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Case Report

Acute myelitis as a neurological complication of Covid-19: A case report and MRI findings

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ABSTRACT

During the recent outbreak of coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 coronavirus, there is rising concerns about neurological complications of COVID-19. Fever, headache, and anosmia may occur early during the disease course. Other neurological sequelae such as encephalitis may occur in later phases. We report a case of acute myelitis in a 32-year old male COVID-19 positive patient who presented with a 2-day history of flu-like symptoms then sudden onset paraplegia and urinary retention. The incidence is not known and the pathogenesis of the disease behind this manifestation is still not fully understood. Nevertheless considering the broad differential diagnosis of acute myelitis, prompt clinical, and diagnostic work up was crucial to exclude other causes. Patients presenting with neurological symptoms such as loss of consciousness, ataxia, convulsions, status epilepticus, encephalitis, myelitis or neuritis should raise concerns for COVID-19 infection during this pandemic prompting early diagnosis and initiation of proper management.

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Introduction

Coronavirus disease 2019 (COVID-19) continues to spread across the world with critical challenges for the public health and medical communities; as of May 2020, the number of confirmed COVID-19 cases globally has climbed up to more than 5 million cases and the confirmed deaths more than 350 thousand cases worldwide [1]. All available evidence for COVID-19 suggests that it has a zoonotic origin [6]. Sequence and evolutionary tree analysis has shown that SARS-

CoV-2 is an enveloped, positive-sense single-stranded RNA virus [6].

Case Report

A 32-year old Asian male previously healthy, presented to the emergency department complaining of 1 day duration of sudden onset of bilateral lower limb weakness, difficulty in sitting up, and in passing urine. He noticed these symptoms upon

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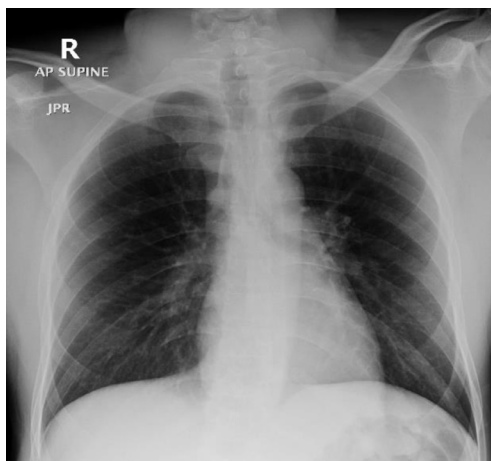


Fig. 1 – Chest X-ray in the frontal view with no evident consolidation or pleural effusion. Cardiothoracic ratio within normal limits.

waking up from sleep in the morning. There were no associated bulbar symptoms, sensory deficit nor upper limbs weakness or back pain. The weakness involved the whole lower limbs proximally and distally equally.

These symptoms were preceded by a 2-day history of high-grade fever and flu-like symptoms, which was not associated with shortness of breath or cough and was managed in the outpatient clinic. He denied any history of trauma or a previous similar episode. There was no significant past medical or surgical history. Family history was negative for any neurological disorders.

On physical examination, the patient was vitally stable and afebrile. He was alert and oriented to time, place, and person. His chest auscultation was clear and heart sounds S1 & S2 were normal. Abdomen was soft with a palpable distended urinary bladder. There were no signs of skin or joint involvement.

Neurological examination revealed intact cranial nerves examination, intact sensory system examination, normal muscle tone in upper limbs, and hypotonic in both lower limbs, muscle power in upper limbs proximally were 5/5 and distally were 3-4/5 while in lower limbs muscle power was 0/5 in all muscle groups. There was also trunk weakness without involvement of the neck muscles.

Reflexes were 2+ in upper limbs and 1+ in lower limbs. Planters response reflexes were equivocal bilaterally.

A foleys catheter was inserted in the emergency department and almost 1.5 L of urine was drained.

The patient was admitted to the hospital as a case of suspected acute myelitis vs spinal cord infarction for further investigation and management.

A chest x-ray in the frontal view was done and was normal with no evidence of consolidation, pleural effusion or cardiomegaly. (Fig. 1)

Laboratory results showed normal white blood cell count ($9.9 \times 3/UL$). Hemoglobin was decreased (10.7 g/dl). Inflammatory markers C-reactive protein was elevated (42 mL/l) However, the erythrocyte sedimentation rate was normal [7].

