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Recurrent Arterial Thrombosis in Young Adult, as Complication of Covid-19 Infection: A Case Report and Review of Literature

Kazim Mohammed [α], Abdullahi Bashir H Mohamud [σ], Mulham Mustafa [ρ], A. Sumeen [ω], R. Abdelgadir [¥], Muhammad Mohsin Khan (MD) [§] & Dr. Ali Raza [χ]

Abstract- **A 30-year-old male with no significant past medical history developed a stroke on day 15th of his COVID-19 Positive result with investigations showing Thrombosis of Left ICA/MCA. The patient underwent mechanical thrombectomy with adequate recanalization yet presented with a recurrent thrombus the next day. Hypercoagulable state is one of the unusual complications seen in COVID-19 positive patients with multiple pieces of literature pointing towards increased risk of venous thromboembolism, with stress towards VTE prophylaxis[1,2]. Arterial thromboembolism is a lesser-known sequela, often involves larger blood vessels correlating with increased inflammatory markers and severity of the disease, and such patients may need prolonged anticoagulation therapy.**

I. Introduction/background

In late December 2019, the first case of the novel coronavirus was first identified in Wuhan, China, and on Mar 11, 2020, the WHO officially declared it a worldwide pandemic. Since then, the world has faced many challenges to overcome and adapt. The novel Coronavirus can present in a spectrum ranging from asymptomatic to the critically ill, with 81% exhibiting mild symptoms[3]. Its high infection rate has left the medical world at unprecedented times with new aspects of the virus observed in each specialty and requires a multi-disciplinary approach to treat the many organs affected. Many studies point to the primary pathogenesis in ARDS/Multiorgan failure in these patients is a Hypercoagulable/Prothrombotic state. We want to present an otherwise healthy 30-year-old COVID-19 positive patient developing an Acute Stroke involving the ICA/MCA.

II. Case Presentation

A 30-year-old male with no known significant past medical history works as a construction worker presented to the ED by complaining of a fever, dry cough, headache, and a sore throat. He has a history of contact with his roommate, who was also experiencing similar symptoms. He denied shortness of breath or chest pain and tested positive for COVID-19 by real-time reverse Transcriptase- Polymerase Chain reaction Swap test (RT-PCR). The examination was unremarkable, a selective blood workup including CBC, CMP, CRP, and a G6PD screening, all of which showed no significant abnormalities. An initial chest x-ray performed at admission was unremarkable, and the patient transferred to the quarantine facility as per the CDC protocol.

On admission to the quarantine facility, repeat blood work was done, including an ECG and a repeat chest x-ray, which showed patchy consolidation in the left lower lung zone. The patient has remained stable, and without any complaints until the day 15th post positive COVID-19 PCR test, the patient collapsed and was unresponsive initially with a GCS score of 11. Vital signs were measured, showing a blood pressure of 99/62 mmHg, Heart Rate of 107 bpm, Oxygen Saturation of 92%, Random Blood Sugar 100 mg/dL, and the patient was afebrile. On examination, the patient showed right-sided facial palsy and hemiplegia with a power of the right upper limb and right lower limb of 0/5 and 2/5, respectively, left upper and lower limbs were 5/5 with intact sensation. The patient was immediately transferred to a specialized stroke unit by ambulance.

III. Investigations

Upon arrival to the ED, vitals were as follows: BP 120 /72, HR 100, oxygen saturation 93 % on room air, and picked up to 97% on 3 L nasal cannula, respiratory rate of 23, and afebrile. On examination, the patient was confused with global aphasia and muteness, right hemianopia, right gaze deviation, right facial weakness, and right hemiplegia (arm 0/5, leg 2/5). NIHSS score- 22 and mRS – 0. A repeated chest x-ray was done, noting air space opacity in the middle and lower lung zones bilaterally (figure 4). His Labs showed WBC-7.8, HCT47.5, INR1.1, Pt-12.5, APTT-25.9, CPR-58.7, Ferritin-619. Unfortunately, the D-Dimer sample was not sent to the lab.

