the right upper and lower limbs. Thereafter, a rapid improvement of clinical status and biohumoral tests highlights, with a clear reduction in oxygen requirements, as if there was a thrombotic problem also in the pulmonary circulation. The case report supports the idea that thrombotic disease in the COVID-19 is a multiorgan problem [6].

## 2. Introduction

Disease due to SARS-Cov2 infection is characterized by severe interstitial pneumonia with respiratory failure that might need invasive ventilatory support. A state of hypercoagulability often occurs with pulmonary embolism or other systemic thrombotic manifestations. For this reason, the anticoagulant therapy is now considered a cornerstone of treatment in patients with COVID19.

It is not yet clear why a state of hypercoagulability develops but it seems that inflammatory state and endothelial damage are the main determinants.

Here, we report the case of a young man with COVID19 with interstitial pneumonia in which an ischemic stroke occurred. Fibrinolytic treatment solved the brain problem and significantly improved respiratory function.

## 3. Case Presentation and Follow Up

A 57-year-old male (DTN 1/10/1962) was hospitalized on March 2020 for SARS-Cov2 related interstitial pneumonia. He had no remarkable medical history except previous bilateral saphenectomy for chronic venous disease and concomitant therapy with benzodiazepine for insomnia. Body mass Index (BMI) was 37 (Obesity grade II).

Admitted to Emergency Room, He reported low-grade fever and marked asthenia for about a week, followed by dry, irritating cough and dyspnea. Moreover, He reported a contact with positive SARS-CoV2 subject 10 days before. The admission to the emergency room was justified by sudden worsening of symptoms with the onset of dyspnea at rest and desaturation (Finger pulse Oxymetry 82%).

Chest x-ray showed a bilateral interstitial-alveolar pneumonia and Blood gas analysis (BGA) in room air a severe respiratory insufficiency (pO<sub>2</sub> 46 mmHg, pH 7.41)

Entry blood tests revealed increased in CRP (26.88 mg/dL), LDH (549 U/L) and CK (708 U/L). D-Dimer level was slightly increased (762 mg/dL), such as transaminases. Complete blood count and renal function were normal. Nasopharyngeal swab was positive for

SARS-CoV2.

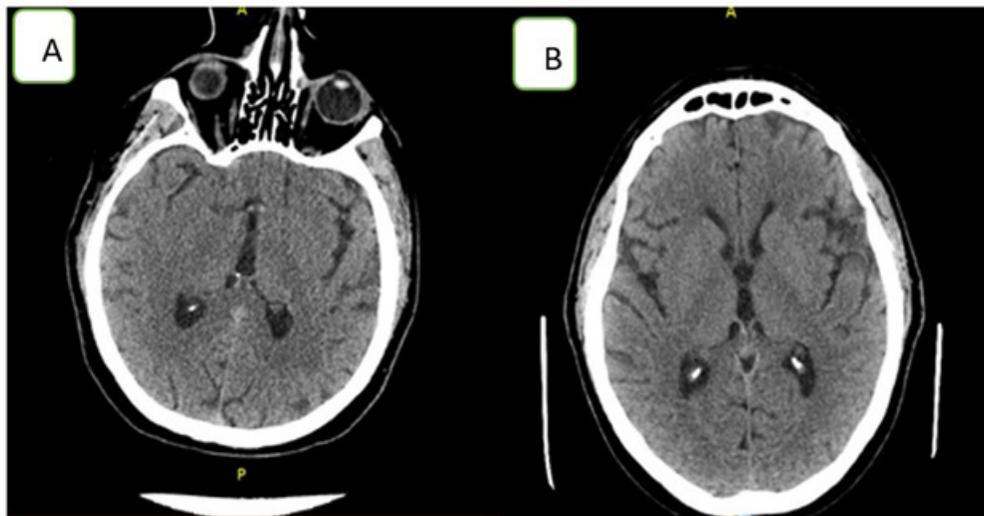
The evidence of the severe respiratory insufficiency requiring high oxygen flows with a reservoir mask at 15 l/min up to continuous positive airway pressure (CPAP) after only 48 hours of hospitalization. Therapy with ceftriaxone, azithromycin, hydroxychloroquine, dual antiretroviral, morphine and heparin prophylaxis (Clexane 4000 IU sc every 24 hours) was also set.

Moreover, we started enteral nutrition with naso-gastric probe (SNG).

