Tumefactive Acute Disseminated Encephalomyelitis after Recent Covid-19 Infection: A Case Report

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**ABSTRACT**

**Objective:** To report a case of a patient with recent mild to moderate COVID-19 infection who developed tumefactive acute disseminated encephalomyelitis.

**Methods:** Patient data were obtained from medical records from the University of Wisconsin – Madison Hospitals in Madison, WI, USA.

**Results:** We report a 59-year-old man with past medical history notable for atrial fibrillation, biventricular pacemaker, end-stage renal disease secondary to idiopathic fibrillary glomerulonephritis, on hemodialysis awaiting transplantation, who presented with ongoing cognitive changes and pneumonia. He was repeatedly COVID-19 positive with minimal symptoms for 4 weeks prior to admission. He developed right sided hemiparesis and persistent, progressive encephalopathy manifesting primarily with disorientation, agitation, and aggression. CSF was notable for cell count of 7, protein of 48, and glucose of 65. Anti-MOG antibody and AQP-4 antibody were negative. A series of CT/CTA head imaging with and without contrast showed progressive multifocal supratentorial areas of white matter hypodensity and MRI head with and without contrast demonstrated progressive multi-focal large ovoid T2 FLAIR hyperintensities, partially ring enhancing on contrasted portion of study, consistent with tumefactive demyelinating disease. Significant improvement in mental status and right sided hemiparesis symptoms was observed with initiation of corticosteroids.

**Conclusion:** This case study provides neuroimaging evidence and clinical correlation to support that SARS–CoV-2 and resultant COVID-19 infection can lead to tumefactive acute disseminated encephalomyelitis. This complication has not been previously documented associated with recent COVID-19 infection.

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**Introduction**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the novel coronavirus responsible for the COVID-19 pandemic affecting. COVID-19 pandemic has infected over 38 million people with over a million deaths [1]. In COVID-19 cases, the most commonly reported neurological manifestations are disruptions and/or loss of smell and taste, vertigo, headache, impaired consciousness, seizures, ataxia, and acute cerebrovascular disease. One of the rare sequelae include acute disseminated encephalomyelitis (ADEM). Tumefactive ADEM, a rare variant of ADEM, had never been previously described or associated with COVID-19 infection.

ADEM is a rare autoimmune disease that affects the central nervous system and often occurs after systemic illness. Incidence is estimated to be 1 to 250,000 yearly, and in up to 75% associated with a preceding infection [2]. The hallmark symptoms for this disease are multifocal neurologic symptoms and encephalopathy. The most common viral infections that have been linked to ADEM are influenza, measles, mumps, rubella, herpes simplex, varicella-zoster, Epstein Barr virus, and cytomegalovirus [2]. The pathophysiology is uncertain but is thought to be a cell-mediated response or auto-antibodies cross-reacting with myelin antigens in the CNS. ADEM is typically responsive to immunosuppression with high-dose intravenous glucocorticoids but intravenous immune globulin (IVIG), plasma exchange, or cyclophosphamide may be effective for refractory cases. ADEM can mimic initial presentations of other primary CNS demyelinating diseases such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMO.). ADEM is a subset of myelin-oligodendro-glycoprotein (MOG) encephalomyelitis [3]. Tumefactive acute disseminated encephalomyelitis is a rare form of demyelinating disease that is most frequently seen in multiple sclerosis [4]. There have been case reports of tumefactive ADEM in non-multiple sclerosis patients, and none in recent COVID-19 positive patients [5-8]. Tumefactive ADEM is not frequently reported as a post-viral sequela, with a small number of case reports showing association to HIV, H1N1 influenza virus, and following HPV vaccination [9]. There have been no case reports to date linking COVID-19 infection to tumefactive ADEM. The patient in the following case report manifested with altered mental status and right sided hemiparesis symptoms associated with COVID-19 infection.