Stroke protocol was activated, and an urgent CT scan along with a perfusion scan. A plain CT scan showed subtle hyperdensity in the left MCA *(Figure 1a)* with no apparent intracerebral or subarachnoid

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hemorrhage with normal ventricles in position and size subarachnoid spaces looked unremarkable. CT perfusion revealed CBF and CBV *(Figure 1b and 1c)* apparent mismatch in the left cerebral hemisphere, mainly in the left frontoparietal region in the left MCA territory with a delay in MTT/T max images, suggestive of tissue at risk. While in CT angiogram, there was the small filling defect of in the left CCA in the neck proximal to the bifurcation, plus partial filling defect left ECA in the neck along with narrowing of the lumen of the left CCA in petrous and cavernous segments with no opacification in the supra-clinoid part of the left CCA and also non-visualized M1 segment of the left MCA, suggestive of a partial block. In contrast, the right ACA/MCA and posterior circulation looked unremarkable.

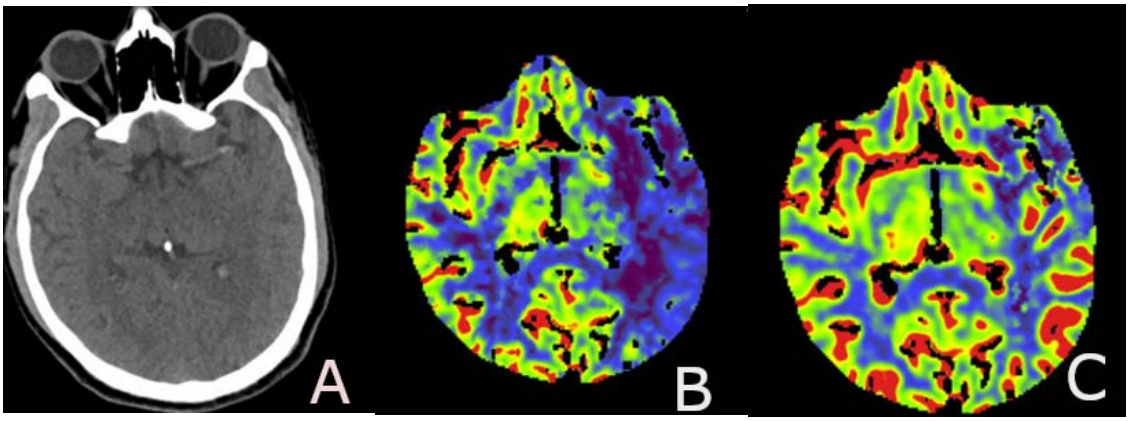


Figure 1A: Plain CT scan showed subtle hyperdensity in the left MCA

Figure 1b and 1c: CT perfusion revealed CBF and CBV apparent mismatch in the left cerebral hemisphere, mainly in the left frontoparietal region in the territory of the left MCA

IV Thrombolysis was initiated as per protocol with a bolus of Alteplase 6.3 mg, followed by an infusion of 56.7 mg. A neuro-interventionist was involved, and the patient underwent mechanical thrombectomy. Simultaneously, as per Qatar CDC guidelines, he was started on Azithromycin, Hydroxychloroquine, and Oseltamivir combination as part of his Covid-19 treatment based on worsened chest X-ray, after ensuring the QTC is below 450 on ECG in such patients.

A filling defect (floating thrombus) noted in the distal left CCA before bifurcation. Total occlusion of the Left ICA and MCA by a large thrombus load starting from the distal cavernous segment. Aspiration thrombectomy; which cleared up the floating thrombus using Solumbra technique (combined aspiration and mechanical thrombectomy) using Solitaire 6X40mm stent; two trials were made and cleared up the ICA and MCA with a final control angiogram revealing adequate recanalization TICI 3. 10 mg Verapamil was injected to overcome spasm in the Left ICA and Left M1 segment. The clots recovered were sticky and soft, suggestive of the embolic source. The intracranial vessels did not show any atherosclerotic features, and there is no evidence of carotid dissection. *(Figure 2a, 2b and 2c)*.