D-Dimer was high (20 ug/mL) and coagulation profile PT(16.8 sec), APTT(51.3 sec), and INR(1.33) were prolonged. Anticoagulant proteins; Protein C, Antithrombin III, and activated Protein C resistance were within normal limits except for a mild decrease in Protein S (42%). Creatine phosphokinase CPK (252U/L) and procalcitonin (0.13ng/mL) were also both elevated. Ferritin levels were within normal range.

A PCR nasal swab gave a positive result for the novel COVID-19).

Other viral PCR screening including Adenovirus, Herpes Simplex virus (type 1&2), Epstein Barr virus, Cytomegalovirus, and Human Immunodeficiency virus yielded negative results. Serology of other viruses such as Influenza virus A and B, Parainfluenza 1-4, Respiratory Syncytial virus, Enterovirus, and Rhinovirus were also negative. Bacteria associated with acute myelitis such as: Chlamydia Pneumoniae, Bordetella Pertussis, Mycoplasma Pneumoniae, and Borrelia antibodies gave negative results.

Autoimmune immunological screening was positive for Lupus anticoagulant and in conjunction with the low Protein S levels the hematologist advised repeating the test after 12 weeks as this result might be due to the anticoagulation treatment that the patient has received. Other tests such as Anti-Neutrophil Cytoplasmic antibodies, Rheumatoid factor, Anti Cardiolipin, and Anti Beta 2 Glycoprotein were all negative.

An urgent Gadolinium-enhanced magnetic resonance imaging of the whole spine was done and revealed extensive diffuse hyperintense signal involving predominantly the grey matter of the cervical, dorsal, and lumbar regions of the spinal cord. Mild enlargement and swelling of the cervical cord were also noted. No evidence of spinal cord or nerve root enhancement upon contrast administration was seen. Diffusion weighted imaging DWI and Apparent Diffusion Coefficient ADC revealed areas of restricted diffusion. No apparent hemorrhagic components were depicted. Conus medullaris appeared normal. (Figs. 2 and 3)

Findings were suggestive of acute myelitis likely as direct damage or a sequelae of a post infectious process of the novel corona virus (COVID-19) as all other commonly associated viruses and immunological disorders were excluded. Spinal cord ischemia or infarction was less likely as to the MRI findings. He was started on a pulse dose of IV methylprednisolone 1g/d for 5 days, Acyclovir 750 MG IV TDS, and Enoxaparin 40 mg daily.

A day after admission the patient became tachycardic and tachypneic and considering the elevated D-Dimer levels a pulmonary CT angiography was done to rule out pulmonary embolism. It revealed a filling defect completely occluding the posterior and lateral basal segmental branches of the right lower lobe pulmonary artery and a partial thrombus in the right interlobular artery and in basal segmental branches of the left lower lobe. RV/LV ratio was normal (0.89). Nevertheless no areas of consolidation or pleural effusion were observed. (Fig. 4). The patient was commenced on a higher dose of Enoxaparin 80 mg BD. LP was not done as the patient was started on anticoagulants for pulmonary embolism.

