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Catatonia in the Setting of Suspected COVID-19 Associated Autoimmune Rhomboencephalitis in a Patient With no Known Psychiatric History: A Case Presentation

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Case:

We present the case of a 42-year-old female with no significant past medical or psychiatric history who presented to the emergency department via emergency medical services (EMS) with altered mental status, upper extremity contractures and urinary incontinence. Upon initial evaluation, she was found to be COVID-19 positive and was worked up for status-epilepticus. She was given ativan and responded with positive effect. Once hospitalized, she was started on keppra for seizure prophylaxis and steroids for COVID-19. Magnetic Resonance Imaging (MRI) on day 8 showed rhombencephalitis. On day 15, a nursing member suspected catatonia due to posturing and psychiatry was consulted. Patient underwent an ativan challenge and responded. Patient was trialed on high dose steroids, intravenous immunoglobulin (IVIG) and plasmapheresis with no significant improvement to mental status. On day 63, the patient started electroconvulsive therapy (ECT), after 9 sessions improvement was seen, however the patient has not completely returned to baseline.

Introduction:

Encephalitis is the presence of inflammation in the brain, usually due to an infection or autoimmune response. Although inflammation can occur in any part of the brain the temporal lobe, frontal cerebral cortex, basal ganglia, and thalamus are most commonly affected (Aziz et al., 2021). Autoimmune encephalitis typically takes weeks to months to present, whereas infectious causes of encephalitis tend to present within several days to weeks.

Autoimmune encephalitis has been linked to voltage gated potassium channel (VGKC) antibodies, both gamma - aminobuyrtic acid (GABA) A and B receptor antibodies, and most commonly, N-methyl-D-aspartate (NMDA) receptor antibodies (Dade et al., 2020). First line treatments include methylprednisolone, intravenous immunoglobulin, and plasma exchange.

Since the inception of Coronavirus (Sars-COV-2) in 2019, there have been few documented cases of patients experiencing neuropsychiatric symptoms with coinfection of COVID-19. It is unknown whether these neurological manifestations are a result of direct infection of COVID-19 or due to post-infection neuroinflammation sequelae. In previously documented cases, symptoms have included delirium, psychosis, depression, and suicidal thoughts. There are even fewer documented cases of patients experiencing associated catatonia.

Catatonia is defined as a state of muscular rigidity or other motor disturbances, extreme over activity or adaptation of bizarre posturing (American Psychological Association). Catatonia is believed to be caused by disturbances in the transmission pathways of serotonin, dopamine, glutamate, and GABA. Most cases of catatonia are associated with psychiatric disorders. However, approximately 25% of catatonia cases are associated with neurological conditions such as parkinson's disease (PD) and encephalitis. Unfortunately, due to the common misconception that catatonia is solely associated with psychiatric disorders, a diagnosis of catatonia can often be overlooked by providers in patients who do not present with significant psychiatric history.

Once diagnosed, the first line treatment for a catatonic state is administering benzodiazepines. Treatment should begin promptly, regardless of underlying cause. This treatment is successful in 70-80% of patients (Sienaert et al., 2014). If a patient does not respond to the benzodiazepines, electroconvulsive therapy (ECT) is then considered as second line therapy. ECT is a potent psychiatric treatment modality that sends small electric currents through the brain to intentionally trigger a brief seizure. ECT is a relatively safe treatment option with no absolute contraindications. When catatonia is not diagnosed and treated promptly, malignant catatonia can occur.

Overall, clinicians caring for patients diagnosed with COVID-19 should consider a diagnosis of catatonia for individuals who present with a recent change in behavior, mental status or function. Delayed catatonia diagnosis is associated with higher morbidity and mortality and therefore, an increased awareness of the potential of COVID-19 to cause neuropsychiatric sequelae is important for early identification and treatment. (Styan et al., 2022). In this paper we will present the case of a patient who presented with pharmacologically treatment-resistant catatonia in the setting of COVID-19-related encephalitis.

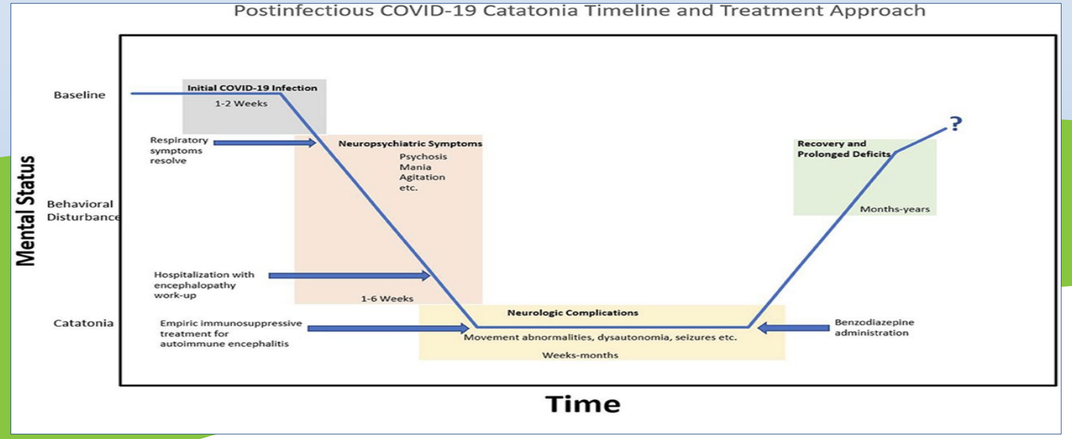
Case Presentation:

Patient is a 42-year-old female with no significant past medical or psychiatric history who presented as a prehospital stroke alert. She had awoken with aphasia, upper extremity contractures, and urinary incontinence. Family reported that the patient had been experiencing a viral-like prodrome for 2 days. Upon arrival, she was found to be afebrile, hemodynamically stable on room air, and unresponsive with upper extremity contractures. Computed tomography (CT) of the brain and chest x-ray were negative for acute pathology. Reverse transcription polymerase chain reaction (RT-PCR) nasopharyngeal swab was found to be positive for COVID-19. Ammonia level was 62. C-reactive protein was 313.8. Creatinine kinase was 419. Urine toxicology was negative.