Due to clinical and biohumoral worsening (stable CRP at 24 mg/dl), tocilizumab (800mg) was performed on 03/24/2020 (no contraindication), after acquiring patient's informed consensus. The Resuscitation evaluation agreed for continuation of ventilatory support with the CPAP helmet.



**Figure 1:** Chest-Xray



**Figure 2:** Cerebral\_CT before (A) and after (B) Thrombolysis

We observed an initial improvement in respiratory exchanges and the oxygen requirement was reduced to reservoir mask (15 L/min). In the evening, after 96 hours of hospitalization, the patient was found lying on the ground, prone, without oxygen therapy, unconscious and cyanotic. At the medical examination, he has a clear hyposthenia / hemiparesis of the right hemisome whit hyperreflexia, confused and with slowed speech.

For suspected ischemic stroke, a basal brain CT scan was performed that excluded ongoing bleeding events. In conjunction with evidence of a significant increase in D-Dimer (from 2599 µg/L to 95090 µg/L - vn <500 µg / l), it was decided to start the systemic thrombolysis with Alteplase (Alteplase 9 mg as a bolus and 81 mg as an infusion in one hour).

The morning after, we could see a slow and gradual recovery of the motility of the right upper and lower limbs. The speaking was normal. 24 hours later, a control brain CT scan was performed, which did not reveal any changes compared to the previous exam.

Antiplatelet and lipid-lowering therapy began.

Thereafter, a rapid improvement of clinical status and biochemical tests highlights, with a clear reduction in oxygen requirements. The patient began physiotherapy and ten days after was discharged at home with a negative nasopharyngeal swab.

#### 4. Discussion

This is a dramatic case of PCR confirmed COVID-19 infection presenting with a cerebrovascular accident. In the study of Mao et al., the patients with COVID-19 and neurological symptoms in Wuhan was 36.4 % of 214 patients. Neurological symptoms included headache, impaired consciousness, ataxia, acute cerebrovascular disease, seizures, hyposmia, hypogeusia and neuralgias. The patients with severe systemic presentations of COVID-19 were more likely to have neurologic symptoms in comparison with those with milder forms of the infection (acute cerebrovascular diseases 5.7 % vs. 0.8%)<sup>6</sup>. In a study by Li Y et al., the incidence of stroke in COVID-19 patients was about 5% with a median age of 71.6 years [8]. Average time of onset of stroke after COVID-19 diagnosis was 12 days and the levels of CRP and D-dimer, indicating a high inflammatory state and abnormalities with the coagulation cascade, was elevated [8].

In this case, the patient had high CRP levels (26.88 mg/dL in ER) and moderately elevated D-dimer levels (762 mg/dL); the onset of neurological symptoms occurred 11 days after the onset of COVID-19 symptoms.

The exact pathophysiology behind these cerebrovascular accidents is still to be determined.

Angiotensin converting enzyme-2 (ACE) receptors are the major entry points for SARS-Cov-2. Although ACE-2 receptors are present in the nervous system, alternate pathways have been proposed to explain the entry of SARS-CoV-2 into the nervous system, including direct injury to blood brain barrier, hypoxic injury, and immune-related injury [9].

Moreover, Kloka et al. demonstrated that 31% of critically ill ICU patients with COVID-19 develop thrombotic complications<sup>10</sup> and multiple reports of pulmonary emboli are currently available in the literature [11]. Recent autopsy studies have highlighted a thrombotic microangiopathy in multiple organs especially in the lungs and kidney [12,13].

With this evidence, the likely mechanism of early cerebrovascular accidents could be hypercoagulability leading to macro and micro thrombi formation in the vessels. Other pathophysiology could be directly related to the infection or hypoxia.

In this reported case, of patients with hypertension and obesity as vascular risk factors, we postulate that the SARS-CoV-2 induced hypercoagulability may be the most important mechanism of the cerebrovascular disease. The exceptional response to fibrinolytic therapy is a clear confirmation.

#### 5. Conclusion

Considerable evidence indicates that COVID-19 is associated with a hypercoagulable state, but the current data do not suggest the use of full-intensity anticoagulation doses unless otherwise clinically indicated. We discussed about a case of stroke in patient with Covid-19 that required fibrinolysis; fortunately, the patient had no complications and fully recovered motor function; we note that after the fibrinolytic treatment we have seen a marked improvement in lung function as if the treatment had been effective on issues of pulmonary microcirculation.

The case report supports the idea that thrombotic disease in the COVID-19 is a multiorgan problem [6,12,13].

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