Acute Arterial Ischemic Stroke Secondary to COVID-19 Infection

Abdullah Ismail, MD[1]; Phillip J Gross, MD MPH[1]
[1]: Northeast Georgia Medical Center- Department of Internal Medicine

Northeast Georgia Medical Center
GRADUATE MEDICAL EDUCATION

Objectives

- Recognize the association between COVID-19 and hypercoagulability
- Understand the pathogenesis of COVID-19 associated hypercoagulability
- Recognize complications of these thrombotic events such as ischemic strokes
- Recognize possible treatment and prophylaxis for future cases
- Understand how this case serves as a unique example of new complications associated with this novel disease

Introduction

- COVID-19 rates are increasing rapidly especially with the presentation of new variants
- Current total cases in the United States alone are approximately 42 million, with a death total over 670,000
- New complications are being discovered daily and long term sequelae are not fully understood
- Thrombotic complications are increasing in occurrence, and may lead to worse overall outcomes
- Incidence of thrombotic disease in COVID infected patients are up to 31%

Diagnosis

- COVID-19 PCR to confirm infection
- Symptoms of COVID-19 respiratory infections present
- Symptoms of acute CVA
- Lab studies including elevated D-dimer, prolonged PT/INR, increased Fibrinogen
- Infarctions found on imaging such as CT and MRI brain

Pathogenesis

- Pathogenesis not fully known, multiple mechanisms are being evaluated
- SARS-CoV-2 binds to ACE2 receptor which leads to upregulation of coagulation cascade factors
- Increased production of FGF and PLA2 lead to fibrinogen production
- SARS-CoV-2 binds TLR9 which stimulates multiple inflammatory mediators
- SARS-CoV-2 also activates TBXAS which assists in the production of Thromboxane A-2, leading to platelet aggregation
- Combination of these factors lead to increased fibrin production therefore leading to hypercoagulability

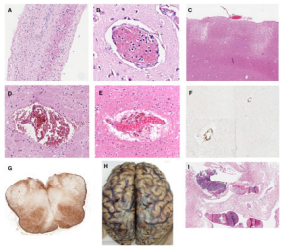

Figure 1: B) Microthrombi in small intraparenchymal blood vessels in brain stem C) Ischemic areas in occipital cortex D-E) Microhemorrhages and hemosiderin laden macrophages in vessels of brain stem I) Leptomeningeal vessels with septic thrombi (Image from Fabbri et al., 2020)

Labs and Imaging

Sodium	137
Potassium	3.1
CO2	23
Chloride	105
BUN	13
Creatinine	1
Glucose	279
AST	25
ALT	70
Protein	6.4
Albumin	2.8
Bilirubin	0.4
Calcium	8.2
ALP	74
AG	9
EGFR	80.3

SARS-COV-2 PCR	Positive
RSV PCR	Negative
Influenza A	Negative
Influenza B	Negative

CRP	7.1
Sedimentation Rate	67
Ferritin	541.3
D-Dimer	0.544
Fibrinogen	604

PT	14.1
INR	1.23
APTT	24.6

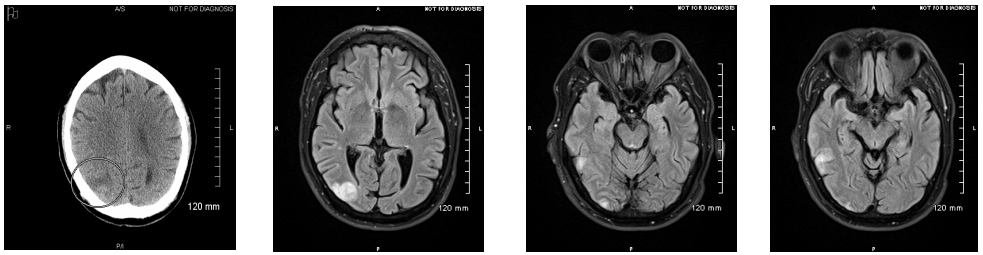

Figure 2: A) CT Brain Without Contrast: Focal area of decreased attenuation extending through the cortex in the posterior parietal region on the right B-D) MRI Brain With/Without Contrast: Focal Abnormal T2 FLAIR high signal involving the cortical aspects of the right occipital lobe and right temporal lobe