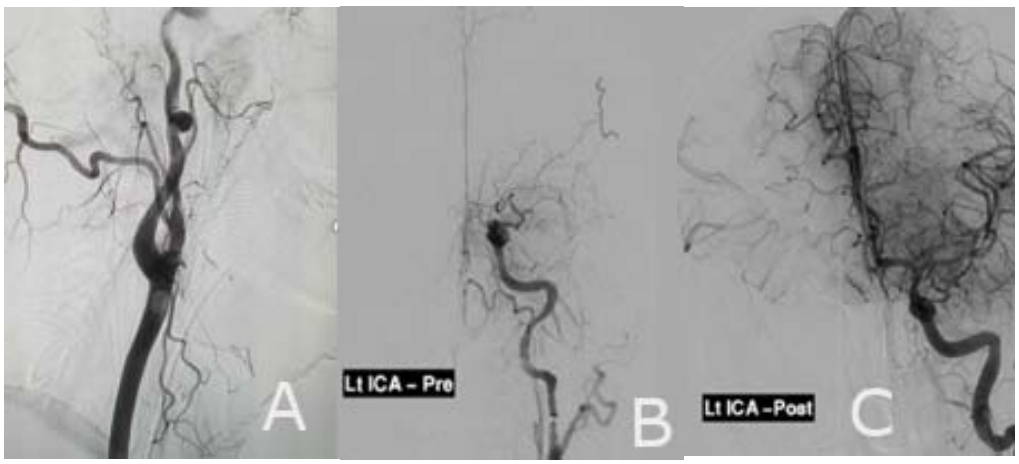


Figure: 2a showing a floating thrombus in the left CCA

Figure: 2b, and 2c show DSA Pre and Post Thrombectomy.

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The patient was admitted to the ICU in a monitored bed and continued to receive care according to the stroke management protocol; he remained aphasic with right-sided hemiplegia. There were No arrhythmias or ECG abnormalities. Follow up CT scan done 24 hours after the thrombectomy showed hyper-density in the left MCA, suggestive of recurrent thrombus. Repeat CT and CTA showed a significant interval increase in the extent of vascular occlusion, involving the entirety of the left internal carotid artery beyond the bifurcation and the M2 and M3 segments of the left MCA (previously only in the M1). Redemonstrations of the small filling defect in the left external carotid artery with no significant interval change. The right CCA, ICA, MCA, and both ACAs appear patent with no evidence of occlusion, and the vertebrobasilar system appears patent with no evidence of occlusion as well *(figure 3)*.



Figure 3: CTA done post thrombectomy reconfirming the recurrence of the thrombus in the Left ICA, MCA.

A cardiac echo done to rule out any source of thrombo-emboli was unremarkable. Serology work up for Lupus anticoagulant showed the first sample to be negative; however, the repeated sample tested positive with negative anticardiolipin and negative Anti Glycoprotein. His Protein C, Protein S, and ATA were normal. Connective Tissue disorder workup was done, with ANA, full ENA panel, which was healthy.

IV. Differential Diagnosis

In this case, the primary etiology of stroke is COVID 19 related thrombo-inflammation leading to stroke or coagulopathy related to the virus, less likely cause is ischemic stroke as the patient is young without any co-morbidities.

V. Treatment

The patient was started on anticoagulation (enoxaparin and followed by warfarin) with an INR target of 2-3, with a plan to repeat DSA after four weeks of anticoagulation treatment. He was tested negative on two samples of the COVID-PCR swab test, taken 24 hours apart on day 25th, with repeat chest x-ray showed regression of the bilateral pulmonary consolidation and infiltration, and the patient is more alert and awake, started verbalizing but has slurred speech.

VI. Outcome and Follow-up

The patient is still undergoing treatment understroke and rehab unit, with an active rehab session, and is expected to be transferred tothe rehabilitation unit.

VII. Discussion

Thromboinflammation or COVID-19-associated coagulopathy (CAC)[4], is a term coined for Hypercoagulable state in Covid-19, characterized by an elevation in procoagulant factor levels including fibrinogen, and an increase in D-dimers correlated with higher mortality. The occurrence of thromboembolic events in Covid-19 disease has been proven by Post-mortem examination of COVID19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings of lungs and other organs suggesting vascular dysfunction[5].

Oxley TJ et al. [6] presented 5 cases of Young adults (all aged between 33-40 years) who have developed stroke due to large vessel involvement and tested Coivd-19 PCR positive. While our example is also

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a young adult without any co-morbidities, it is interesting to note that his chest X-ray progressed to worse on the day of the stroke and even the inflammatory markers were highest on the day of the stroke, raising a high level of suspicion of association between COVID-19 related inflammation and stroke *(Figure 4, & 5)*. Further investigational studies are required to know if early treatment in such a patient could prevent stroke, as in our case, even though he was tested positive, he was started on Covid-19 Treatment protocol only after he developed stroke and repeat X-ray showed B/L pneumonia.



Figure 4: Chest x ray done at Day 1 of Covid-19 PCR positive results, Day 3 showing Left basal Patch and Day 15 when patient developed Stroke, Showing Progression of the Pneumonia.

