Clinical Presentation of Immune-Mediated Post SARS-Cov-2 Encephalitis and Vasculitis

Mancilla TR, MD, PhD; Lee J, BS; Hills W, MD; Stanford P, MD

EASTERN IDAHO REGIONAL MEDICAL CENTER

Background

- Acute viral encephalitis accounts for 20-50% of encephalitis hospitalizations with the most common etiologies being HSV, VZV, enteroviruses, and arboviruses[1].
- Prognosis is typically poor with worse outcomes in the elderly, pediatrics, or patients presenting with a Glasgow score 3-8[2].
- Treatment is primarily supportive with airway and fluid management. There is poor evidence for the use of steroids to control inflammation[4].
- It was noted early in the COVID-19 pandemic that SARS-Cov-2 could present with neurological manifestations[1,5-6].
- Autopsy of one patient with neurological manifestations of COVID-19 revealed SARS-CoV-2 in the CSF and brain tissue[8].

Case Presentation

A 19-year-old female presented status post-COVID-19 infection with sporadic episodes of numbness, urinary incontinence, nausea, and diarrhea. Two weeks prior the patient had been worked-up for new onset migraines and found to incidentally have COVID-19. The patient's past medical history includes polycystic ovarian syndrome with NuvaRing, prediabetes, and depression. The patient denied smoking or vaping.

Shortly after being found COVID-19 positive the patient developed intermittent, alternating, one-sided weakness usually lasing 10 minutes. The patient sought care after an episode of right-sided weakness that had not resolved for over 24 hours. She reported chest pressure without shortness of breath and had one episode of urinary incontinence. She also complained of blurry vision, diplopia, and flashing lights.

The neurological exam was positive for confusion, difficulty differentiating left and right, and a word-finding deficit. Physical exam demonstrated decreased sensation to the right hemibody, proximal right upper extremity strength 3/5, distal right upper extremity strength 5/5, and right lower extremity strength (distal and proximal) 0-2/5. Left upper and lower extremity strength were both 5/5.

An MRI of the brain demonstrated multiple areas of restricted diffusion and a CT angiogram of the head and neck showed intracranial vessels to have an irregular appearance with multiple areas of focal stenosis. She had elevated inflammatory and autoimmune markers, but viral RNA was not found in the patient's CSF. A viral and bacterial panel of the CSF was pan-negative as well. The patient was diagnosed with a Post-COVID immune-mediated encephalitis and cerebral vasculitis.

The patient was treated with levetiracetam 500 mg BID, Dexamethasone 4 mg every 6 hours, IVIG 0.4 mg/kg for 5 days, and Tocilizumab 400 mg once. She responded almost immediately to treatment, but a full recovery was slow and required continued physical and occupational therapy in inpatient rehabilitation.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Results

Coagulation	Value
D-Dimer	0.51 (0.00-0.49)
LA PTT Screen	27
LA dRVVT screen ratio	48
Immunology	**Value**
ESR	23, 63 (0-20)
Sjogren's antibody	a: 3.7; b <0.1

Table 1. Pertinent Positive Labs. As seen below, the patient had many negative or normal labs screening for autoimmune diseases. However, she had an elevated D-dimer and elevated LA (lupus anticoagulant) dRVVT screen indicating an increased coagulability. This is inconclusive for LA and would require further work-up to confirm the presence of LA in the blood.

The immunology portion of the table demonstrates an elevated ESR. The labs were performed on 1/24 and 1/26. The ESR may have peaked at a larger value. A repeat on 2/5 had returned to normal at 19. Sjogren's A antibody is found in 60-80% of Sjogren's patients while the B antibody is found in only 30-50%.

Pertinent Negative/Normal Labs

- Chemistry: ACE, TSH, FT4, CRP, Ferritin
- Immunology: Rheumatoid Factor, ANA, ANCA, anti-proteinase 3, anti-myeloperoxidase, Beta-2-GPI IgG/A/M, anti-cardiolipin IgG/A/M, phosphatidylserine IgG/A
- Serology: PRP, HIV, TB
- Coagulation: Protein C, Protein S, Antithrombin III Activity, Factor 5 Mutation
- Miscellaneous: Factor II Mutation, Il-6, Lysozyme

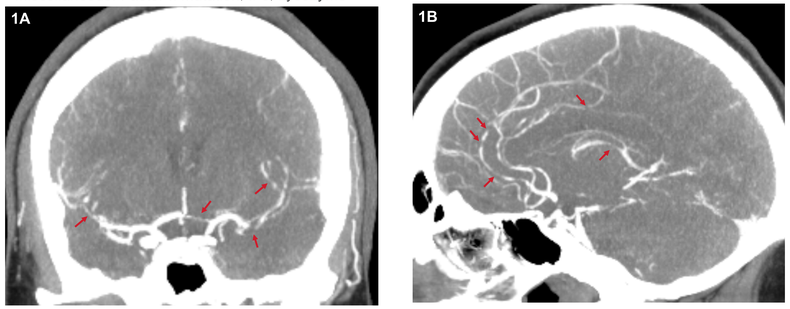

Figure 1. CT Angiography of the Head

1A coronal and **1B** sagittal representative slices of vessel abnormalities from patient presentation on 01/23/2023. Arrows indicate some examples of focal stenosis.