**Case Report**

A 59-year-old male was admitted to outside hospital after presenting with 2 weeks of cognitive changes, including memory loss and disorientation. His past medical history was notable
for atrial fibrillation, biventricular pacemaker, end-stage renal disease secondary to idiopathic fibrillary glomerulonephritis, on hemodialysis awaiting transplantation. He was COVID-19 positive 4 weeks prior to admission after being screened prior to a hemodialysis appointment and was asymptomatic. Upon presentation, the patient had repeated COVID-19 testing which remained positive. Head CT was obtained for altered mental status and demonstrated multifocal supratentorial areas of white matter hypointensity, deemed to be nonspecific but likely to represent microangiopathic white matter disease. He was treated for community acquired pneumonia with intravenous cefepime. This was changed to intravenous piperacillin/tazobactam after 4 days due to worsening confusion and agitation with concern for possible cefepime encephalopathy. Additionally, acyclovir was started empirically with concern for herpes encephalitis. A lumbar puncture was performed not felt to be consistent with bacterial meningitis. CSF returned notable for cell count of 7, protein of 48, and glucose of 65. HSV later returned negative and acyclovir was thus discontinued. Given the patient’s persistent altered mental status, head CT was repeated and was found to be stable. At request of family, the patient was transferred to our facility.

Upon arriving at our facility, the patient was tested again for COVID-19 and was found to be negative, 10 days after prior positive test. He was agitated and uncooperative to complete neurological examination. Exam was notable for disorientation, difficulty following commands, moving all four limbs spontaneously against gravity, hyperactive reflexes diffusely, and upgoing plantar response bilaterally. Metabolic screen was notable elevated BUN (114), it was felt ongoing encephalopathy was secondary to cefepime and uremic encephalopathy. Repeat surveillance CT imaging was obtained 4 days later and demonstrated progressively increased conspicuity of subcortical rounded foci of hypointensity throughout the bilateral frontoparietal regions without mass effect. The size of the lesions was unchanged compared to initial head CT. The patient’s exam was largely limited due to agitation, was similar to previous but now demonstrated possible mild right sided hemiparesis.

One-week post-transfer patient showed consistent confusion and clinical progression of right sided weakness. Specifically, the patient was minimally verbal, unable to follow commands, with a right facial droop but was spontaneously moving all extremities. CT imaging CT/CTA of head and neck with and without contrast demonstrated multi-focal hypoattenuating lesions observed to partially ring enhancing on the contrasted portion of the study, suggestive of demyelinating disease. To better delineate the ring enhancing lesions, MRI head and cervical spine with and without contrast redemonstrated multi-focal hypointensities lesions observed to progressively increase in size over the subsequent weeks. The patient was initiated on methylprednisolone a 5-day course with plans to be followed with tapering methylprednisolone therapy. The patient’s exam was largely limited due to agitation, was similar to previous but now demonstrated possible mild right sided hemiparesis.

Discussion
This case is an important addition to the literature in regard to neurological complications related to COVID-19. The literature includes several cases of ADEM related to COVID-19 however this is the first known case of tumefactive ADEM associated with COVID-19.

Take Home Points
- SARS-CoV-2 is a novel virus with an increasing number of neurological complications, and it is imperative to continue to document all associated conditions.
- Tumefactive ADEM is not normally seen as a post-infectious complication unlike ADEM. This possible speaks to COVID-19 and its unknown pathophysiology and evolving literature surrounding neurological complications from infection.
- This patient had a recent COVID-19 infection and was tested negative when the tumefactive ADEM developed. This is important so that clinical suspicion does not lessen even after testing negative for COVID-19.
- The severity of disease in this patient with genetic susceptibility to autoimmune processes as evidenced by his idiopathic fibrillary glomerulonephritis highlights how much COVID-19 can affect genetically susceptible patients, increasing clinical suspicion for complications.
- This is the first documented case of severe tumefactive acute disseminated encephalomyelitis post-COVID-19 infection to date.

References
of neurologic conditions.