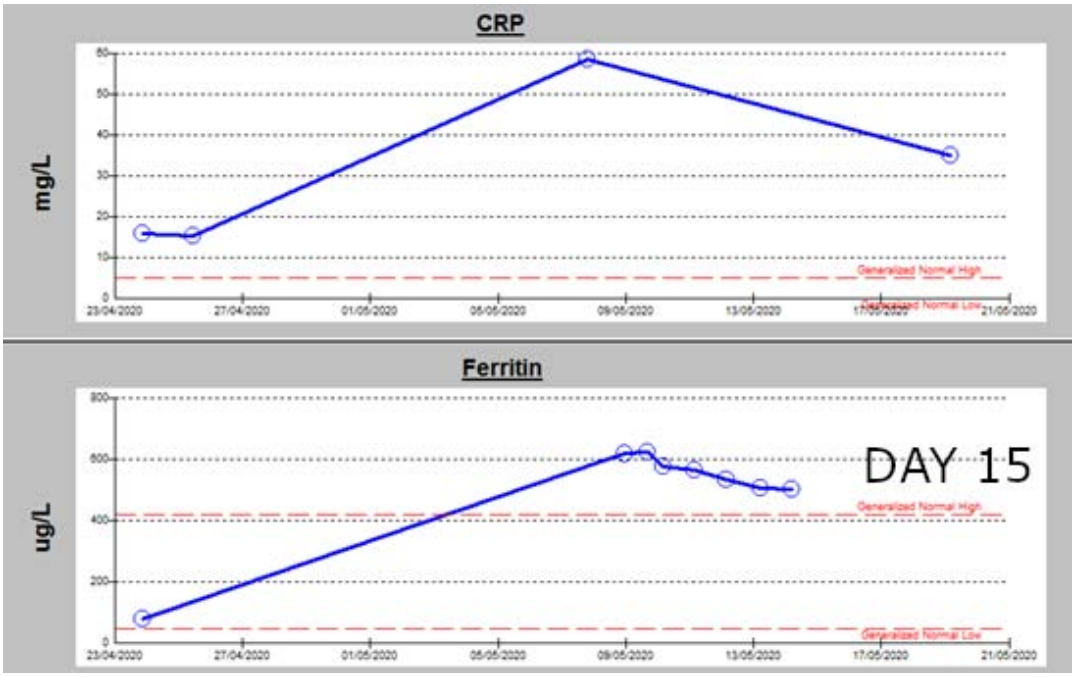


Figure 5: Graph co-relating the highest peak of inflammatory markers to the day of the stroke.

Although Serology workup for Lupus anticoagulant came positive on the repeated second with negative anticardiolipin and negative anti Glycoprotein, the underlying antiphospholipid syndrome (APS) is still suspicious considering the high rates of false positives rates of lupus anticoagulant, and the presence of Lupus antibodies (aPL) in other settings including infection, bacterial/Viral, Medications, Malignancy besides APS, either transiently or persistently[7]. McNally T,8, in his report, "The use of an anti-beta 2-glycoprotein-I assay for discrimination between anticardiolipin antibodies associated with infection and increased risk of thrombosis," concluded that the alpha-beta 2GPI assay is harmful in patients with transiently positive ACL assays associated with infection. We plan to repeat the Anti-lupus anticoagulant test after 12 weeks. However, it would be interesting to know if Covid-19 disease does increase the occurrence of Anti-phospholipid syndrome and related thrombotic events. Though limited data of just 6 cases of COVID infection-related large vessel stroke, including ours, Anterior circulation (ICA/MCA) is the most common site of thrombus occurrence. In contrast, just one case involving posterior circulation is reported in the cases described by Oxley TJ et al6.

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Though Oxley et al6, in his case, reported complete resolution of the thrombus after ten days of anticoagulation, our situation was complicated with the recurrence of thrombus the next day. We plan to repeat DSA after four weeks of anticoagulation treatment.

VIII. Learning Points/Take Home Messages

- Large Vessel thrombus in Covid-19 positive patient could be a new etiology of stroke.
- The association between the Inflammatory peak, the formation of thrombus, and stroke occurrence need to be further investigated.
- Along with the effectiveness of anticoagulation and early treatment of Covid-19 infection in preventing such stroke is yet to be determined.

Conflict of Interest:

All authors declare no potential conflicts of interest to disclose related to the publication of this case series.

Author Contributions: KM, AH identified the cases, obtained informed consent and wrote the initial manuscript. MMK assisted in the literature review and manuscript writing. AH reviewed the case as infectious disease experts. Rest contributed to the manuscript writing, literature review and discussion. was also involved in image selection and critically revising the manuscript to its final form. All authors approved the final version for submission.

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