Lumbar puncture revealed normal opening pressure, normal white blood count, and mildly elevated protein level (64 g/dL). Autoimmune encephalitis panel was negative except for anti-GAD65 antibodies (.06 nmol/L). An MRI of the brain completed on day 8 revealed persistent FLAIR signal abnormality in the pons and bilateral hippocampi without pathologic enhancement. CT chest, abdomen and pelvis were negative for malignancy.

The patient was initially worked up for status epilepticus and was administered 2mg of Ativan on day 1 which resulted in improvement in the patient's upper extremity contractures. Keppra 1000mg was started. She was then started on a 6-day course of methylprednisolone 80mg Q12H on day 2 which was then tapered down to 30mg on day 10. Over the following days, the patient remained largely unresponsive. On day 15, she was noted to be posturing and circling the unit on her tiptoes. Psychiatry was then consulted for agitation, combativeness, and medical management. Upon examination, the patient exhibited mutism, stupor, and was not reactive to painful stimuli; therefore, catatonia was suspected. An ativan challenge resulted in a positive response. She was then started on IV 2mg Ativan TID and showed moderate improvement over the next 2 days; following commands and talking, although her speech was difficult to understand. She was uptitrated to 4mg Ativan TID. This was titrated back down to 2mg due to concerns of over sedation on day 18. The patient was started on a 5-day course of IV 1000mg methylprednisolone on day 16. A 3-day course of IVIG 45g was initiated on day 21. On day 24, a 5-day course of plasmapheresis was initiated, and Ativan was uptitrated to 5mg TID which was later uptitrated to 6mg and subsequently 7mg TID by day 29. She was subsequently restarted on 60mg prednisone whilst on plasmapheresis.

After completing plasmapheresis there were no significant improvements. Psychiatry recommended a trial of ECT. On day 63, the patient was transferred for ECT. The regimen included 3 sessions of ECT per week. After nine treatments a significant improvement was seen; however she has not returned to baseline. Her seizure medication was discontinued to promote adequate seizures. An ativan taper was also initiated and continued in the outpatient setting. Due to concern for post- ECT confusion, ECT was discontinued after these nine sessions.



Discussion:

The exact cause of the patient's catatonia could not be concretely determined to be of autoimmune or COVID-19 origin. The patient had no known medical or psychiatric history and was determined to be COVID-19 positive upon admission. Her prodrome was known to be mild. Earlier in the patient's treatment course. GAD-65 antibodies were suspected as the cause of encephalitis due to the patient having a CSF value of .06 n/mol (normal .02). Although this value is not as high as seen in most patient cases which is usually a 100-fold greater than normal (Dade et al., 2020), it was greater than the normal range. In order to treat the suspected autoimmune encephalitis, the patient was given three first line treatments; methylprednisolone, IVIG and plasmapheresis. However, no significant improvement in neuropsychiatric symptoms were seen. Although the patient did respond to ativan, the response was minimal and she did not return to baseline, despite titration up to 7mg TID. For this reason, ECT was suggested. With ECT, the patient did demonstrate significant improvement.

Another significant challenge in this case was that this patient experienced a delay in her treatment, as catatonia was not suspected until day 15 of the hospital course. The initial reason for stiffness was believed to be due to seizures as the patient was found to have upper extremity contractures when found by EMS, which responded to ativan. Due to the patient's lack of psychiatric history, seizures were suspected to be the cause and the patient was started on a prophylactic regimen with keppra; which did not resolve the contractures. Fortunately in this case, the patient did not experience any life-threatening symptoms of malignant catatonia. In order to improve future patient outcomes, we must do a better job in educating providers, outside the realm of psychiatry, on how to recognize, assess and differentiate catatonia from other diagnoses that may have overlapping symptoms. Catatonia has been historically linked to psychiatric disorders causing many practitioners to forgo catatonia as a differential, however, patients without psychiatric backgrounds, as in this case, can also present with catatonia. Without prompt treatment the outcome can be fatal.

This case demonstrates the importance of working as an interdisciplinary team. In this patient's case, internal medicine, neurology, and psychiatry all worked together to create the best patient outcome. Healthy discussion between specialists was vital to ensure the best outcome for the patient. In our patient's case, the use of electroconvulsive therapy as a treatment option was met with concerns from neurology. These concerns included the patient potentially entering status epilepticus. These concerns were valid. However, at this point, the patient was already tried on high dose prednisone, IVIG and plasmapheresis to help treat the encephalitis with only minimal improvement. This team was able to work together and discuss the treatment progress and options with the patient's family to make a well-informed decision to pursue ECT.

Conclusion:

Catatonia is a symptom that can be seen in various disease processes. Although most commonly seen in psychiatric illnesses, it is pertinent for all clinicians to be able to identify catatonia as the implications of untreated catatonia can be deadly. Clinicians caring for patients diagnosed with COVID-19 and demonstrating recent changes in behavior, mentation and/or motor function should consider catatonia as a diagnosis. In this particular case, the delayed suspicion, identification and subsequent treatment may have led to an increase in suffering as a delayed catatonia diagnosis has been associated with a higher morbidity and mortality (Llesuy et al., 2018).

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