Case Presentation

- A 62-year-old patient with a past medical history of hypertension and insulin-dependent diabetes presented to the ED with seizure like activity
- Spouse reported that he was about to take a nap after dinner and began shaking, foaming in mouth, bit his tongue, and was staring blankly
- Reportedly experienced multiple seizure-like episodes over a 30-minute time span, and then had another en route to the ED
- Was given a sedative during transport and was at baseline mentation upon admission
- Recent medical history was notable for having COVID-19 infection for the past 14 days. Patient stated that he had lost 14 pounds during this time period, attributing it to the infection and associated diarrhea
- At presentation to the ED, patient denied any current symptoms of infection and was vitally stable other than an increased pulse of 106 and blood pressure of 166/89
- Labs were notable for a potassium of 3.1, A1C 9.1, glucose of 279, ESR 67, CRP 7.10, TSH 0.306, and THC value of 171
- CT brain without contrast was done and showed focal area of decreased attenuation extending through the cortex
- MRI brain with and without contrast further showed early subacute infarction of the right occipital lobe and right temporal lobe, with no hemorrhagic transformation.
- CTA head and neck was unremarkable
- EKG conducted at admission showed sinus tachycardia
- TTE and venous duplex scan were also unremarkable
- Telemetry was negative for arrhythmias
- TEE was conducted and showed no thrombus at the left atrial appendage, but a small PFO on atrial septum was present on color flow with left to right shunting. On saline bubble study the shunt was further confirmed with coughing
- With consultation of neurology, a diagnosis of acute ischemic stroke due to hypercoagulability associated with COVID-19 infection was made
- No subsequent seizure like activity was reported during hospital stay
- Patient discharged with recommendations to take Eliquis starting at a 10 mg dose for one week, then titrating to 5 mg on the second week, for a total 1-month course. Patient was also instructed to continue with Aspirin 81 mg and Lipitor 40 mg daily

Discussion

- In this patient, the acute cerebral vascular event was likely due to the hypercoagulation associated with COVID-19 infection
- Patient was COVID-19 positive for 14 days prior to thrombotic event
- Imaging confirmed subacute infarctions in multiple regions of the brain, which emphasizes the importance of evaluating the association between this infection and hypercoagulability
- During hospital stay, patient presented with no further thrombotic or neurological events
- Patient was discharged with Eliquis which was titrated down, and eventually switched to Aspirin
- COVID-19 has become an important topic in the medical field due to its rapid spread and increased mortality rates
- With infection rates continuing to reemerge, it is imperative to further analyze these associations as more cases of thrombotic related events may occur

Conclusion

- Hypercoagulability is a sequelae of COVID-19 infection
- Current research has shown that the use of anticoagulation may significantly decrease the risk of mortality in these patients
- Current medications of choice include unfractionated heparin, which also is known for its suppression of inflammatory mediators such as IL-6/IL-8
- Mechanisms behind the hypercoagulable state are not fully understood, and need to be evaluated further
- Future use of additional modalities for coagulation status should be implemented for COVID-19 patients, such as thromboelastography (TEG)

References

Centers for Disease Control and Prevention. (n.d.). *CDC Covid Data tracker*. Centers for Disease Control and Prevention. Retrieved September 19, 2021, from https://covid.cdc.gov/covid-data-tracker/#datatracker-home.

Fabbri, V. P., Foschini, M. P., Lazzarotto, T., Gabrielli, L., Cenacchi, G., Gallo, C., Aspide, R., Frascaroli, G., Cortelli, P., Riefolo, M., Giannini, C., & D'Errico, A. (2020). Brain ischemic injury in covid-19-infected patients: A series of 10 post-mortem cases. *Brain Pathology*, *31*(1), 205–210. https://doi.org/10.1111/bpa.12901

Fabbri, V. P., Foschini, M. P., Lazzarotto, T., Gabrielli, L., Cenacchi, G., Gallo, C., Aspide, R., Frascaroli, G., Cortelli, P., Riefolo, M., Giannini, C., & D'Errico, A. (2020, November 2). *Brain ischemic injury in covid-19-infected patients: A series of 10 post-mortem cases*. Wiley Online Library. Retrieved September 19, 2021, from https://onlinelibrary.wiley.com/doi/10.1111/bpa.12901.

Ilonzo, N., George, J. M., Choinski, K., & Ting, W. (2021). Anticoagulation, statins and "arterial thrombotic Sequalae after covid-19: Mind the gap." *Annals of Vascular Surgery*. https://doi.org/10.1016/j.avsg.2021.05.025

Johansson, A., Mohamed, M. S., Moulin, T. C., & Schiöth, H. B. (2021). Neurological manifestations of covid-19: A comprehensive literature review and discussion of mechanisms. *Journal of Neuroimmunology*, *358*, 577658. https://doi.org/10.1016/j.jneuroim.2021.577658

Kichloo, A., Dettloff, K., Aljadah, M., Albosta, M., Jamal, S., Singh, J., Wani, F., Kumar, A., Vallabhaneni, S., & Khan, M. Z. (2020). Covid-19 and hypercoagulability: A Review. *Clinical and Applied Thrombosis/Hemostasis*, *26*, 107602962096285. https://doi.org/10.1177/1076029620962853

Rico-Mesa, J. S., Rosas, D., Ahmadian-Tehrani, A., White, A., Anderson, A. S., & Chilton, R. (2020). The role of anticoagulation in covid-19-induced hypercoagulability. *Current Cardiology Reports*, *22*(7). https://doi.org/10.1007/s11886-020-01328-8