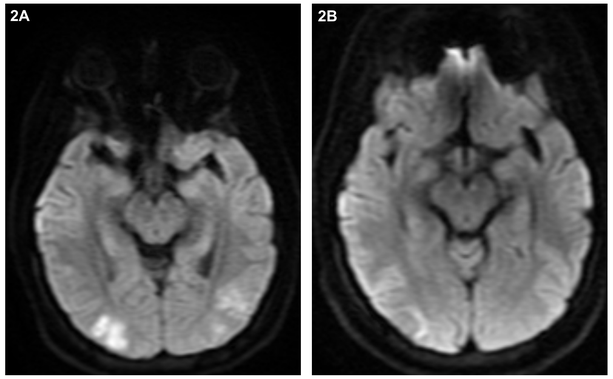

Figure 2. Diffusion-Weighted Chronologic Comparison

2A MRI taken 01/23/22 upon presentation. Representative example of restricted diffusion secondary to inflammation and swelling. **2B** MRI taken 03/04/22 after resolution of symptoms.

Discussion

- Young adult female presented with highly atypical symptoms almost two weeks after being diagnosed with COVID-19
- Initial symptom that prompted testing was new onset migraines
- Imaging found encephalitis and cerebral vasculitis
- CSF was negative for COVID-19 by PCR
- Positive results for some indicators of an autoimmune process
- Likely genetic predisposition to autoimmune disease
- Good response to IVIG, steroids, and tocilizumab
- Highlight: CNS damage likely due to immune response to COVID-19 infection and responded well to aggressive therapy

Conclusion

Neurological manifestations of COVID-19 infection, including encephalitis, were abundant during the pandemic. Cerebral vasculitis is a less common finding. Given that the majority of cases are in patients > 50 years of age, our patient's predisposition to an autoimmune disease may explain why she developed the encephalitis/vasculitis.

It is important that patient's with COVID-19 associated neurological symptoms be treated for their COVID-19 infection, as well as tested/treated for an autoimmune process. It is well-documented that viral illnesses can precipitate autoimmune diseases. Symptoms can progress quickly, so aggressive and early treatment is imperative.

References

1. Tyler KL. Acute viral encephalitis. N Engl J Med. 2018 Aug 9; 379(6):557-566.
2. Shives KD, Tyler KL, Beckham JD. Molecular mechanisms of neuroinflammation and injury during acute viral encephalitis. J Neuroimmunol. 2017 Jul 15; 308:102-111.
3. Collantes MEV, Espiritu AI, Sy MCC, Anlacan VMM, Jamora RDG. Neurological manifestations in COVID-19 infection: A systematic review and meta-analysis. Can J Neurol Sci. 2021 Jan 15; 48(1): 66-76.
4. Graham EL, Koralnik, IJ, Liotta EM Therapeutic approaches to the neurologic manifestations of COVID-19. Neurotherapeutics. 2022 July 21; 19: 1435–1466.
5. Yousuf F, King R, Ainger T, Hessler A. Autoimmune encephalitis following recovery of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Neurology. 2021 Apr 13; 96: 2756.
6. Khoo A, McLoughlin B, Cheema S, Weil RS, Lambert C, Manji H, Zandi MS, Morrow JM. Postinfectious brainstem encephalitis associated with SARS-CoV-2. J Neurol Neurosurg Psychiatry. 2020 Sep; 91(9):1013-1014.
7. Montaut, V, Madigan S, Pugin D, Clerc, O, Haesler L. Corticosteroid responsive encephalopathy: prolonged coma in catients late in the course of dreadful severe acute respiratory syndrome Coronavirus 2 infection. Critical Care Explorations. 2020 Oct ; 2(10): e0248.
8. Timmons GM, Rempe T, Bevins EA, Goodwill V, Miner A, Kavanaugh A, Ritter M, Graves JS. CNS lymphocytic vasculitis in a young woman with COVID-19 Infection. Neurol Neuroimmunol Neuroinflamm. 2021 Jul 28; 8(5): e1048.

HCA Healthcare®