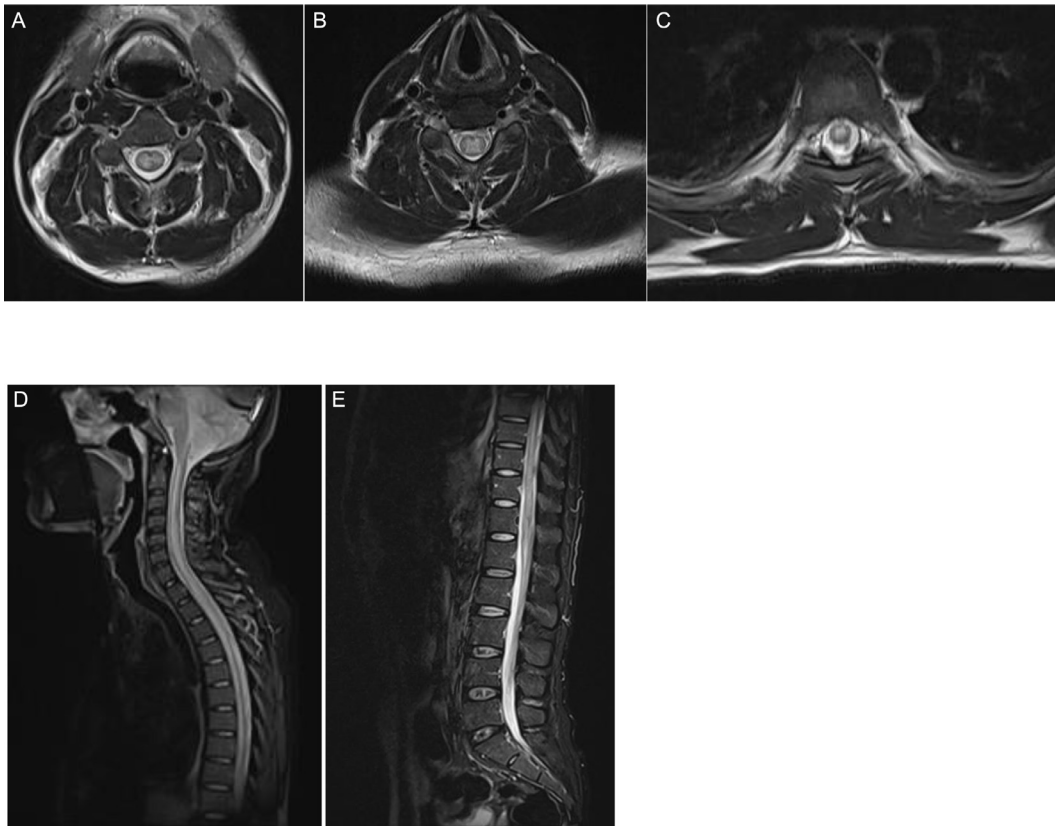


Fig. 2 – A-C: Axial T2 images of the cervical and dorsal spine showing central hyperintense signal of the cervical and dorsal spinal cord at multiple levels. D&E: Sagittal STIR images of the cervical, dorsal and lumbar spine showing hyperintense longitudinal signal involving a long segment of the spinal cord starting at the level of C2.



Fig. 3 – A: T1 Gadolinium enhanced MRI of the cervical and upper dorsal spine in sagittal view showing no evidence of abnormal enhancement of the spinal cord. B&C: DWI and ADC sagittal images show evidence of restricted diffusion.

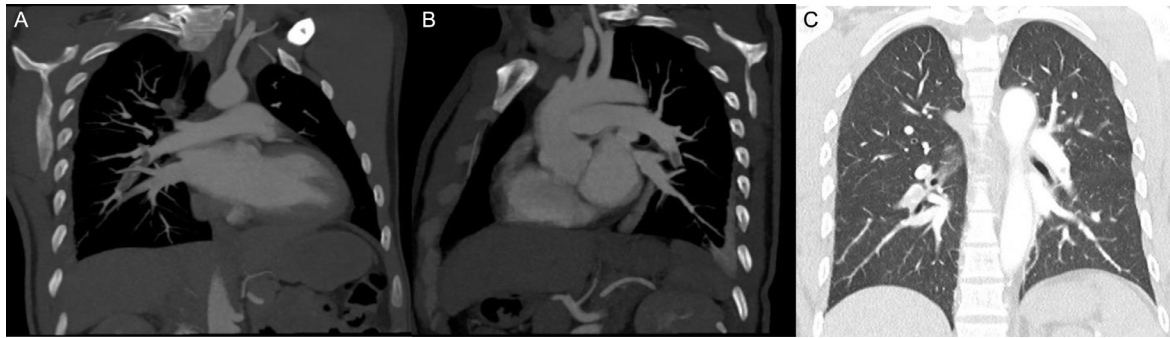


Fig. 4 – A&B: Pulmonary CT angiography Maximum Intensity Projection in the right and left oblique views. A. Segmental upper and lower lobe thrombi in the right pulmonary artery. B. Segmental left lower pulmonary artery thrombus C: Coronal lung window images showing clear lungs with no evidence of consolidation or pleural effusion.

Soon afterwards the patient's general condition improved and his vitals stabilized. Creatine phosphokinase CPK and procalcitonin also normalized. A marked improvement of his neurological deficit was noted over a period of five days of treatment with IV methylprednisolone, he regained power in his upper limb 4+/5 and bilateral lower limbs 4/5. He was also started on bladder training.

Discussion

The clinical manifestations of COVID-19 are highly related to inflammation of the respiratory tract with the most common symptoms including a high grade fever (98%) and cough (76%), that can rapidly be complicated by acute respiratory distress [2,6]. Such cases are hypothesized to be related to a Cytokine storm with overproduction of early response proinflammatory cytokines. There is an increased risk of vascular hyperpermeability, multiorgan failure, and eventually death in these patients [13].

There is also a disruption of the procoagulant-anticoagulant balance which increases the risk of developing microthrombosis and disseminated intra vascular coagulation. Thus as with our patient, pulmonary emboli are more prevalent [13].

