

# Post Covid-19 delayed cytokine storm manifesting with ARDS and multifocal stroke

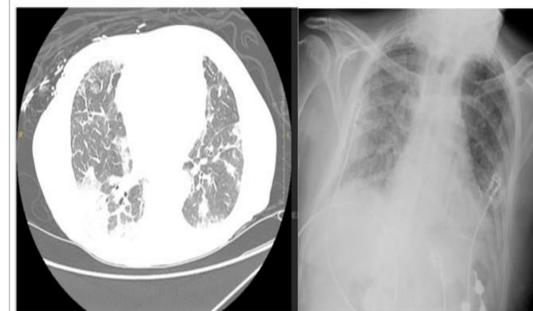
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## BACKGROUND

- While we are getting familiar with the acute manifestations of COVID-19 disease, the long-term effects remain uncertain. The term “long Covid syndrome” is used to describe the heterogenous symptomatology of patients who recovered from acute Covid-19 disease <sup>1</sup>.
- Although there are case reports on large ischemic stroke linked with Covid-19<sup>7</sup>, the literature on multifocal embolic CVA (cerebrovascular accidents) in "long-COVID" patients is almost nonexistent.
- We present a case of an elderly male previously hospitalized for covid-19 pneumonia who developed delayed cytokine storm culminating in ARDS and multifocal CVA.

## CASE REPORT

- An 84-year-old male with past medical history of diabetes and hypertension presented with fever, malaise, and hypoxia 2 weeks after hospitalization for COVID-19 pneumonia. Of note, he earlier received 2 doses of the COVID-19 vaccine three months prior to his initial hospitalization for COVID-19.
- Initial labs were unremarkable. Chest CT showed advanced peripheral pulmonary ground-glass infiltrate with more dense consolidation at the lung bases. He was diagnosed with post-viral bacterial pneumonia and treated with empiric intravenous broad-spectrum antibiotics.
- He did not improve despite adequate antimicrobial therapy, further work up was necessitated. CXR showed worsening pulmonary infiltration. Urine streptococcal and legionella antigens, HIV1/2, hepatitis screen, blood cultures, MRSA culture, sputum Gram stain and culture were all negative.



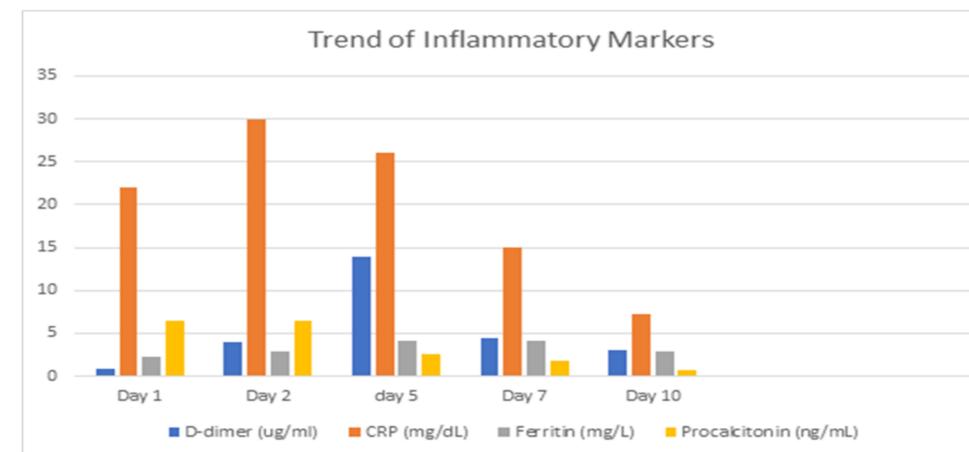
Initial Chest CT with peripheral ground-glass opacities (Left), with subsequent Chest Xray reflecting worsening infiltrates(right)

- Due to the persistent elevation of inflammatory markers and end-organ dysfunction, a diagnosis of post-covid delayed cytokine storm was made. He received systemic steroids and tocilizumab immunotherapy. There was gradual improvement in inflammatory markers with no corresponding improvement in oxygen requirement.

- He subsequently developed weakness of the right arm and left leg while on prophylactic anticoagulation. CT scan of the head showed bi-occipital and bi-parietal attenuation with some left caudate hypodensities, concerning for subacute multifocal CVA. There was atherosclerotic disease of the aortic arch and great vessels with no evidence of intracranial stenosis, aneurysm, or dissection. Thrombolytic therapy was not offered due to unclear duration of symptoms. TTE was negative and patient was in sinus rhythm.
- Due to worsening respiratory status and DNI/DNR status, he chose for continued non-invasive ventilation. He was discharged on home hospice.

## DISCUSSION

- Our patient was hospitalized and discharged for COVID-19 pneumonia and did not require oxygen supplementation at that time. His rehospitalization highlights the pervasive and unpredictable nature of Covid-19 related cytokine storm.
- Cytokine storm or cytokine release syndrome describes the life-threatening SIRS (Systemic Inflammatory Response Syndrome) associated with elevated levels of circulating cytokine and secondary end-organ dysfunction <sup>3</sup>. Various processes have been proposed as the mechanism with most underpinned at cytokine dysregulation involving mast cells and macrophages. <sup>4</sup>
- Repeat COVID-19 PCR was negative emphasizing a delayed inflammatory component. In an animal study reported by Song et al, delayed cytokine reactions were seen more in older subjects compared to younger subjects <sup>5</sup>. Although there was improvement in inflammatory markers with the tocilizumab and intravenous steroid, there was no corresponding improvement in clinical status.



Trend of Inflammatory markers

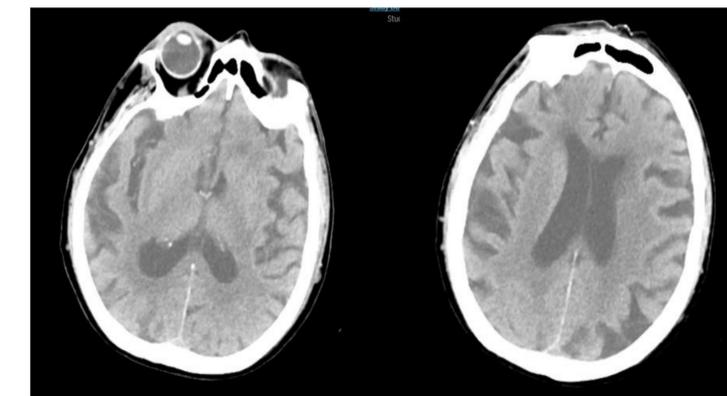
- Although there are increasing reported cases <sup>1,6,7</sup> of stroke in Covid-19 with a predominant feature reflecting extracranial thrombotic phenomenon, our patient had multifocal ischemic areas reflecting a possible embolic process. This case is unique in that this patient manifested features of acute covid-19 infection while repeatedly confirmed covid-19 negative. Therefore, this hypothesizes that sero-conversion does not prevent known covid-19 morbidities in elderly patients with elevated inflammatory markers.

## CONCLUSION

- The long-term effects of Covid-19 remains uncertain. Inflammatory markers could be assessed in elderly patients recently discharged from acute care settings in a bid to identify those at elevated risk for decompensation. In addition, this highlights the need for healthcare providers to consider delayed cytokine storm as a differential in poorly responsive patients.

## REFERENCES

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Non-contrast CT Head showing bi-occipital and bi-parietal attenuation with some left caudate hypodensities