In a cohort study done by Helms et al., it was found that more than 95% of COVID-19 patients had elevated D-dimer and fibrinogen levels. Almost 87% had positive Lupus anticoagulant during their ICU stay as to our patient [16]. In another study done by Harzallah et al, Lupus anticoagulant was positive in 45% [14]. It is also worth mentioning that there is a well-documented transient increase in Lupus anticoagulant in cases of acute infections associated with a number of viral infections such as: hepatitis C virus, Human Immunodeficiency virus, Cytomegalovirus, Varicella Zoster, Epstein-Barr virus, Adenovirus, and Parvovirus B [15].

Recently, a few studies have described neurological complications associated with COVID-19. A retrospective study done in China by Mao et al. has reported COVID-19 associated neurological symptoms involving both the central nervous system (CNS) and the peripheral nervous system (PNS)

in 214 patients [3]. Headache, dizziness, impaired consciousness, ataxia, acute cerebrovascular disease, and epilepsy were the most commonly reported cases of neurological sequelae of COVID-19 [3]. CNS manifestations were more common in the more acutely ill patients [3].

There were a few recent case reports also associating SARS-CoV-2 with acute encephalitis in patients who have symptoms of impaired consciousness [8]. There has also been reports by Zhao H et al. associating COVID-19 viral disease with Guillain-Barré syndrome where neurological symptoms occurred without any preceding respiratory symptoms suggesting a para-infectious rather than the post-infectious neuronal injury [8, 9].

The incidence of acute myelitis associated with COVID-19 infection is unknown. Three case reports of similar cases were published in the literature up to the current date of writing this report linking COVID-19 to acute myelitis as a neurological complication [4,6,18]. The first is in Wuhan, China where COVID-19 was first reported and is by Kang Zhao et al.[6]. The second in Boston where the patient presented with symptoms of upper respiratory tract infection then developed acute myelitis 7 days later by Sarma et al.[4]. Nevertheless it is still debatable whether the myelitis occurs directly from the viral infection or as an autoimmune sequelae [5].

The pathogenesis of the disease behind this manifestation is not fully understood yet. There is a strong evidence suggesting that the COVID-19 virus uses angiotensin-converting enzyme2 (ACE2) as its receptor to interact with host cells. This evidence is based on the previous extensive SARS-CoV structural analyses that showed interactions between the SARS-CoV virus and ACE2 receptors and because of the marked sequence similarities between COVID -19 and the SARS-CoV virus it is hypothesized that the pathogenesis is comparable [5,7].

The ACE2 receptors are expressed on alveolar epithelial cells, intestinal enterocytes and arterial and venous endothelial cells; however, in the brain only the vascular cells express ACE2 as a cell receptor not the neurons; yet this could be a potential mechanism for dissemination of the virus into the brain by the blood circulation [12].

It is also hypothesized that the virus can disseminate into the nervous system through the olfactory bulb in which sen-

sory neurons connect the nasal cavity to the CNS by the axons, which terminate in the olfactory bulb and passes through the cribriform plate [12]. This route must be taken into consideration in cases of early-phase COVID-19-affected patients who exhibit loss of smell and taste [17]. Furthermore, in advanced stages of the disease the neurological signs and symptoms observed in the COVID-19 cases could be due to the effects of hypoxia, respiratory and metabolic acidosis [17].

The imaging modality of choice for the diagnosis of suspected cases of acute myelitis is magnetic resonance imaging. T2-weighted fast spin-echo and short-tau inversion recovery (STIR) are the best sequences to view the spinal cord lesions, the latter being the most sensitive sequence [10,11]. The role of MRI is not confined to demonstrate spinal cord lesions but also to rule out other pathologies that may present with similar clinical symptoms [11]. In acute myelitis signal changes tend to affect the central region of the cord and involves more than two-thirds of the cords diameter as well as extends longitudinally over more than 1 segment [11]. The affected spinal cord segments appear hyperintense on T2 and short-tau inversion recovery sequences with associated cord swelling and show variable contrast enhancement [10,11].

In conclusion, COVID-19 has been associated with several neurological complications. We presented a case of acute myelitis as a neurological complication of COVID-19 infection that was admitted with paraplegia and urinary retention. The patient eventually improved and regained motor functions. In the current pandemic Status; COVID-19 should be considered a differential diagnosis in patients presenting with loss of consciousness, ataxia, convulsions, status epilepticus, encephalitis, myelitis, or neuritis [8].

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